ICBMB 2022

Abstracts Book

The 17th National Congress of Biochemistry & 8th International Congress of Biochemistry & Molecular Biology

TEHRAN - IRAN

23-26 August 2022

17th National Congress of Biochemistry & 8th International Congress of Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

Page | - 1 -

'In The Name of God'

Dear Colleagues

On behalf of the organizing committee, I am honored and delighted to welcome you to the 17th National and 8th International Congress of Biochemistry and Molecular Biology (ICBMB2022) which is going to be held on August 23-26, 2022, in Tehran, Iran. The congress will be held under the auspices of the International Federation of Clinical Chemistry (IFCC). The ICBMB2022 covers a wide range of critically important scientific sessions from basic and clinical research to innovations in the field of biochemistry and molecular biology. More than 16 sessions containing 5 expert panels by IFCC, will be included in the program. We have also tried to provide an opportunity for all researchers to display/talk about their research achievements and contradictions in front of the experts and budding scientists. Our program offers state-of-the-art lectures, oral presentations of abstracts, panel discussions, and poster sessions. We are proud to offer the opportunity in continuing medical education for the attendances.

I hope that this congress would provide valuable, useful and informative ideas to the participant students, researchers and other experts. I convey my best wishes for the success of the event.

With Kind Regards

Dr. Reza Meshkani

Congress President

17th National Congress of Biochemistry & 8th International Congress of Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

Page | - 3 -

Dear Colleagues

It is with great pleasure to proudly announce the 17th National Congress of Biochemistry and 8th International Congress of Biochemistry and Molecular Biology. This Congress presents a unique opportunity to bring together biochemists, laboratory medicine specialists and industry partners to discuss the latest advances in the science and technology related to biochemistry.

Currently we are in an exhilarating and fast evolving era in the field of biochemistry and laboratory medicine and this conference provides an excellent opportunity to present and discuss the latest advances in these fields, gain knowledge from the experts from various countries and connect with colleagues from different universities and research centers.

This proceeding highlights the diversity and scope of the many exciting pieces of research presented at the congress. It includes the abstracts presented by keynote speakers, as well as the abstracts that present novel research findings and were selected among numerous abstracts, after careful blind reviews. Topics of this congress include clinical biochemistry and molecular diagnosis, novel methods in laboratory sciences, cancer biochemistry, nutritional biochemistry, biochemistry of drugs, pure and structural biochemistry, nano-biochemistry and molecular biology. The focus of the congress is on the topics that impact human well-being, with emphasize on the clinical value of the research. A range of science-related educational topics as well as an exhibition from commerce are also included in the program.

I would like to thank everyone who worked timelessly to enable this congress to take place and I hope that this event would be a milestone of a new reality in which we can get back together personally and share all the experiences that enrich us as professionals and human beings.

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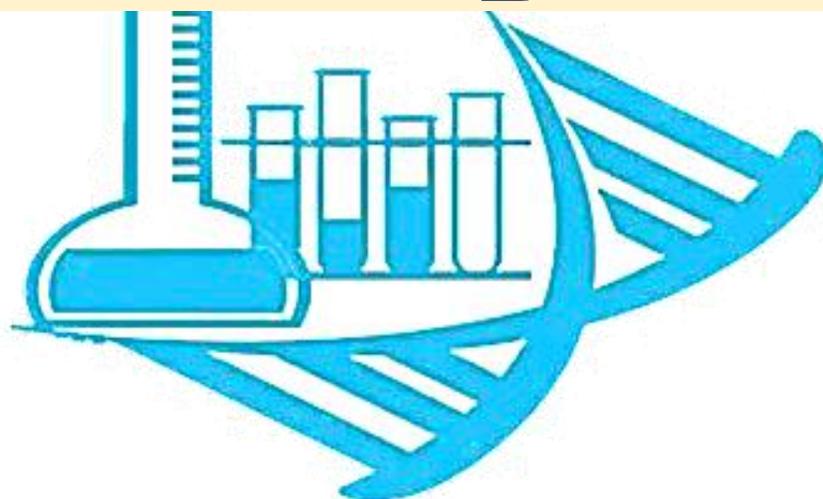
Tehran - Iran
23-26 August 2022

Biochemical Society of Iran

17th National Congress of Biochemistry & 8th International Congress of Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

Page | 9

Establishment and management of the national laboratory network for COVID-19

Alireza Biglari, MD PhD, Professor of Medical Genetics, Tehran University of Medical Sciences, Tehran, Iran. Pasteur Institute of Iran, Tehran, Iran.

Pasteur Institute of Iran, which has played a lasting role in controlling the infectious diseases such as rabies, plague, cholera, tuberculosis and hepatitis in the country for a century, is recognized as one of the main public health centers working on research and diagnosis of emerging infectious diseases. This institute has always been an influential authority in promoting Iranian public health and well-being.

In the Covid-19 crisis, the Pasteur Institute of Iran has been at the front of diagnosing and controlling this destructive virus based on its historical mission and national duty. Weeks before the detection of the first cases of the disease in Iran, the institute had conducted a study on this virus and especially the design of appropriate diagnostic methods, relying on local knowledge and facilities available in the country, taking into account the existing restrictions, including international sanctions. Therefore, from the beginning of the crisis, the responsibility of the national laboratory diagnosis committee for the corona virus was assigned to this institute with the aim of creating and directing the national laboratory diagnosis network of the new corona virus. In the first weeks of the crisis, samples suspected of being infected with Covid-19 were sent from all over the country to the Pasteur Institute of Iran. In a short period of time from the beginning of the epidemic, under the guidance of the Pasteur Institute of Iran, more than 500 laboratories were established in different parts of the country. Virus mutations have also been monitored in this network by the Pasteur Institute of Iran. Moreover, the Pasteur Institute of Iran provided a great opportunity for the country's self-sufficiency by evaluating the quality of diagnostic kits produced by domestic companies and granting approval to provable products.

Surveillance of SARS-CoV-2 variants

Mostafa Salehi-Vaziri, COVID-19 National Reference Laboratory, Pasteur Institute of Iran

The evolution of SARS-CoV-2 has resulted in the emergence of numerous variants. Some of the SARS-CoV-2 variants such as Alpha, Beta, Gamma, Delta, and Omicron showed new characteristics such as increased transmissibility, escape to natural or vaccine-derived immunity and decreased susceptibility to therapeutics antibodies. Continuous genetic sequencing is of paramount importance to follow the emergence and impact of the challenging SARS-CoV-2 variants. Surveillance of variants is suggested to be done through two strategies including Routine surveillance and Unusual Events based (such as vaccine breakthrough, prolonged infections in immunosuppressed individuals, rapidly spreading outbreaks, cases with unusual clinical presentations and gene target failure in PCR) surveillance. These two strands of evidence should be brought together in a timely fashion to provide a broad understanding of viral evolution and its potential impact on disease control, in order to guide public health response. Ideally, sequences should be reported with linked information called "metadata" to provide laboratory, clinical and epidemiologic data for characterization of public health risks of SARS-CoV-2 variants. Timely and accurate sharing of SARS-CoV-2 sequencing information in public databases such as GISAID is critical to understanding of virus evolution patterns and control of the pandemic. Employing these strategies, the COVID-19 National Refernce Laboratory at Pasteur Institute of Iran managed to identified Variants of Concern including Alpha, Beta, Delta and Omicron promptly following the emergence each variant.

Role of Laboratory in the clinical trials of COVID-19 vaccines

Tahmineh Jalali, Arboviruses and viral hemorrhagic fevers Department, (National Reference Laboratory), Pasteur Institute of Iran

Vaccine development for COVID-19 during public health emergencies (PHEs) is compressed in time and continues to be fast-tracked globally. WHO published guidance to best design, implement and analyze the vaccine trials during PHEs. According to global guidelines, the role of laboratory was explained during the process of vaccine evaluation. Also some examples of available laboratory test design were outlined that were used in COVID-19 vaccine trials.

In vaccine trials, the most common primary endpoint is clinical disease with laboratory confirmation. Direct detection of SARS-COV-2 using reverse transcriptase polymerase chain reaction (RT-PCR) or antigen-detection assays confirm the infection. In some symptomatic cases, seroconversion can be used as a confirmatory test of infection for which multiple specimen collection and testing are needed. It is worth to mention that the feasibility of multiple blood draws, transportation and storage of samples, and the types of diagnostic assays used are the main concerns and challenges. Due to the effect of unspecific results which can influence the estimated vaccine efficacy, highly specific tests are required to maximize the precision of an estimate. The poor laboratory infrastructure or using inappropriate assays with missing or failed confirmatory tests may result in undercounted cases. Diagnostic methods are evolving fast in PHEs, so the availability of a specific test may be a challenge. Therefore, the proper storing strategy for specimens may be necessary to retest.

Collection of immunogenicity data along with efficacy data is highly recommended to identify correlates and potential surrogates of protection. Monitoring the vaccine-induced immune response during clinical trial typically includes a baseline blood sample and post-vaccination sample(s) to measure the immune response, its magnitude and its longevity. The occurrence of infection, with or without clinical symptoms, also could be detected by seroconversion using baseline (pre-vaccination) and follow-up samples. The relationship between prior immunity and vaccine efficacy can be examined using baseline immunogenicity data as well as assessment of potential correlates of protection and susceptibility of the study population. The immunogenicity data is also important for evaluation of potential correlates of protection.

17th National Congress of Biochemistry & 8th International Congress of Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

Page | 12

Laboratory abnormalities in children with novel coronavirus disease 2019

Giuseppe Lippi, Section of Clinical Biochemistry and School of Medicine, University of Verona, Verona, Italy; Chair of the IFCC Task Force on COVID-19

One of the most important aspects of COVID-19 pathophysiology that has now emerged clearly, is that SARS-CoV-2 seems to affect children less severely compared to adults, with an estimated low mortality rate, even if children are at least as susceptible as adults to become infected and thereby to contribute to spread the infection. The clinical picture of COVID-19 in childhood entails mostly fever, symptoms of upper respiratory tract infection and headache. The cumulative hospital admission rate is slightly higher than 5%, with only 0.8% of all children developing severe disease. More or less like in adults, the risk of developing severe disease is especially higher in children bearing important comorbidities. As concerns laboratory abnormalities in children, in a first meta-analysis that we carried out at the beginning of the pandemic we highlighted that the number and extent of the changes were milder compared to adults, and the most frequent encompassed leukocytosis, neutrophilia, lymphopenia, thrombocytopenia, along with increased values of C reactive protein and creatine kinase. In following meta-analyses, other the authors that the most frequently altered laboratory tests in children with SARS-CoV-2 infection were D-dimer, creatine CK-MB, LDH, erythrocyte sedimentation rate and procalcitonin. The laboratory parameters mostly associated with unfavorable clinical progression of SARS-CoV-2 infection in children have are leukocytes, prothrombin time, D-dimer creatine kinase, lactate dehydrogenase, aspartate aminotransferase, red blood cell distribution width (RDW).

17th National Congress of Biochemistry & 8th International Congress of Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

Page | 13

Errors in Clinical Laboratories or errors in laboratory medicine?

Mario Plebani,
Honorary Professor of Clinical Biochemistry and Clinical Molecular Biology, University of Padova-Italy
Adjunct Professor, Department of Pathology, University of Texas Medical Branch, Galveston, USA

Errors in laboratory medicine have a completely different meaning today than they had a century ago. At that time the term referred to defects in the analytical performance of the test itself, the so-called analytical phase. A dramatic change in addressing the issue of errors in laboratory medicine started at the end of the 1990s, when a body of evidence has been accumulated demonstrating vulnerability in the pre- and post-analytical phases. The "take-home" message of the papers published is the need to consensually develop and adopt standard operating procedures (SOP) for safely performing patient identification and preparation, test requesting, sample collection and handling and that harmonization initiatives should be performed to improve procedures and processes at the laboratory-clinical interface. In addition, the Working Group "laboratory errors and patient safety" of the IFCC developed a model of harmonized quality indicators (MQI) to control and improve all steps of the testing process. It seems likely that only a small proportion of laboratory errors results in actual patient harm and adverse events thanks to the several barriers and defensive layers present between the release of laboratory information, the decision-making process and, ultimately, the action on the patient. However, from a risk management viewpoint, even the great majority of laboratory errors with little direct impact on patient care provide important learning opportunities. In fact, any error, regardless of its apparent triviality, might indicate weaknesses in policies and procedures that may not lead to adverse events in their particular context, but might cause the patient harm in slightly different circumstances. An importance step in the journey towards the reduction of the error rates in laboratory medicine is the implementation of a valuable quality system according to the International Standard ISO 15189:2012 and of reliable quality indicators (QIs) covering all steps of the intra- and extra-analytical phases of the total testing process (TTP).

It has been demonstrated that performance and outcome measures improve the quality of patient care and, in particular, QIs represent valuable tools for quantifying the quality of selected aspects of care by comparing it against a defined criterion. The measurement and monitoring of QIs in laboratory medicine serves many purposes as they make possible to: a) document the quality of the service provided; b) improve performance and patient safety; c) make comparison

17th National Congress of Biochemistry & 8th International Congress of Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

Page | 14

(benchmarking) over time between laboratories; d) make judgments and set priorities (corrective actions to be performed); e) support accountability, quality improvement and accreditation. The set of QIs consensually defined may allow clinical laboratories to measure and improve the quality of all steps of the TTP. The journey towards quality and patient safety continues as the outcome-based approach should be developed to assure more visibility and better clinical outcomes to individual patient and the entire community.

Bio Sketch:

Prof. Plebani is full Professor of Clinical Biochemistry and Clinical Molecular Biology at the School of Medicine, University of Padova and Chief of the Department of Laboratory Medicine at the University-Hospital of Padova. He served as President of the International Society of Enzymology for four years (2004-2008), as President of the Italian Society of Clinical Biochemistry and Molecular Clinical Biology for five years (in 2003 and from 2007 to 2009) and President of the Federation of Italian Societies of Laboratory Medicine (FISMeLAB) from 2009 to 2012. He is Editor-in-Chief of Clinical Chemistry and Laboratory Medicine, and Editor in Chief of Diagnosis and has published 1100 full papers, more than 900 abstracts and several books and book chapters, HI 90 (20.351 citations with an average per year of 371 citations), and an Impact Factor of 984.495 in the last three years.

17ᵗʰ National Congress of Biochemistry & 8ᵗʰ International Congress of Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

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Misuse of laboratory testing

Janne Cadamuro
Department of Laboratory Medicine, Paracelsus Medical University, Salzburg, Austria.

Alongside increased life expectancy, healthcare costs have risen to unsustainable levels. Especially in laboratory medicine, the demand increases steadily every year, mostly more than patient numbers. One of the main reasons surely is the ease of test ordering, by which availability triggers demand. However, more is not always better. Patient safety is in danger when needed tests are not ordered (underuse) or when not needed tests are ordered (overuse). In the former case, consequences might include incorrect diagnosis and missed treatment options, while in the latter case unnecessary follow-up diagnostics or treatments may arise. Numbers of over- and underuse are being reported as high as 70% and 40% of all laboratory orders, respectively. Apart from jeopardising patient safety, laboratory misuse may contribute substantially to inadequate healthcare costs.

In order to overcome this issue, laboratory specialists need to refocus on the medical part of the profession. Several strategies, all of which surmised under the term "laboratory demand management" have been proven to be efficient to reduce inappropriate laboratory testing. Most of these strategies focus on control overuse, while only laboratory diagnostic algorithms are capable of defying laboratory underuse. However, the development and implementation of such algorithms is very labour intensive and ideally requires the assistance of artificial intelligence models. Despite of the chosen strategy, a solid evidence basis and close collaboration with clinical colleagues is key for a successful implementation.

Bio sketch:

Dr. Janne Cadamuro studied medicine in Vienna, Austria, moved then to Linz (2001) and thereafter to Böblingen (2003), Germany, to begin my education as laboratory physician. In 2008 I finalized it in the University Hospital of Salzburg, Austria, where he is until today. He interim headed the Department of Laboratory Medicine in this hospital in the years 2011-2013. He is the current chair of the EFLM Working Group of Pre-Analytics and a member of the EFLM Working Group Post-Analytics. Extra-analytics, including laboratory demand management and artificial intelligence are my core scientific interest in which he have published about 100 articles.

17th National Congress of Biochemistry & 8th International Congress of Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

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Addressing the robustness of our pre-analytical processes to improve patient safety

Vincent De Guire

PhD, DEPD, CSPQ, Clinical Biochemist, Maisonneuve-Rosemont Hospital; Optilab Montreal-CHUM Network, Quebec, Canada

Quality improvement and monitoring of our pre-analytical processes is essential for patients' safety and required for ISO15189 accreditation. Assessment of the robustness of our processes through benchmarking and laboratory comparison should be a priority. Standardization of our pre-analytical processes is also part of the solution. In this presentation international guidelines, national standardization initiatives as well as specific strategies applicable in our laboratories will be discussed.

Bio Sketch:

Dr Vincent De Guire is a clinical biochemist in Maisonneuve-Rosemont Hospital in Canada and clinical assistant professor at the University of Montreal. He is a member of the Working Group on Laboratory Errors and Patient Safety of the International Federation of Clinical Chemistry and act as an expert on the Working Group of the Preanalytical phase of the European Federation of Laboratory Medicine. Dr De Guire is notably the chair of the Special Interest Group on Quality Improvement through Quality Indicators Monitoring of the Canadian Society of Clinical Chemists and the president of the Program for Quality Indicators Comparison of the Quebec Society of Clinical Biology. He is also leading multiple provincial and regional committees translating international guidelines on quality improvement in the laboratory field.

17th National Congress of Biochemistry & 8th International Congress of Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

Page | 17

A review of the challenge in measuring hemoglobin A1c measurement

Farideh Razi. MD.AP.CP
Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Science

Diabetes mellitus is one of the major health problems, consuming a considerable part of the healthcare budget. Diabetes diagnosis in the early stage has important influences on the patient's life with better glycemic control and decreasing the risk of devastating complications. Until recently, the HbA1c test was used as one of the best markers for patient management since it reflects the average blood glucose levels over the past three months, and a rising HbA1c level is associated with an increased risk of diabetes complications. In 2010 ADA suggested an HbA1c level of 6.5% as a cut-off that can be used to diagnose diabetes. HbA1C tests have a number of advantages, including no need for fasting, rapid testing, lower variability, better stability in three months, and less affected by diet and stress. Nevertheless, it is costlier, and in various clinical conditions, HbA1c measurement is arguable because of analytical, physiological, and pathological interferences. HbA1c test is affected by iron deficiency anemia, accelerated red cell turnover, and some medications such as salicylic acid, ethnicity, and age. There are many methods for Hba1c measurement, and their results might not be identical even on the same sample. With the goal of standardizing the methods and reducing the variation among them, the National Glycohemoglobin Standardization Program (NGSP) was established that evaluates and certifies methods/ kits for the measurement of HbA1c and provides a list of certified methods regularly. Despite all these efforts, non- NGSP methods are still produced and used in many countries, which shows hard-working is required to implement the standardization program worldwide.

Ensiyeh Nasli Esfahani, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Science

Hemoglobin A1c, which is given as a percentage of total hemoglobin concentration, is a gauge of how much hemoglobin is glycosylated in erythrocytes. It depicts the irreversible, time- and concentration-dependent exposure of erythrocytes to glucose. HbA1c levels indicate the average blood glucose concentration over the previous 2-3 months, including both pre- and postprandial glycaemia. The most extensively used biomarker of long-term glycemic management is the test of HbA1c since blood glucose levels vary greatly throughout a 24-hour period and from day to day in people with diabetes. The amplitude or frequency of short-term changes in blood glucose, which are especially significant in type 1 diabetes, cannot be determined by the HbA1c level. In general, there is a strong correlation between FPG, PPG, and mean plasma glucose (MPG), which is the average of numerous measures of glucose obtained during the day, and HbA1c. Conversely, there is a poor correlation between postprandial glucose excursions (PPGEs), also known as the change in glucose concentration from before to after a meal, and the incremental glucose area, also known as the area under the glucose curve above the pre-meal value, and HbA1c.

According to a recent study in patients with type 1 diabetes, the correlation between HbA1c and plasma glucose varied slightly during the day (r = 0.66-0.76), with night and after-lunch plasma glucose associated with HbA1c the most significantly, and fasting and post-breakfast plasma glucose correlating less strongly. Other studies conducted in patients with type 2 diabetes showed that correlations between HbA1c and FPG and PPG measurements taken at 1 and 2 hours after an oral glucose load or a test meal were unremarkable (r = 0.6–0.7). However, in another randomized clinical trial, FPG was found to be correlated best with HbA1c (*r* = 0.62–0.67) and there was no significant correlation between HbA1c and PPGE. Due to insufficient data regarding the relative contributions of FPG and PPG to HbA1c, it appears that FPG is somewhat better than PPG in predicting HbA1c.

Basis of HbA1c measurement methods

Hamid Reza Joshaghani
Department of Laboratory Sciences, Golestan University of Medical Sciences, Gorgan, Iran

A hemoglobin A1c (HbA1c) test measures the amount of blood sugar (glucose) attached to hemoglobin and shows what the average amount of glucose attached to hemoglobin has been over the past three months. Therefore, measurement of HbA1c concentration is considered a valuable diagnostic tool for monitoring long-term glycemic control. The basis of HbA1c measurement is actually the chemical (electrical) charge that exists on the HbA1c molecule, and the amount of charge is different from the charges of different components of hemoglobin. Many tests have been developed to determine the HbA1c concentration. Currently, common laboratory methods to recognize glycated proteins are Chromatography based HPLC assay, Antibody based immunoassay, Enzyme based enzymatic assay and Electrophoresis. In Chromatography, Assay uses an HPLC instrument and ion exchange or affinity column to separate HbA1c molecules from another hemoglobin molecules. Based on the ratio of HbA1c peak area to the total hemoglobin peak areas. Immunoassay method uses a specific antibody (usually monoclonal) to the glucose and the first 5 to 10 amino acids of the β-chain. This antibody is latex coated. The agglutinator reacts with the antibody to give a scattering of light and an increase in absorbance. In Enzymatic method, lysed blood samples are subjected to proteolytic digestion. Glycated valines are released and serve as substrate for fructosyl valine oxidase. The produced hydrogen peroxide is measured using a horseradish peroxidase-catalyzed reaction with a chromogen. The enzymatic method currently available measures HbA1c by using an enzyme that specifically cleaves the N-terminal valine. Point-of-care testing (POCT) instruments are also being developed today, which have the advantage of providing results to the doctor during the patient's visit. Despite the methods that exist to measure HbA1c, each of them has limitations and there are challenges such as standardization, defining global reference values in this case. Therefore, methods with lower limitations and costs and higher speed, accuracy and sensitivity are still needed.

17th National Congress of Biochemistry & 8th International Congress of Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

Page | 20

Laboratory diagnostic chalenges in kidney transplantation

Mahboobeh Freidoon

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Kidney transplantation is the treatment of choice for end-stage renal disease. Patients require close monitoring to ensure that the graft is functioning optimally and to assess for complications due to side effects of immunosuppressive medications. Some laboratory tests should be checked regularly at each visit. The most redoubtable complications is allograft rejection. therefore, discovering biomarkers of acute impairment in renal transplanted patients is required. The routine evaluation of renal allograft function typically involves monitoring the serum creatinine level and screening for proteinuria. creatinine is a poor marker to establish the kidney injury. Estimated glomerular filtration rate together with creatinine is ready to approximately measure the kidney function. Quantification of plasma levels of dd-cfDNA has been proposed as a noninvasive test for the early diagnosis of acute renal allograft rejection. Some patients with evidence of renal allograft dysfunction and/or proteinuria may require a renal biopsy to determine the cause of these abnormalities.

Posttransplant screening for the development of DSAs may also permit the early detection of acute ABMR and allograft dysfunction, it is recommended that, in addition to histology, C4d staining, and the presence of DSA be evaluated in suspected cases of rejection.

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Page | 21

CKD and Biomarkers

Saghar Chehrazi,
Azad university of medical science, Tehran

Chronic kidney disease (CKD), characterized as renal dysfunction, is recognized as a major public health problem with high morbidity and mortality worldwide. Unfortunately, there are no obvious clinical symptoms in early-stage disease until severe damage occurred.

The traditional chronic kidney disease (CKD) biomarkers (eGFR based on serum creatinine, sex and age and albuminuria) cannot predict a patient's individual risk for developing progressive CKD. For this reason, it is necessary to identify novel CKD biomarkers that will be able to predict which patients are prone to develop progressive disease and discriminate between disease processes in different parts of the nephron (glomeruli or tubules). A good biomarker should change before or simultaneously with lesion development and its changes should correlate strongly with lesion development. Also, there should be a close relationship between severity of injury and amount of detectable biomarker and its levels should decrease with diminishing injury. The most promising biomarkers are NGAL and KIM-1, MCP-1, MMP-9, clusterin, MMP-9, TIMP-1, Procollagen I alpha 1 and suPAR.

All these, have been studied as biomarkers for prediction of CKD progression in cohorts of patients with chronic kidney disease of different stages and various aetiologies (proteinuric and non-proteinuric, glo- merulonephritides, diabetic, hypertensive and polycystic kidney disease). There is evidence that these molecules could be useful as biomarkers for progressive chronic kidney disease, however, the available data are not enough to draw final conclusions. Further studies with large cohorts and long follow-up are required to identify appropriate biomarkers, that will be able to accurately and reliably define the risk for progressive chronic kidney disease.

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MEDICAL SCIENCES

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Biomarkers of Acute kidney injury (AKI); which and when? Different states and diseases, such as infections, toxins, ischemia, metabolic or genetic disorders, autoimmune diseases, can cause kidney damage, which may be manifested as acute kidney injury (AKI) or chronic kidney disease (CKD). Acute kidney injury (AKI) is a common clinical syndrome, estimated to occur in nearly one-quarter of all hospitalized patients worldwide; that has been consistently linked with increases in short-term mortality and health-care resource use. AKI has been reported to complicate 1% to 7% of all hospital admissions and 1% to 25% of intensive care unit (ICU) admissions and the incidence of AKI has increased greatly over time. Identifying patients early is of paramount importance in order to offer a prompt intervention and to improve the prognosis. The standard metrics used to define and monitor the progression of AKI, such as serum creatinine and blood urea nitrogen levels, are insensitive, nonspecific, and change significantly only after significant kidney injury and then with a substantial time delay. New biomarkers have the potential to identify earlier patients with AKI and in the future potentially intervene to modify outcomes.

17th National Congress of Biochemistry & 8th International Congress of Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

Page | 23

New Biomarkers in Renal Disease Diagnosis

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Biomarker is a measurable characteristic that is considered as an indicator of biological processes, pathogenesis or response to an intervention .High sensitivity and specificity of a biomarker make it reliable as a diagnostic biomarker. Currently, evaluation of renal function is based on conventional poorly-sensitive and specific markers, such as serum creatinine and urea levels. Therefore, there is an unmet need for new diagnostic and screening biomarkers.

Two groups of biomarkers have been introduced in renal diseases. The first group of biomarkers is identified based on predefined hypothesis. Biomarkers such as Cystatin C, KIM-1, NGAL and adiponectin are well known in different renal diseases; however the practical use of most biomarkers remains unclear.

Development of new "omics" techniques has been provided the possibility to discover novel hypothesis-free biomarkers by studying on whole genome, proteome, transcriptome and metabolome. Immune factors, microRNAs and collagen fragments are examples of biomarkers obtained by these new methods.

Although many biomarkers have been identified in kidney diseases, due to the lack of validation, differences in the type of technique and study population in most studies, there is still no clear consensus on a unique biomarker. To improve this assessment, research is underway to find reliable biomarkers. Here in this review, top diagnostic biomarkers in renal diseases will be discussed.

17th National Congress of Biochemistry & 8th International Congress of Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

Page | 24

Reference Interval Harmonization in Clinical Laboratories: Harnessing the power of Big Data Analytics

Khosrow Adeli, PhD FCACB DABCC
President, IFCC, Professor and Head, Clinical Biochemistry, The Hospital for Sick Children, University of Toronto, Toronto, ON, Canada

Harmonization in laboratory medicine from specimen collection to result reporting is critical to ensure consistent and accurate clinical decision-making. Harmonized or common RIs refer to using one interpretative recommendation for an analyte across several laboratories, regardless of analytical assay or patient population. Harmonized or common RIs should therefore only be considered for assays that demonstrate minimal bias across considered methodologies. Several national surveys have reported wide variation in reference intervals across healthcare centres in certain regions, even those using the same analytical platform for test measurement. There is a high risk of inappropriate test result interpretation when reference intervals are not appropriately harmonized. The Canadian Society for Clinical Chemistry (CSCC) Working Group on Reference Interval Harmonization was established in 2015 to develop evidence-based harmonized/common reference intervals (hRIs) and support their implementation in laboratories across Canada. After comprehensive review of the literature, our group established a novel approach to reference interval harmonization in adults involving: extraction of data from outpatient community reference laboratories across Canada, 2) assessment of outliers and monthly instability, 3) statistical evaluation of age, sex, and centre-specific differences, 4) derivation of preliminary harmonized reference intervals using a new indirect method (Truncated Maximum Likelihood method), 5) comparison of established harmonized reference intervals to direct a priori data in the healthy Canadian population and 6) verification through a cross-Canada prospective program. Thus far, this approach has led to the development of harmonized reference intervals for 17 biochemical and immunochemical markers. In this presentation, we will discuss the work completed by CSCC hRI WG, challenges encountered, and future plans to support implementation.

Bio Sketch:

Dr. Adeli is a Senior Scientist in the Molecular Medicine Program of the Research Institute, as well as the Head of Clinical Biochemistry in the Department of Paediatric Laboratory Medicine, at the Hospital for Sick Children. He is also a Full Professor in the Departments of Laboratory Medicine and Pathobiology (LMP), Biochemistry, and Physiology at the University of Toronto. He currently serves as the Director of the Point of Care Testing Program at SickKids and Vice Chair of Quality in LMP at the University of Toronto. He is the current President Of the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC).

17th National Congress of Biochemistry & 8th International Congress of Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

Page | 26

Reference measurement services for medical tests: current state of play and future perspectives

C.M. Cobbaert, PhD, Pharm, EuSpLM, Head of the Department of Clinical Chemistry and Laboratory Medicine, Leiden University Medical Center, Department of Clinical Chemistry and Laboratory Medicine, Leiden, the Netherlands

Reference measurement services are essential for global comparability of medical tests results. Especially disease defining tests and tests that use clinical decision limits for reaching on-treatment goals rely on being anchored to higher order reference measurement systems that produce test results that are sustainable in time and space. Examples of such tests are HbA1c, cholesterol and LDL-c, neonatal bilirubin, PT/INR and haemoglobin. Clinical decision limits for some of these tests have been determined in Randomized Control Trials. To make these limits useful within specific target populations, longitudinal test accuracy is key. To that end the concept of metrological traceability, described in ISO 17511:2020, has to be implemented and monitored. In ISO 17511 six calibration hierarchies are described to accomplish either test standardization or test harmonization, from highest to lower order of metrological hierarchy.

To apply the metrology concept properly IFCC, BIPM and ILAC founded the Joint Committee on Traceability in Laboratory Medicine (JCTLM) in 2002. Since then, about 10% of routinely used medical tests are globally standardized by means of JCTLM - endorsed reference materials and reference measurement procedures. The success story is the HbA1c standardization, implemented by a global standardization network that enabled to reduce interlaboratory CVs from > 30% to about 3%. The uptake of the metrology concept by the IVD -industry is monitored in periodic surveys by EQA organizers. Those EQA organizers who use commutable and value assigned EQA samples can evaluate the degree of adoption and the accuracy of medical test results. Examples will be presented.

Yet, many more tests have to be standardized. To that end, enabling technology which allows molecular detection and quantitation of the analytes of interest is needed. Examples of the diversity of (glyco) proteoforms hidden behind proteins determined with activity and immunoassays will be discussed. Many more efforts are needed to standardize biologically relevant protein measurands in the future.

17th National Congress of Biochemistry & 8th International Congress of Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

TEHRAN UNIVERSITY
OF
MEDICAL SCIENCES

Bio Sketch:

Christa Cobbaert is a Laboratory Specialist in Clinical Chemistry and Laboratory Medicine and heads the Department of Clinical Chemistry and Laboratory Medicine at LUMC, Leiden. She is vice-chair of the International Federation of Clinical Chemistry Scientific Division Executive Committee and chair of the European Federation of Laboratory Medicine Working Group on Test Evaluation. She is an expert in metrology, i.e. the science of measurement, which is essential for global standardization c.q. harmonization of medical tests.

Risk Management of Total Testing in Clinical Chemistry

Tony Badrick
Royal College of Pathologists of Australasia Quality Assurance Programs

Risk management is a key process in Quality Management to introduce proactive error identification and mitigation. Rather than reacting to error, the concept is to consider where these may occur and re-engineer the process to reduce the error and the risk.

The requirements of the technique understand your work processes in detail, identifying in this workflow where error is most likely to occur and then changing that workflow.

Most errors in the total testing cycle occur in the pre- and post-analytical phases, so laboratories need to measure these errors. There may be many of these, not all having the same impact on patients. Therefore, it is important to not just measure the frequency of errors, but also the risk of patient harm.

Then once the risk of each type of error has been identified, and then possible improvements to the workflow should be implemented. As an example of this concept, reducing phlebotomy related hemolysis will be presented.

Laboratories should monitor pre- and post-analytical error and identify trends in rates. Ideally, laboratories should also benchmark these errors against other laboratories to try and identify better workflows or practices.

Bio Sketch,

Professor Tony Badrick was Associate Professor, Faculty of Health Sciences and Medicine at Bond University for 4 years before becoming the CEO of the RCPAQAP in 2015. He is an Adjunct Professor School of Pharmacy and Pharmacology, Griffith University, Gold Coast, Honorary Associate Professor, National Centre for Epidemiology and Public Health Australian National University College of Health and Medicine, Honorary Associate Professor, Faculty of Medicine, Bond University, Gold Coast, and Visiting Fellow, Australian Institute for Health Innovation, Macquarie University.He was also President of the Australasian Association of Clinical

17th National Congress of Biochemistry & 8th International Congress of Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

TEHRAN UNIVERSITY
OF
MEDICAL SCIENCES

Biochemists (2003-2007), Chair of the Faculty of Science RCPA (2012-2018) and is Chair of the Education and Laboratory Management Committee of the Asian Pacific Federation of Clinical Biochemistry, and currently the Chief Examiner of the Faculty of Science of the Royal College of Pathologists of Australasia.Tony has published over 150 peer-reviewed articles mainly on the themes of Quality Control, Quality Management and Clinical Biochemistry.

17th National Congress of Biochemistry & 8th International Congress of Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

Page | 30

The strengths and limits of local and circulating stem cell markers in diagnosis of primary bone tumors

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Primary bone tumors are considered as non-frequent mesenchyme-originated solid tumors which affected individuals at all age ranges. The dynamic of bone tissue-dependent on the tissue's physiological and pathological condition which makes it susceptible to cellular re-arrangement, tumor cell formation, and tumor cell implantation. Despite recent improvements regarding primary bone tumor diagnosis and therapeutic strategies, still nonspecific symptoms besides late patient referring and early detection failing are prominent drawbacks that cause cancer-induced morbidity and mortality. Therefore, the development of novel and efficient biomarkers for primary bone cancers is of grave importance. We designed a connected series of projects to unravel the relevance of cancer stem cell markers in the pathogenesis and diagnosis of different types of primary bone tumors including osteosarcoma, Ewing's Sarcoma, chondrosarcoma, osteochondroma, Giant Cell Tumor, and exostosis tumors at both local and liquid biopsy samples of patients. The simultaneous increase in the expression of the several cancer stem cell markers in tumor tissue and in circulating blood cells and their relationship with tumor severity indicates the possible promoting role of these markers in primary bone tumor pathogenesis. Moreover, these markers might be involved in the early detection of primary bone tumors and can be considered as a potential biomarker to bone cancer diagnosis.

17th National Congress of Biochemistry & 8th International Congress of Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

Page | 31

Intracellular crosstalk between four main cell death pathways: necroptosis, ferroptosis and autophagy as backup death routes

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Abstract

Apoptosis necroptosis, ferroptosis and autophagy are four major processes to determine cell fate ·The interaction between these routes determines the balance of cell death and cell survival. The engagement of regulated cell deaths is tightly controlled by a complex network of signaling mechanisms that often exhibit cross talk between receptors, enzymes, and downstream signaling products. Networking of cell death pathways show that a cell can divert to an alternative pathway even in the presence of inhibitors of the primary pathway. These findings hold promising implications in the design of novel therapeutics for the treatment of numerous diseases, ranging from neurodegenerative disease to cancer. Here, we explore the emerging idea of cell death as a signaling network, considering connections between four main cell deaths pathways.

17th National Congress of Biochemistry & 8th International Congress of Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

TEHRAN UNIVERSITY
OF
MEDICAL SCIENCES

Page | 32

Association of some Organochlorine pesticides with oxidative-stress factors and some epigenetic alterations in Breast, Colorectal, Bladder, Blood, Gastric and Thyroid cancers in Kerman province

Gholamreza Asadikaram[*], Parisa Paydar, Moslem Abolhassani[2], Neda Motazavi, Fatemeh yusefi, Fuzieh Salimi, Arash Rafienia, Mojtaba Abbasi, Mohammad Reza Ashrafi, Vahid Moazed.

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Objectives: Among the numerous agents, genetic factors and environmental elements such as pesticides have an important role in cancer incidence. We aimed to investigate the probability role of some organochlorine pesticides (OCPs) and organophosphorous pesticides (OPPs) in patients with Breast, Colorectal, Bladder, Blood, Gastric and thyroid cancers.
Methods: In this case-control studies, patients with different cancers and healthy subjects were selected. The serum levels of some OCPs (αHCH, βHCH, γHCH, 2,4DDT, 4,4DDT, 2,4 DDE and 4,4 DDE) were measured by gas chromatography method. Serum levels of malondialdehyde (MDA), and total antioxidant capacity (TAC) and the enzyme activity of acetylcholinesterase (AChE) and arylesterase activity of Paraoxonase-1 (PON-1) were evaluated in all participants. The methylation specific PCR (MSP) assay was used for determining the methylation status of CpG island of several important genes. Furthermore several acetylation and methylation of histones in patients were investigated.

Results: The mean serum levels of some OCPs were significantly higher in the patient groups compared to the control group ($P < 0.05$). The AChE and arylesterase activity of PON-1 in the patient groups were significantly lower than the control groups ($P < 0.05$). The mean serum levels of MDA and TAC in the serum of the patient groups were significantly higher than the control groups. The current findings demonstrated alters in methylation of some important genes and acetylation and methylation of histones in cancer patients. Moreover, a positive correlation between some OCPs and studied epigenetic changes were observed in the most studied cancers.

Conclusion: Regarding the higher levels of some OCPs in cancer patients, along with epigenetic changes, diminishing in AChE and PON-1 activity and increasing in oxidative stress factors, it may be concluded that OCPs and OPs play an important role in the induction of cancers in southeastern Iran.

17ᵗʰ National Congress of Biochemistry & 8ᵗʰ International Congress of Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

TEHRAN UNIVERSITY OF MEDICAL SCIENCES

Page | 33

Targeting autophagy & unfolded protein responses to treat cancer: research facilities and capabilities

Pooneh Mokarram

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Cellular stress, induced by external or internal signals, activates several processes designed at either restoring cellular homeostasis or committing to cell death. Among the numerous factors, the unfolded protein response (UPR) and autophagy, are part of the ER stress (ERS) response. Here we demonstrate how crosstalk among Autophagy and UPR sensitize cancer cells to chemotherapeutic agents.

Firstly, one study was designed to improve survival of 5-Fluorouracil (5FU) non-responder patients who suffer from a form of colorectal cancer (CRC) characterized by high level of microsatellite instability (MSI-H). Our findings showed that combination treatment with 5-FU and D4476 (CK1α inhibitor) sensitized HCT 116 CRC cells (RAS-mutated/MSI-H cell line) to 5-FU chemotherapy by autophagy flux inhibition. In parallel, we also investigated the effects of BAMLET (bovine α -lactalbumin made lethal to tumor cells) on AKT/Phospho-ß-catenin/Autophagy pathway in HCT 116 cell line. Our findings demonstrate that BAMLET hampers autophagy flux and leads to apoptosis induction, possibly, by reducing the expression of CK1α and attenuation of the AKT/Phospho-ß-catenin axis.

In other study, we defined novel research on Glioblastoma (GBM) which is the most prevalent malignant primary brain tumor with a very poor survival rate. Temozolomide (TMZ) is the common chemotherapeutic agent used for GBM treatment. We recently demonstrated that simvastatin (Simva) increases TMZ-induced apoptosis via the inhibition of autophagic flux in GBM cells. Considering the role of the unfolded protein response (UPR) pathway in the regulation of autophagy, we investigated the involvement of UPR in Simva–TMZ-induced cell death by utilizing highly selective IRE1 RNase activity inhibitor MKC8866, PERK inhibitor GSK-2606414 (PERKi), and eIF2α inhibitor salubrinal. Simva–TMZ treatment decreased the viability of GBM cells and significantly increased apoptotic cell death when compared to TMZ or Simva alone. Simvastatin sensitizes GBM cells to TMZ-induced cell death via a mechanism that involves autophagy and UPR pathways. More specifically, our results imply that the IRE1 and PERK signaling arms of the UPR regulate Simva–TMZ-mediated autophagy flux inhibition in U251 and U87 GBM cells.

Finally, we presented an overview of our recent advances in therapeutic strategies involving autophagy/UPR modulators in CRC and GBM cancers.

17th National Congress of Biochemistry & 8th International Congress of Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

TEHRAN UNIVERSITY
OF
MEDICAL SCIENCES

Nonalcoholic fatty liver disease; diagnosis and treatment

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Obesity is associated with a clinical spectrum of liver abnormalities collectively known as nonalcoholic fatty liver disease (NAFLD) .The abnormalities include steatosis (increased liver fat without inflammation) and nonalcoholic steatohepatitis (NASH; increased liver fat with inflammation and hepatocellular injury). It may lead to fibrosis, cirrhosis, and ultimately liver failure. The pathogenesis of NAFLD is multifactorial.

NAFLD is closely associated with elements of metabolic syndrome, including abdominal obesity, insulin resistance, diabetes, dyslipidemia, and hypertension, as well as with polycystic ovary syndrome and obstructive sleep apnea, independent of the degree of obesity. NAFLD can also occur in nonobese individuals, often accompanied by insulin resistance and dyslipidemia, or in lipodystrophy syndromes. Several single-nucleotide polymorphisms have been associated with increased risk of NAFLD, and among lean children, genetic risk factors may be a stronger predictor of liver fat than cardiometabolic markers.

NAFLD should be suspected in a child with typical clinical features (obesity and persistent mild elevations of serum alanine aminotransferase [ALT], typically one to six times the upper limit of normal [ULN], or ALT 25 to 200 units/L), and no other symptoms of liver disease. A provisional diagnosis of NAFLD can be made by excluding other causes of liver disease through a focused history, physical examination, and laboratory evaluation. The timing and extent of the evaluation depends upon the degree of ALT elevation and whether any atypical features are present.

A definitive diagnosis of NAFLD can only be made by liver biopsy, but this is not always necessary for clinical management. For children and adolescents with NAFLD and obesity, we recommend interventions to reduce overweight and obesity. The first-line approach in youth is counseling directed at improving diet and exercise habits. Pharmacotherapy options for weight management in children are limited. Weight loss surgery may be appropriate for selected adolescents with severe obesity, especially if liver biopsy shows evidence of advanced NAFLD.

No medication or supplement is recommended or approved for routine treatment of NAFLD in children. Limited evidence suggests that vitamin E has beneficial effects on some histologic features of NAFLD in children. For patients with biopsy-proven steatohepatitis (with or without fibrosis), a decision to treat with vitamin E should be made on a case-by-case basis, after a discussion of the potential benefits and risks with the patient and family.

17th National Congress of Biochemistry & 8th International Congress of Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

Page | 35

Laboratory findings of Pancreas insufficiency

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Exocrine pancreatic insufficiency (EPI) is a condition due to pancreatic and nonpancreatic etiologies, causing food maldigestion. The pancreatic juice consists of bicarbonate and water which are secreted by ductal cells and several enzymes secreted by acinar cells, having the specific capacity to digest proteins, carbohydrates and fats. The most important symptoms and clinical complications of pancreatic insufficiency is caused by lipase deficiency, because it has the poorest stability in the gastrointestinal lumen.

According to the severity of pancreas tissue destruction, clinical presentation differs. Patients with mild insufficiency may be asymptomatic or have mild abdominal discomfort, with normal-appearing bowel movements. Moderate to severe insufficiency results in maldigestion of fat and protein and weight loss. Overt Steatorrhea occurs when 90 percent of glandular function lost. Steatorrhea causes loose, greasy, foul-smelling stools that are difficult to flush. Vitamin deficiency and metabolic bone disease have been observed in patients with pancreatic insufficiency.

Exocrine pancreatic insufficiency investigations include blood and stool tests, malabsorption and pancreatic function and imaging tests. Macrocytic and microcytic anemia is seen in the blood test. Patients develop electrolyte imbalances and metabolic acidosis, hypoproteinemia, hypoalbuminemia and edema due to protein malabsorption. The gold standard for the diagnosis of PEI is three-day fecal fat quantification and determination of the coefficient of fat absorption. Fat malabsorption can lead to low serum levels of triglycerides, cholesterol, and alpha- and beta-carotene.

EPI investigation includes direct and indirect tests. Direct tests are the most sensitive diagnostic tests. They involve secretin test, endoscopic test, and CCK test .Fecal elastase-1, fecal chymotrypsin, sand erum trypsinogen are indirect tests for EPI investigation that are simpler, easier to perform and less expensive compared with direct pancreas function tests. Advanced tests of pancreatic exocrine function can usually be avoided in patients with a well-established CP diagnosis based on clinical picture of PEI.

17th National Congress of Biochemistry & 8th International Congress of Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

Page | 36

Celiac disease and diagnostic challenges

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Celiac disease is a digestive and autoimmune disorder, with 1% prevalence, that can damage small intestine. It occurs in genetically susceptible individuals, and is triggered by well-identified environmental factors such as gluten and related prolamins present in wheat, rye, and barley, as well as the autoantigens. This disease primarily affects the small intestine, where it progressively leads to the flattening of the small intestinal mucosa.

Celiac disease is classified as follows. Typical form is characterized by GI signs and symptom, small intestinal mucosa damage and positive autoantibody. In Atypical form, GI symptoms are minimal or absent, extraintestinal manifestations are present, and serology and pathology findings are positive. In the Silent form of the disease, the small intestinal mucosa is damaged and autoimmunity can be detected with serology; however, no symptoms are present. In potential disease, specific autoimmune serology is positive, symptoms may or may not be present, the mucosa morphology is normal, and full-blown celiac disease may develop at a later stage in some or all of these individuals. The latent form is the rarest with normal mucosal morphology and gluten-dependent enteropathy may occur at a time point.

The diagnosis of celiac disease is based on combination of symptoms, autoantibodies, HLA status, duodenal biopsy and histologic findings. After history taking and physical examination laboratory test should be done. Tissue transglutaminase (TTG) and the endomysium (EMA)-IgA tests are both highly sensitive and highly specific, with values for both parameters exceeding 96% in most studies. In clinical practice, it is recommended to obtain first serologic tests for celiac disease and then to proceed with the intestinal biopsy samples taken by endoscopy, to diagnose the condition in positive cases. Multiple biopsy samples (at least four) are recommended because celiac disease may be patchy and areas of villous atrophy may be adjacent to normal areas. Biopsy from the duodenal bulb is also recommended, as about 2-3% of celiac children may have changes only in that area. New guidelines allow avoiding the confirmatory duodenal biopsy in selected cases, characterized by a child or teenager with gastrointestinal symptoms consistent with celiac disease, a compatible HLA status, levels of tissue TTG elevated more than 10-fold, and positive EMA. The only treatment is strict adherence to a gluten free diet, requiring a wheat , barley and rye free diet.

17th National Congress of Biochemistry & 8th International Congress of Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

TEHRAN UNIVERSITY
OF
MEDICAL SCIENCES

Page | 37

Key points in the laboratory tests for the evaluation of liver and pancreatic disorders

Zahra Hesari

Laboratory Sciences Research Center, Golestan University of Medical Sciences, Gorgan, Iran

Liver function tests (liver panel) are blood tests that measure various enzymes, proteins, and other substances made by the liver. These tests check the overall health of liver. Different substances are often tested on the same blood sample at the same time and may include: albumin and total protein, ALP (alkaline phosphatase), ALT (alanine transaminase), AST (aspartate aminotransferase) and gamma glutamyl transferase (GGT), Bilirubin, Lactate dehydrogenase (LD), which is released into the blood when cells are damaged by disease or injury, and prothrombin time (PT). If the level of one or more of these substances is outside the normal range, it may be a sign of liver disease. Serum protein electrophoresis (SPEP) is a cheap and easy method to identify some liver diseases. The serum sample is subjected to electric current and proteins are separated based on charge. After common staining, each fraction is then quantified using a densitometer. Serum protein components are divided into five main parts. Albumin and globulins are the two main components of the electrophoresis pattern. Albumin, the largest band, is closest to the positive electrode (anode). The changes of these bands can be seen in different conditions, including: inflammation, liver dysfunction, and etc.

The pancreas is a glandular organ located behind the stomach that produces digestive juices. Inflammation of the pancreas, also called pancreatitis, usually causes high levels of amylase and lipase in the bloodstream. Amylase or lipase results that are more than three times the normal level probably mean pancreatitis or damage to the pancreas. To evaluate these tests, 8 to 12 hours of fasting is needed. A stool test is another type of pancreatic function test. If symptoms persist for a while or subside, stools test helps diagnose a more chronic condition. If elastase is low, it means that the pancreas no longer produces enough digestive enzymes to break down food in the small intestine, called exocrine pancreatic insufficiency (EPI). Excess fat in the stool is another possible symptom of pancreatic insufficiency. In patients with pancreatic cancer measuring the levels of CA19-9, or CEA, can be used for monitoring the treatment.

17th National Congress of Biochemistry & 8th International Congress of Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

Page | 38

Interpretative Commenting in Laboratory Medicine

Dr. Samuel Vasikaran, MD, FRCPA

Path West-Laboratory Medicine Western Australia, Perth, Australia

The aim of the clinical laboratory is to improve patient health through accurate diagnosis. While accurate and timely measurement of tests are crucial aspects of this service, the diagnostic laboratory also has a role and a responsibility to assist clinicians in the interpretation of the results they generate in order to make the right diagnosis and management decisions. There is evidence that clinicians value interpretative advice from the laboratory due to gaps in their knowledge and abilities to select appropriate tests and make correct interpretation of laboratory results.

There is wide variation internationally in the extent of provision of individualized narrative interpretative comments, even though there is evidence that interpretative assistance from the laboratory may improve clinical outcome.

This lecture will outline current status on commenting, the needs of clinicians for interpretative support, the evidence for improvement in outcomes as a result of interpretative commenting and the need for clinical laboratory to improve the quality of the interpretative service currently offered, through education and training. Illustrative case studies will be included.

Bio sketch,

Dr. Samuel Vasikaran is a Consultant Chemical Pathologist at PathWest –Laboratory Medicine, Western Australia. He has a special interest and expertise in bone turnover markers, with over 130 peer reviewed publications and book chapters. Dr Vasikaran chaired the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) Working Group on Bone Marker Standards which, in collaboration with the International Osteoporosis Foundation, designated serum PINP and CTX as the reference bone turnover markers in osteoporosis. He is currently member of the IFCC Committee on Bone Metabolism.

17th National Congress of Biochemistry & 8th International Congress of Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

TEHRAN UNIVERSITY OF MEDICAL SCIENCES

Page | 39

Big Data, AI and the future of diagnostics interpretation

Damien Gruson [1,2]

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2 Department of Laboratory Medicine, Cliniques Universitaires St-Luc and Université Catholique de Louvain, Brussels, Belgium.

Laboratory Medicine is at the heart of a changing health ecosystem where emerging technologies, smart testing, remote monitoring, and data science are playing a central role. Consolidated clinical laboratories are also space for routine integration of multi-omics platforms (including genetics, epigenetics, transcriptomics, metabolomics, and proteomics), providing new services and pathophysiological insights to physicians. The resulting "augmented" laboratory medicine should have benefits for the management of patients and clinical outcomes. To develop powerful integrative approaches, the use of artificial intelligence and computational biology is mandatory to improve the diagnosis, prognosis, and treatment of complex diseases. Clinical laboratories, specialists in laboratory medicine and coalition of caregivers assisted by AI companions for data integration will provide key components and expertise for the transition to clinical practices, with a high potential for new ways of caring complex diseases.

Bio Sketch,

Prof. Damien Gruson is head of the department of Clinical Biochemistry of the Cliniques Universitaires Saint Luc, Brussels, Belgium. He a member of the Endocrinology, Diabetes and Nutrition research unit of the Catholic University of Louvain, a board member of the Belgian Society of Laboratory Medicine and the French Society of Laboratory Medicine and a Fellow of the European Society of Cardiology. He is also a member of the division on emerging technology of the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) and the endocrinology division of the American Association of Clinical Chemistry (AACC).

17th National Congress of Biochemistry & 8th International Congress of Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

Page | 40

Failure Mode and Effect Analysis (FMEA) in Laboratory Medicine

Sedef Yenice, Ph.D., MBA,

Professor of Biochemistry and Clinical Chemistry, Gayrettepe Florence Nightingale Hospital, Istanbul, Turkey

Failure Mode and Effects Analysis (FMEA) is one of the core tools for effective quality management and conducting a systematic, proactive analysis of a process where damage may occur. In an FMEA, an interdisciplinary team representing all areas of the process and subprocess under review meets to predict and record where, how, and to what extent the system could fail. Then, team members with the appropriate expertise work together to develop improvements to prevent those failures - especially failures that would likely occur or cause serious harm to patients or employees.

The FMEA tool asks teams to review, evaluate and record the following:

Steps in the process

- Failure modes (What could go wrong?)
- Failure causes (Why would the failure occur?)
- Failure effects (What would be the consequences of each failure?)

In comparison, root cause analysis (RCA) is a structured method for solving problems after they occur. Teams, on the other hand, use FMEA to examine processes for potential failures and to prevent them by correcting the processes proactively rather than reacting to adverse events after failures have occurred. This emphasis on prevention can reduce the risk of harm to patients and staff. FMEA is particularly effective in evaluating a new process before implementation and in assessing the impact of a proposed change on an existing system. The process develops activities and outcome measures that management must agree to.

To date, insight into and application of FMEA in laboratory medicine has been quite limited, even though proactive risk assessment is mentioned in several guidelines for organizing laboratories. For example, sections 4.11 and 4.14 of the guideline ISO 15189 state that medical laboratories should conduct risk assessments to investigate potential failures in their processes, alluding to the investigation of activities and processes in a preventive manner by employing useful tools.

In this context, this presentation will provide an understanding of the basic steps of performing FMEA and an overview of how FMEA can be performed as part of risk assessment.

17th National Congress of Biochemistry & 8th International Congress of Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

TEHRAN UNIVERSITY
OF
MEDICAL SCIENCES

Bio sketch:

Dr. Sedef Yenice is professor of Biochemistry and Clinical Chemistry, Chair, EFLM Working Group on Laboratory Medicine Credit Points (WG-LMCP) (2021-present), Chair, IFCC Abbott Visiting Lecturer Program (VLP) (2021-present), Executive Member of IFCC Education and Management Division (EMD)(2020-present), Expert and Advisor, IFCC EMD, Committee on Clinical Laboratory Management (2020-present), Member, CLSI ExP on Clinical Chemistry and Toxicology (CHEM) (2020-present), Chair, IFCC Education and Management Division, Committee on Clinical Laboratory Management (2014–2019).

17th National Congress of Biochemistry & 8th International Congress of Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

Page | 42

Probiotics and neurodegenerative diseases

Ebrahim Abbasi

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The age-related disorders such as Alzheimer disease (AD), are becoming more common, especially due to the elderly population that has grown in recent years. Studies have reported that the gut microbiota participates in the neurodegenerative disorders and diverse cognitive functions by regulating the gut-brain axis. There are bi-directional interactions between the gastrointestinal system and the brain. The brain has a vital role in maintaining appropriate gastrointestinal function and the gastrointestinal has been reported to critically affect brain function. Gut microbial can affect all aspects of physiology, including the brain function, brain-gut communication, and behavior. Gut microbiota can alter brain function and the brain affects the composition of the microbiota by influencing digestion. Probiotics are recognized to have useful effects on the gut microbiota gut-brain axis. Moreover, it has been documented that probiotics can regulate inflammatory processes, oxidative stress, and alter gut microbiota. Additionally, microbiota influence the host physiology by modulating host gene expression through miRNAs. Dysregulation of miRNAs can affect gut physiological functions leading to neurodegenerative disorders. About 60% of protein coding mRNAs are regulated by miRNAs, including several of the regulatory proteins related with diseases. Probiotics can modulate many miRNAs in the gut-brain axis. Furthermore, it has been shown that probiotics have significant effects in personalized medicine.

17th National Congress of Biochemistry & 8th International Congress of Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

TEHRAN UNIVERSITY
OF
MEDICAL SCIENCES

Page | 43

Prebiotics in the Management of Obesity and Associated Metabolic Disorders

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The prevalence of obesity and metabolic comorbidities has considerably increased worldwide over the past decades. Despite tremendous efforts to tackle obesity, current therapeutic approaches are disappointing and call for alternatives. Imbalanced gut microbiota or dysbiosis is thought to be a principal factor in the development of obesity and metabolic consequences as the cross-talk and cross-feeding interaction processes between the intestinal microbiota, the host, and the surrounding network of these bacteria contribute to regulating the immune system, inflammatory pathways, and energy homeostasis. Nowadays, the approach of modulating the gut microbiota using oral supplementation with prebiotics has received the lion's share of attention for its beneficial effects on the management of obesity and associated metabolic disorders. Prebiotics are defined as "indigestible food ingredients fermented by gut microbes, that serve as a substrate that is selectively utilized by host microorganisms conferring a health benefit". However, recent attempts at increasing knowledge of intestinal microbiota have opened the door for novel prebiotic foods such as polyphenols, minerals or vitamins, and polyunsaturated fatty acids.

Preclinical and clinical studies have reported the benefits of prebiotics in combatting obesity and metabolic abnormalities, through various mechanisms of action. However, the results are inconsistent and further studies, to correct conclusions are required. Personalized nutrition and precision medicine are beginning to influence the application of prebiotics, with growing interest in the modulation of microbial signatures of health and disease. In conclusion, the possible role of both "true" prebiotics" and "novel" ones - either individually or in combination - in cellular, molecular, psychological, and physiological behavioral aspects of obesity as a heterogeneous condition is needed to unravel the role of modulation of microbial signatures in the management of obesity and metabolic comorbidities.

17th National Congress of Biochemistry & 8th International Congress of Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

Page | 44

Structural and functional effects of natural products, and food components on protein aggregation involved in neurodegenerative (Alzheimer's, Parkinson's, etc.) diseases

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David Geffen School of Medicine, UCLA, CA.

Intrinsic and extrinsic stimuli may alter overall homeostasis and promote inflammation. Activation of compensatory mechanisms ultimately leads to maintaining healing or results in cell and tissue damage. Nowadays, it is widely accepted that both endoplasmic reticulum (ER) stress and autophagy play critical roles in controlling inflammatory signaling cascades. The role of natural products originated from different sources including plants, animals, etc. to treat diseases has been known from ancient times, in many cultures. Different families of natural products have been administered as drugs or functional foods to treat diseases and/ or prevent their progression. Some of these compounds have been approved by FDA and are routinely used to treat some types of cancer, diabetes, and so on. Although there is no known cure for neurodegenerative diseases, some drugs originating from natural products are administered to inhibit or prevent the progression of these harmful diseases. Here, some new findings about the roles, mechanisms, and interactions of some natural products with both ER stress and autophagy regulators, as well as the breakdown of protein aggregates will be discussed in neurodegenerative diseases. Applying these compounds in food preparations increases the hope for the prevention of Alzheimer's, Parkinson's, and other diseases with a similar mechanism.

17th National Congress of Biochemistry & 8th International Congress of Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

TEHRAN UNIVERSITY
OF
MEDICAL SCIENCES

Page | 45

Split-luciferase complementary assay of NLRP3PYD interactions revealed inflammasome inhibitors during inflammation

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Inflammasomes are a member of multiprotein complexes that represent critical elements of a type of imflammation related cell death. The Nod-Like Receptor (NLRP3) inflammasome comprises the NLRP3 molecular sensor, the apoptosis-associated speck-like protein containing a caspase recruitment domain (ASC) adaptor protein, and pro-caspase-1. The NLRP3 protein contains an N-terminal pyrin domain (NLRP3PYD), a central NACHT domain containing a nucleotide-binding domain (NBD) (crucial for oligomerization of NLRs upon activation), and a C-terminal leucine-rich repeat (LRR) domain. Upon activation, the NLRP3 protein homo-oligomerizes via NLRP3PYD homo-interactions and interacts with the ASC protein via NLRP3PYD–ASCPYD interactions. The dysregulation of the best-characterized complex, the NLRP3 inflammasome, has been linked to diseases such as multiple sclerosis, type 2 diabetes mellitus, Alzheimer's, and cancer. In spite of some reported inhibitors specific for the various components of inflammasome complexes, specific targeted NLRP3PYD homo-oligomerization inhibitors has not been reported yet. We describe here a new assay targeting Pyd domain of NLRP3 based on split luciferase complementary assay, thereby used to identify QM380 and QM381 as NLRP3PYD homo-oligomerization inhibitors after screening small molecules from a library. It is shown that these NLRP3PYD inhibitors interfere with ASC speck formation, inhibit pro-inflammatory cytokine IL1-β release, and decrease of pyroptotic cell death. We employed spectroscopic techniques and computational docking analyses to confirm the experimental results and predict possible mechanisms underlying the inhibition of NLRP3PYD homo-interactions.

17ᵗʰ National Congress of Biochemistry & 8ᵗʰ International Congress of Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

Page | 46

Epigenetic alteration of two important subunits of cytochrome oxidase genes and their expression levels in EAE mice brains and their correlation with biochemical characteristics

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Background: Multiple Sclerosis (MS) is a chronic neurological disorder of CNS characterized by inflammation and demyelination. Mitochondrial dysfunction is involved in the process of neurodegeneration and neuronal cell death in this disease. The aim of this study was to examine the promoter methylation of two important subunits of cytochrome oxidase (COX) genes and also other related biochemical factors in mice brain tissues of the experimental animal model of MS (EAE) in comparison with control mice.

Methods: Twenty-one C57BL/6 female mice were used at 7 weeks of age in this study (9 mice for induction EAE, 6 for control group and 6 for sham group). Activity of COX, amount of ATP and HIF1-a levels were measured. Methylation analysis was done using bisulfite-sequencing PCR on two promoters of the Cox5a and Cox5b genes and finally gene expression levels of both of them were also determined using Real-time PCR in whole brain tissues of all three experiments groups.

Results: The attenuated gene expression level of COX and its activity in EAE mice compared to controls correlated with hypermethylation of Cox5b and Cox5a promoter genes by affecting on several transcriptional factors. Decreasing ATP content accompany with significant elevation of HIF1-a in EAE mice brains were also detected. HIF-1α induction may provide prevention of more neuronal death by compensating energy loss under hypoxia-like conditions in EAE mice brains.

Conclusion: These novel data suggest that Cox5a/Cox5b promoter hypermethylation associated with inactivating of COX enzyme and energy loss due to the mitochondrial dysfunction in EAE mice brains providing new approach for managing of this disease.

Clinical Proteomics and Biomarker Discovery Using Two-Dimensional Shotgun Proteomics

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Mechanistic insights from a holistic approach at the systems level have great potential to advance our understanding of human disease and to aid in the identification of novel therapeutic targets and disease biomarkers. While the genome is considered to be largely static, the proteome exhibits considerable plasticity owing to alternative splicing events and protein modifications. Hence, in the postgenomic era, proteomics is essential for deciphering how molecules interact as a system and for understanding the functions of cellular systems in healthy and disease states. Analyses at the protein level hold even higher promise for identifying changes that go along with illness and for defining a fitting treatment. Clinical proteomics encompasses a spectrum of activity from pre-clinical discovery to applied diagnostics. Proteomics are applied to clinically relevant materials to determine quantitative and qualitative profiling of proteins and peptides that are present in clinical specimens like human tissues and body fluids. In addition, Proteomics is addressing a clinical question or need such as discovery, analytical and preclinical validation of novel diagnostic or therapy related markers.

Urine proteome of patients with lupus nephritis (LN) were analyzed using high resolution LC/MS/MS to identify non-invasive diagnostic candidate biomarkers. To increase the depth and accuracy of the proteome analysis, samples proteins were digested and labeled with TMT-10plex isobaric label reagents. The 10-plexed digests were injected into the multi-junction capillary isoelectric focusing device (pI-Trap) as a first dimension of separation, fractionated into 10 fractions and subjected to LC-MS/MS analysis using data-dependent acquisition method. Over 1100 unique proteins were identified in urine proteome. Thirteen proteins with highest fold change and AUCs were selected as candidate biomarkers (AFM, TF, CP, SERPINA1, ORM1, ALB, SDC2, CD44, DEFB1, TFF2, VMO1, FSHB, LRRC15). The suggested panel of urinary biomarkers can precisely discriminate patients with lupus nephritis from SLE patients and healthy volunteers. The results demonstrated that urinary proteins can be less invasive markers to distinguish LN patients.

17th National Congress of Biochemistry & 8th International Congress of Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

TEHRAN UNIVERSITY OF MEDICAL SCIENCES

Page | 48

Introduction to Emerging technologies in clinical laboratory

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The term "emerging technologies" is used extensively, and many have proposed definitions on the internet and in published literature. Key phrases used in definitions include "innovation", "relatively fast-growing", the "future impact", socio-economic domains", and "uncertainty". In Laboratory Medicine, an Emerging Technology is a technology that needs translation into broad clinical practice. The most attractive and promising "emerging technology" for Laboratory Medicine in the next decade is "augmented Intelligence". The Total Testing Process is changing too because some Digital Assistants start to be implemented in the pre-preanalytical phase (Intelligent ordering system), in the Pre-analytical phase (Intelligent manager) and in the post-analytical Phase (Intelligent Interpreting and reporting system).

Humans and machine intelligence can interact in a continuum from assisted intelligence, to augmented intelligence. In 1989 the term "Machine learning" was introduced to apply statistical methods in extracting information, knowledge, useful patterns, and actionable insights from large amounts of data (data set) usually to solve a specific problem. Then Machine Learning was applied in Health Care where a big amount of Data is produced from clinical notes, images (X-ray, CT, MRI…), clinical laboratory results, pathology images and reports, medication, genome and family history and, in the next future, omics patterns reports. Then these clinical Data are usually merged with other Data obtained from Recommendations, Guidelines, Best Practice, Current Research, Ongoing clinical trials, New drugs Discovery and Doctors experiences. The application of augmented Intelligence tools in Medicine is growing very: increase in request for care and life expectancy, multi-cronicity, patient's empowering, reduced time with Doctors, Limits in government's investments for Health Care and Increased expenses out pocket. Recently also Laboratory Medicine start to implement Augmented Intelligence tools in Hematology, Autoimmunity, Mass Spectrometry and Cancer diagnosis.

17th National Congress of Biochemistry & 8th International Congress of Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

TEHRAN UNIVERSITY
OF
MEDICAL SCIENCES

Page | 49

Building a Sustainable, Scalable Hospital-Based Clinical Mass Spectrometry Program

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Laboratory developed test (LDT) development is one of the most stimulating and satisfying aspects of our work in clinical biochemistry, allowing us to rapidly address new clinical needs and achieve analytical performance superior to traditional immunoassays. However, as we are developing our innovative assays, we sometimes overlook the possibility that the testing will become more popular than initially anticipated. As we prepare to deploy these new clinical services, we must anticipate our duty to deliver on our promises. In this session we will discuss how to develop and deploy a clinical mass spectrometry assay with optimal use of liquid handling and data automation, which permits technical staff to respond to increasing demand without wearing out. Options for minimizing peak review and patient-specific interventions will also be discussed along with strategies for commercial or in-house developed middleware. These considerations will be applied to simpler assays such as immunosuppressive drug monitoring all the way to complex quantitative protein mass spectrometry methods.

17th National Congress of Biochemistry & 8th International Congress of
Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

Page | 50

Engineering in Precision Medicine

Dr. Ali Khademhosseini

University of California-Los Angeles (UCLA), USA

Engineered materials that integrate advances in polymer chemistry, nanotechnology, and biological sciences have the potential to create powerful medical therapies. Dr. Khademhosseini is interested in developing 'personalized' solutions that utilize micro- and nanoscale technolgoies to enable a range of therapies for organ failure, cardiovascular disease and cancer. In enabling this vision, he works closely with clinicians (including interventional radiologists, cardiologists and surgeons). For example, he has developed numerous techniques in controlling the behavior of patient-derived cells to engineer artificial tissues and cell-based therapies. His group also aims to engineer tissue regenerative therapeutics using water-containing polymer networks called hydrogels that can regulate cell behavior. Specifically, he has developed photo-crosslinkable hybrid hydrogels that combine natural biomolecules with nanoparticles to regulate the chemical, biological, mechanical and electrical properties of gels. These functional scaffolds induce the differentiation of stem cells to desired cell types and direct the formation of vascularized heart or bone tissues. Since tissue function is highly dependent on architecture, he has also used microfabrication methods, such as microfluidics, photolithography, bioprinting, and molding, to regulate the architecture of these materials. He has employed these strategies to generate miniaturized tissues. To create tissue complexity, he has also developed directed assembly techniques to compile small tissue modules into larger constructs. It is anticipated that such approaches will lead to the development of next-generation regenerative therapeutics and biomedical devices.

PLENO-IDEA: New materials for tissue engineering that can mimic natural tissue structure.

Presenters Biography: Ali Khademhosseini is currently the CEO and Founding Director at the Terasaki Institute for Biomedical Innovation. Previously, he was a Professor of Bioengineering, Chemical Engineering and Radiology at the University of California-Los Angeles (UCLA). He joined UCLA as the Levi Knight Chair in November 2017 from Harvard University where he was Professor at Harvard Medical School (HMS) and faculty at the Harvard-MIT's Division of Health Sciences and Technology (HST), Brigham and Women's Hospital (BWH) and as well as associate faculty at the Wyss Institute for Biologically Inspired Engineering. At Harvard University, he directed the Biomaterials Innovation Research Center (BIRC) a leading initiative in making engineered biomedical materials. Dr. Khademhosseini is an Associate Editor for ACS Nano. He served as the Research Highlights editor for Lab on a Chip. He is a fellow of the American Institute of Medical and Biological Engineering (AIMBE), Biomedical Engineering Society (BMES), Royal

17th National Congress of Biochemistry & 8th International Congress of Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

TEHRAN UNIVERSITY OF MEDICAL SCIENCES

Society of Chemistry (RSC), Biomaterials Science and Engineering (FBSE), Materials Research Society (MRS), NANOSMAT Society, and American Association for the Advancement of Science (AAAS). He is also the recipient of the Mustafa Prize ($500,000 prize) and is a member of the International Academy of Medical and Biological Engineering, Royal Society of Canada and Canadian Academy of Engineering, and National Academy of Inventors. He is an author on >650 peer-reviewed journal articles, editorials and review papers, >70 book chapters/edited books and >50 patents/patent applications. He has been cited >90,600 times and has an H-index of 152. He has made seminal contributions to modifying hydrogels and developing novel biomaterial solutions for addressing pressing problems in healthcare. He has founded 2 companies, Obsidio Medical and Biorae. He received his Ph.D. in bioengineering from MIT (2005), and MASc (2001) and BASc (1999) degrees from University of Toronto both in chemical engineering.

17th National Congress of Biochemistry & 8th International Congress of
Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

Page | 52

Communication of scientific and educational information in laboratory medicine: innovative approaches and tools

Dr. Nader Rifai,
Professor of Pathology, Harvard Medical School, Louis Joseph Gay-Lussac Chair of Laboratory Medicine, Director of Clinical Chemistry, Boston Children's Hospital, Boston, MA, USA

Since 1850, over 22 million articles have been posted on PubMed alone; of which 10 millions have been posted since 2000. So the increase in the number of published scientific articles and journals has been exponential. This fact presents a challenge to journal editors regarding how to choose the appropriate articles to publish, how best to present the findings, and most importantly, how to distinguish the information they publish and their journals from what else is found in the literature.

Advancements in technology have greatly influenced the way editors communicate scientific and educational information and helped to address some of the above-mentioned concerns. Information can be easily presented in multiple formats (textual, visual, and audio) at multiple levels of difficulty to better address the needs of the various readers. Electronic platforms have enabled the presentation of supplementary materials, podcasts, videos, and animations to enhance the delivery of information and enrich readers' experience. Technology also enabled the use of novel educational concepts such as adaptive learning, the closest to personalized education. In this lecture, the presenter shares his experience in disseminating scientific and educational information from three products, the journal Clinical Chemistry, the Tietz Textbook of Laboratory Medicine, and NEJM/AACC Knowledge+ for Laboratory Medicine.

Bio Sketch,
Dr. Rifai is a Professor of Pathology at Harvard Medical School, the Louis Joseph Gay-Lussac Chair in Laboratory Medicine, and Director of Clinical Chemistry at Boston Children's Hospital. His research focused on biomarkers of cardiovascular disease. However, in the last decade his main interest shifted to dissemination of scientific information and E-learning. Dr. Rifai is active in national and international societies; he served on the Board of Directors of the AACC, NACB and ABCC, was the Chair of Lipids and Lipoproteins Division, acted twice as the Vice-Chair of the AACC annual meeting, and he is currently the Chair of the IFCC Visiting Lectureship programme and a member of the IFCC Education and Management Division. In addition, he is the Editor-in-Chief of *Clinical Chemistry*, the Founder and Co-Chair of *Clinical Chemistry* Trainee Council, the Senior Editor of Tietz Textbook of Clinical Chemistry and Molecular Diagnostics and the Co-Editor-in-Chief of NEJM Knowledge+/AACC Learning Lab for Laboratory Medicine, an adaptive learning program.

17th National Congress of Biochemistry & 8th International Congress of Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

TEHRAN UNIVERSITY
OF
MEDICAL SCIENCES

Effective Education in Clinical Chemistry in the New Millennium

Roger L. Bertholf, PhD
Houston Methodist Hospital, Houston, Texas, USA

The depth and complexity of clinical chemistry curricula depend on their target audience: medical laboratory technologists, clinical pathology residents, or clinical chemists in professional training programs. There are significant differences in the educational requirements of these three constituencies that influence the choice of an optimal strategy for teaching them clinical chemistry. Practicing clinical biochemists require a comprehensive education in the analytical methods used in a medical laboratory, the medical use and interpretation of laboratory tests, and administrative and regulatory aspects of medical laboratory operation. Clinical pathology residency programs focus primarily on the medical interpretation of laboratory data, but also include a basic knowledge of analytical methods and some understanding of laboratory administration. At the medical technologist level, the focus of clinical chemistry education is chemical analysis and the application of statistical methods to monitor assay performance, although exposure to clinical interpretation and laboratory accreditation and regulation are also important components, particularly at supervisory and managerial levels. This session will present several approaches to improving the effectiveness of clinical chemistry education in these domains.

Bio Sketch:
Dr. Bertholf is the Medical Director of Clinical Chemistry, and Director of the Clinical Chemistry Fellowship program at Houston Methodist Hospital. Prior to his current appointment at Houston Methodist, he was Professor of Pathology and Laboratory Medicine, and Director of Clinical Chemistry, Toxicology, and Point of Care Testing at University of Florida Health Science Center in Jacksonville. Dr. Bertholf has lectured and published on a wide variety of topics, including laboratory statistics, heavy metal neurotoxicity, thyroid function, immunochemical methods, research ethics, medical errors, chromatographic applications in clinical chemistry and toxicology, and urine drug testing in pain management. He serves on the Board of Directors for the American Board of Clinical Chemistry, the AACC Finance Committee, and chairs the Southeast Section of the AACC. Dr. Bertholf is also Editor in Chief of Lab Medicine, published by the American Society for Clinical Pathology.

17th National Congress of Biochemistry & 8th International Congress of Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

TEHRAN UNIVERSITY
OF
MEDICAL SCIENCES

Page | 54

Fundamental principles of laboratory medicine diagnostics that span from past, present, to future technologies

Jude M. Abadie, Ph.D., DABCC, FAACC, DABMGG, FACMG,
Director, Clinical Pathology, Clinical Pathology, Chemistry, Toxicology, and Molecular Diagnostic,
Texas Tech University Health Sciences Center El Paso, USA

Understanding the origin of clinical tests in the context of both patient presentation and technology can provide insights to the future of laboratory medicine. This presentation will describe how the evolution of clinical tests demonstrates advancements in methodology have improved diagnostic robustness in the context of accuracy and speed. Furthermore, the discussion will illustrate examples of how subsequent generations of tests can present new challenges related to interpretation of analyte levels that are detected at greater sensitivities. Concepts in molecular pathology for tumor and exome analysis will demonstrate the essential need for accurate interpretation in order to generate the clinical report. Lastly, through retrospective and prospective observations, this presentation will provide guidance for the clinical laboratory professionals to use educational technology and resources to facilitate their understanding and interpretation of clinical tests that span multiple specialties of laboratory medicine.

Bio Sketch

Dr. Jude Abadie grew up in New Orleans, Louisiana where he graduated from LSU Health Science Center, department of pathology. He is fellowship-trained and board certified in clinical chemistry, clinical toxicology, and clinical molecular genetics. Dr. Abadie served 21 years in the U.S. Army in pathology and lab medicine duty assignments including Madigan Army Medical Center in WA, Walter Reed Army Medical Center in DC, Tripler Army Medical Center in Hawaii, and Brook Army Medical Center in TX. He has held a life-long passion for teaching and working in the field of laboratory medicine. At TTUHSC El Paso and University Medical Center of El Paso, Dr. Abadie's main focus in clinical pathology is on clinical laboratory testing, clinical consultant, director for our outlying clinics, and providing medical education to medical students, fellows, and residents.

17th National Congress of Biochemistry & 8th International Congress of Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

Page | 55

Clinical laboratory technologies, opportunities and challenges

Mohammadjavad Rasaee

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Clinical laboratories all over the world are the main centers of medical diagnostic validations. Laboratory practices account for the big part of medical expenditure. The total expenditure in segments such as diagnosis, drugs and medical care is estimated as 10 trillion $, average 1000 $ per population in which approximately 50 % is spent on treatment (hospitalization, other expenditures) while 25 % goes for drugs and 25% are spent for clinical diagnosis. This comes to be 300 $ per head or 2.5 trillion $ in all sorts of diagnosis. The clinical diagnosis which may accounts for 60 %, which is around 1500 billion $ per annum (200 $ per head). In local currency, around 500 thousand billion Toman, it is estimated for Iran population .This amount would be sufficient to create 400.000 employments in the sector .If the rate of professional employment in such sectors is assumed as 10 % only, an estimated 40.000 employment is very well expected while other related sectors such as service providing in clinical laboratories in the country which accounts for almost 5000 laboratory throughout a big country such as Iran also need at least 15.000 professionals .Therefore one conclude that 50 to 55 thousand professional in different fields of clinical diagnosis including production facilities ,research and development and service providing would be required. While on the bases of estimations, only 10 % of such professionals are active in the field at present. It is however very important to establish more production units, to develop R&D departments in all existing production facilities and to develop accelerators and science and technology parks in the field of clinical diagnosis.

17th National Congress of Biochemistry & 8th International Congress of Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

Page | 56

Antibodies and fragments thereof in molecular diagnosis and therapy

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Monoclonal antibodies due to their high specificities are powerful tools in research and clinic. A classical structure of antibody consists of two heavy and two light chains linked to each other by disulfide bonds. The main interaction between a monoclonal antibody and an antigen resides in complimentary determinant regions (CDRs) recognizing antigenic epitope of 4-6 amino acids. This applies to antibody binding site on an antigen too. In general either antigen or antibody needs interaction of two small parts consists of 4-6 amino acids. Among CDRs the CDR3 loop is the most significant part for antigen binding ranging 5-24 amino acids.

The large structure of an antibody has both advantage and disadvantage in clinical applications either therapy or diagnosis. Disadvantages include the size and the nature of whole antibody as only a small part of an antibody takes part in antigen binding and subsequent function.

While a classical monoclonal antibody like IgG with 150 kDa in size is used in various applications, fragment of antibodies as small as 3kDa have also been used with almost the same functionalities as whole IgG. The antibody fragments including ScFv, Fab, F(ab')2, Minibody, Diabody, and Triabody will be discussed.

17th National Congress of Biochemistry & 8th International Congress of Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

Page | 57

Opportunities to produce knowledge-based products in Iran

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In recent years, the issue of guiding educated people to the path of entrepreneurship and production of knowledge-based products has become serious in our country. However, Iran's universities and research centers are still far from what is called the third generation universities and entrepreneurs, and there is no suitable platform and infrastructure. Despite incubators and accelerators in universities, the relationship between the university and the industry has not been formed, few people have entrepreneurial experience, and many students' theses do not lead to the production of knowledge-based products. Such conditions can be both a challenge and an opportunity to enter the business space and produce knowledge-based products.

Regarding the special conditions of Iran, two proposals are proposed for educated people to enter the entrepreneurial space and gain experience in producing knowledge-based products.

1- Internship and gaining experience of students in start-ups and knowledge-based companies
2- Starting a business with simple ideas and producing products that are not very complicated.

17th National Congress of Biochemistry & 8th International Congress of Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

TEHRAN UNIVERSITY
OF
MEDICAL SCIENCES

Page | 58

The Role of Radiopharmaceuticals in Diagnosis and Therapy of Cancers with emphasis on Clinical Applications and Marketing

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Radiopharmaceuticals are radioactive compounds which have a bound radionuclide in their structure, whose purpose is directing the radionuclide to a location to be treated or to obtain images. Nuclear medicine is the medical specialty that employs radiopharmaceuticals, which has presented itself as a tremendously useful friend for medicine assisting in various diagnoses and treatments, especially for cancer. Progress in nuclear medicine has been always tightly linked to the development of new radiopharmaceuticals and efficient production of relevant radioisotopes. The use of radiopharmaceuticals is an important tool for better understanding of human diseases and developing effective treatments. The availability of new radioisotopes and radiopharmaceuticals may generate unprecedented solutions to clinical problems by providing better diagnosis and more efficient therapies.

Over the last several decades radiopharmaceuticals have emerged as an extremely useful modality for both diagnosis and treatment of disease. Much wider availability of novel radionuclides, more advanced image collection technologies, simplified radiopharmaceutical production technologies, and, most importantly, increased clinical community interest in application of radiopharmaceuticals in patients have created a significant demand for these agents. Human cancer cells overexpress many peptides and mAb receptors as molecular targets. Radiolabeled peptides and mAbs as a novel type of radiopharmaceuticals that bind with high affinity and specificity to the receptors on tumor cells hold great potential for both diagnostic imaging and targeted radionuclide therapy. The advantage of solid-phase peptide synthesis, the availability of different chelating agents and prosthetic groups and bioconjugation techniques permit the facile preparation of a wide variety of peptide-based targeting molecules with diverse biological and tumor targeting properties. Some of these peptides, including somatostatin, bombesin, vasoactive intestinal peptide, gastrin, neurotensin, exendin and RGD are currently under investigation. It is anticipated that in the near future many of these radiolabeled peptides and mAbs may find applications in nuclear oncology. This report presents recent developments in the field of small peptides and mAbs as well as their applications in the diagnosis and treatment of cancer.

17th National Congress of Biochemistry & 8th International Congress of Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

Page | 59

Industrialization of biology: A road map

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2- Department of Medical Biotechnology, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran
3- Department of Research and Development, Parsian Giti Iranian Co., Alborz, Iran

The tremendous progress of biology over the past half century—from the introduction of the DNA molecule to today's astonishing and rapid progress in the field of industrial biology—has set us on the path to significant innovation in the production of bio-chemical materials. New bio-based chemicals, improved public health through improved medicines and new biological diagnostics and techniques, and biofuels that reduce our dependence on oil are all results of research and innovation in the life sciences. In the past decade, we have seen major advances made possible by biotechnology in areas such as rapid and low-cost DNA sequencing, metabolic engineering and high-throughput, high-precision screening, controlled DNA manipulation. The production of chemicals using synthesis and biological engineering can expand even faster. If we are to realize the benefits of the rapidly expanding industrialization of biology, we need a visionary plan, through the development of a technical roadmap similar to those that have fueled the steady growth of the semiconductor industry and our explorations in space.

The industrialization of biology provides such a roadmap for achieving key technical milestones for the production of chemicals via biological pathways. This report examines the technical, economic, and social factors that limit the adoption of addressing biological issues in today's chemical industries, and if overcome, the advanced production of chemicals through industrial biotechnology will be significantly accelerated. By working on chemical synthesis reactions, metabolic engineering, molecular biology, genetic engineering, and synthetic biology, Industrialization of Biology identifies key technical goals for the production of next-generation chemicals, and then gaps in the knowledge, tools, techniques, and systems needed to achieve them. It introduces these goals. And it also makes clear to us the goals and the timetable to achieve them. This report also considers the necessary skills to achieve the goals of the road map and the educational horizon needed to produce the required scientific staff and skilled engineers.

17th National Congress of Biochemistry & 8th International Congress of Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

THEHRAN UNIVERSITY
OF
MEDICAL SCIENCES

Oral Presentations

A-10-1192-1

Comparative evaluation of inflammatory parameters and insulin resistance indices in obese/overweight women with polycystic ovary syndrome

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Introduction: Polycystic ovary syndrome (PCOS) is one of the most important metabolic disorders in women of reproductive age which is characterized by androgen excess and/or ovulatory dysfunction. Indeed, there is an abnormal adipocyte function in PCOS women which may result in inflammation and insulin resistance. Since the obesity impact on secretion of many adipocyte-derived substances (adipokines) as well as insulin resistance, the purpose of this study was to compare the level of adiponectin, insulin resistance, hs-CRP and homocysteine in Iranian obese/overweight women with PCOS.

Methods: A total of 304 PCOS women and 139 healthy non-PCOS women enrolled in this study. Both groups were stratified according to BMI into a normal group (BMI<25) and an obese/overweight group (BMI ≥25). FBS, TG, TC, LDL, HDL were measured using commercial kits. Adiponectin, Free testosterone, LH, FSH, hsCRP, HomoCysteine and insulin levels were determined using ELISA technique. Homeostasis model assessment of insulin resistance (HOMA-IR) was calculated using the related equation.

Results: The levels of adiponectin, insulin, hsCRP and free testosterone in both statuses of normal and obese/overweight women with PCOS were higher than control groups. However, HOMA-IR as a good marker of insulin resistance was increased in obese/overweight women with PCOS in comparison of obese/overweight non-PCOS women. Interestingly, HOMA-IR had higher level in obese/overweight PCOS compared to normal weight non-PCOS women. No significant differences found in FBS, TG, TC, LDL, LH and HomoCys between groups.

Conclusion: According to the obtained results, HOMA-IR is a good biomarker of insulin resistance in obese/overweight among Iranian PCOS women. So, the importance of weight reduction should be considered for treatment procedure of infertile PCOS women.

Keywords: Polycystic ovary syndrome, HOMA-IR, adiponectin, Infertility

A-10-1089-1

Hypertrophic subcutaneous adipocytes in class I obese subjects were associated with ER stress and insulin resistance

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Introduction: The excessive fat deposition in adipose tissue in obesity is associated with metabolic abnormalities. The lipid storage capacity of the adipose tissue prevents ectopic lipid deposition. This capacity varies in people depending on the levels of adipogenic gene expression and provision of the blood supply for tissue expansion through angiogenesis. Here, we studied hyperplasia/hypertrophy of subcutaneous adipose tissue concerning adipogenic gene expression, angiogenesis status, and metabolic parameters in non-obese and class I-III obese subjects with different BMI levels.

Methods: Subcutaneous adipose tissue samples were collected from 80 subjects. Anthropometric parameters, the adipose tissue cell size, serum biochemistry, the ER stress-induced XBP1 level, and the gene expression levels of PPARγ2, WNT10B, and VEGF were measured. The CD31 level was measured by western blotting.

Results: The obese subjects had greater waist circumferences and higher serum TG, TC, insulin, and HOMA-IR than the non-obese group. The class I obese group showed the largest adipocyte size, increased insulin, HOMA-IR and sXBP-1, WNT10B, and VEGF-A expression. The class II/III obesity group showed high PPARγ2 expression and CD31 levels. The class I obesity group with hypertrophic scWAT adipocytes and limited capacity of adipose tissue expansion, presented insulin resistance and higher markers of hypoxia and ER stress.

Conclusion: The results suggest that the capability of adipogenesis with adequate angiogenesis is related to the metabolic status and ER stress.

Keywords: obesity, adipogenesis, ER stress, XBP1, WNT10B, angiogenesis, insulin resistance

A-10-1144-2

Evaluation of IP10 and miRNA 269-a Expression Levels in Peripheral Blood Mononuclear Cell of Coronary Artery Disease Patients and Controls

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Introduction: Coronary artery disease (CAD) is the main cause of death worldwide. Atherosclerosis, the leading underlying cause of CAD, is a progressive inflammatory disease. miRNAs play a substantial role in inflammation. The aim of this study was to investigate the associations of peripheral blood mononuclear cells (PBMCs) gene expression of IP10 and miRNA 296-a and serum levels of IP10 and serum inflammatory cytokines interleukin-6 (IL-6) in CAD patients and controls.

Methods: This is a case–control study conducted on 82 angiography confirmed CAD patients and 82 controls. PBMC expressions of miR-269a and IP10 were evaluated by real-time method, and serum concentrations of IL-6 and TNF-a were evaluated by enzyme-linked immunosorbent assay in the study population.

Results: A significant increase was found for serum IP10, IL-6, and TNF-a levels, and PBMC expression of IP10 and miRNA 296-a genes expression of CAD as comparison with controls. No significant correlation was found between IP10 gene expression and miRNA 296-a. A significant positive correlation was found between PBMC gene expression level of IP10 and serum concentrations of IP10 and cytokines IL-6 and TNF-a levels. Taking together, in PBMC of CAD patients, the IP10 and 296-a miRNA genes expression levels were increased significantly than controls. IP10, IL-6, and TNF-a levels in CAD patients were more than those in controls significantly.

Conclusion: Concerning positive relationship between miRNA 269-a gene expression level and serum concentrations of IL-6 and TNF-a in CAD patients, it is proposed that IL-6 and TNF-a inhibitor could be the main targets of miRNA 296-a and, thereby the IL-6 and TNF-a levels were increased; however, further study is needed.

Keywords: PBMC, miRNA 296-a, coronary artery disease, interleukin-6, IFN-Y–induced protein

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The effect of yttrium oxide nanoparticles on the inflammatory responses induced by streptozotocin in male Wistar rats

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Introduction: Alzheimer's disease (AD) is a neurodegenerative disorder and the most common form of dementia that is characterized by extensive neuronal loss, accumulation of beta-amyloid and tau proteins, increased glutamate toxicity and decreased acetylcholine levels. Moreover, numerous studies have pointed out the strong contribution of neuroinflammation to AD pathogenesis. Yttrium oxide nanoparticles (Y2O3NPs) with anti-apoptotic and antioxidant effects protect nerve cells from several stress and toxins. The aim of this study was to evaluate the protective effect of Y2O3NPs against neuroinflammation induced by streptozotocin (STZ).
Methods: In this study, male Wistar rats weighing 200-250 g were used, which were divided into 4 experimental groups as follows: 1) control 2) Alzheimer 3) Alzheimer+Y2O3NPs 4) Y2O3NPs. The Alzheimer's model was induced by intracerebroventricular injection of STZ (3 mg/kg, 3μl, bilaterally). The expression of factors involved in neuroinflammation (IL-6, IL-1β and TNF-α) was assessed in the hippocampus of rats using quantitative polymerase chain reaction (qPCR). Also, the protective effect of Y2O3NPs (0.5 mg/kg/day, for 21 days, 24 h after STZ injection) on the inflammatory responses was investigated in STZ-treated rats.
Results: Our results revealed that STZ by increasing the expression of IL-6, IL-1β and TNF-α induced neuroinflammation, while treatment with Y2O3NPs significantly attenuated the expression of these factors and suppressed inflammatory responses in the hippocampus of Alzheimer's rats.
Conclusion: These findings show that Y2O3NPs can be considered as important promising therapeutic targets for the treatment of neuroinflammation in neurodegenerative diseases such as AD.

Keywords: Alzheimer, Streptozotocin, Yttrium oxide nanoparticles, Neuroinflammation

17th National Congress of Biochemistry & 8th International Congress of Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

Page | 65

A-10-1608-1

The effects of treatment of Experimental Autoimmune Encephalomyelitis (EAE) mice with stem cells transduced with Klotho gene on clinical scoring and Myelin Basic Protein (MBP) expression in spinal cord

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Introduction: Multiple sclerosis (MS) is a chronic autoimmune disorder leading to demyelination. Cell therapy and gene therapy is one of the strategies that attracted much attention in recent years. In the current study, we investigated the therapeutic effects of Adipose-derived mesenchymal stem cells (Ad-MSCs) carrying the klotho gene on remyelination in the central nervous system of a mouse model of EAE.

Methods: Ad-MSCs were obtained from healthy donors through lipoaspiration. The cells were characterized by flow cytometry and their trans-differentiation potential. After the construction of lentiviral particles in HEKT293 cells using the calcium phosphate method, viral particles were transduced into Ad-MSCs and klotho expression was confirmed using western blotting. Then EAE was induced in C57BL/6 mice by Hooke kit and the mice were randomly divided into control, stem cell-treated, and klotho gene-treatment. Ten days after EAE onset, experimental groups received either PBS, MSCs, or Klotho-Ad-MSCs.Then, on day 25 of EAE development, the mice were killed, their brain and spinal cord tissues were removed, and RNA was extracted to determine the expression of MBP in the spinal cord using Real-Time PCR.

Results: Transfection of transfer and helper vectors was successfully done with high efficiency. Ad-MSCs were transduced with the klotho gene. The results of klotho expression showed that stem cell therapy caused 2-fold increase in MBP in the spinal cord compared to the control group. This increase was 4 fold in samples treated with stem cells carrying the klotho gene. This data was confirmed by the Western blotting technique. Accordingly, stem cell therapy improved body weight and physical activity.

Conclusion: These results suggest that klotho protein can pose neuroprotective effects by increasing MBP expression in the spinal cord of EAE mice

Keywords: Multiple sclerosis, Stem cells, , Klotho, Myelin Basic Protein, EAE model

protective effects of curcumin in an animal model of brain development disease

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Introduction: There is increasing evidence that undesirable circumstances during embryonic development could cause prenatal brain injury. Curcumin, as a natural polyphenol has been introduced to suppress inflammatory process. However, the role of Curcumin on LPS-induced prenatal brain injury remains unknown. The purpose of this study was to examine the beneficial effects of curcumin supplementation on inflammatory status, microglyosis and astrocytosis in this experimental model of prenatal brain disorders

Method: In this study, an in vivo experimental model of prenatal brain injury was produced using LPS a well-known toxic chemical. LPS can induce oxidative stress in the brain. 100μg/kg LPS on 14 day of gestation intraperitoneally injected. In curcumin group, curcumin injected into the lateral ventricle of embryos on second day of gestation. We evaluated the number of microglia cells and astrocytes in brain by immunohistochemistry for GFAP, Iba1, oligo-2 proteins. The effect of curcumin on inflammatory cytokines and chemokines were analyzed by qRT-PCR. In addition, the protective effects of curcumin were investigated by assessment of caspase3 mRNA expression level.

Result: Our data showed that LPS intoxication caused a significant oligodendrocyte loss, and reactive gliosis in the cortex of pups. Curcumin prevented the microgliosis and astrocytosis in cortex as determined by immunohistochemistry staining. Furthermore, we found that the curcumin treatment significantly enhanced the frequency of oligodendrocytes (Olig2+). In addition, curcumin significantly modulated cytokines (TNF, IL-6) and caspase 3 mRNA expression levels in the cortex of mice.

Conclusions: These results provide evidence that curcumin abolishes destructive LPS effects in the mouse brain by restoring oligodendrocyte generation, as well as decreasing astrogliosis and microgliosis and inflammation and apoptosis.

Keywords: prenatal brain injury, Astrogliosis, Microgliosis, LPS

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Effects of hydro-alcoholic extract of Ginger on the paraoxonase1 enzyme activity in hyperlipidemia rats, an experimental and molecular dynamic simulation study

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Introduction: Ginger as a herbal plant is widely used in medicine. This study aims to evaluate the effects of Ginger on the paraoxonase1 (PON1) enzyme in hyperlipidemia rats and investigate the effects of their main compounds via molecular dynamic (MD) simulation.

Methods: In this study, 40 male rats were divided in 6 groups. Negative and positive control groups were fed with routine and fat-enriched diet, respectively. Treated groups were fed with fat-enriched diet along 400 and 800 mg/kg of Ginger hydro alcoholic extract. Serum lipid profile was determined in rats. The effect of extracts on the PON1 enzyme activity in serum was evaluated by aryl esterase activity. Gene expression of the PON1 was determined via qRT-PCR. The MD simulation studies were done using the Auto Dock v.4.2 and the Gromacsv.4.6.1 software.

Results: Ginger extract reduced the serum lipid profile such as triglycerides, total cholesterol Light-density lipoprotein (LDL), Very light-density lipoprotein (VLDL) and increased the high-density lipoprotein (HDL). Also the Ginger extract increased the PON1 Enzyme activity significantly ($P > 0.05$) and increased its gene expression. The simulation results indicated that Gingerol, Paradol, and Zingerol as the main three compounds of Ginger, induce the variation in the secondary and 3-Dimensional structure of PON1 by inducing the MD parameters.

Conclusion: Ginger as a medical plant can moderate the serum lipid profile in hyperlipidemia rats and induce the PON1 activity to protect the ox-LDL. It seems that Gingerol, Paradol, and Zingerol can induce the PON1 enzyme activity by direct effects.

Keywords: Ginger, Hyperlipidemia, PON1 enzyme, Molecular dynamic

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Preventive Effects of Achillea Millefolium, Rosa Damascena and Origanum Majorana Hydroalcoholic Extracts on Breast Cancer in Female Mice

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Introduction: Breast cancer is overally considered as the second most frequently recognized cancer worldwide. Several studies have recently reported the antitumoral properties of some medical herbs such as Yarrow (Achillea millefolium), Marjoram (Origanum majorana) and Rose (Rosa damascena Mill L). Therefore, the current study aimed to evaluate the effect of hydroalcoholic extract of these plants on breast cancer prevention in female mice.

Methods: Mice were classified into five ten-mice groups: normal control (untreated group), tumor group (treated with 4T1 cells) and treatment groups (treated with 4T1 cells+ Yarrow or Rose and/or Marjoram plants). Then, the levels of cancer antigen 15-3 (CA 15-3) and carcinoembryonic antigen (CEA), superoxide dismutase (SOD) and total antioxidant were determined. At final, tumor size was evaluated.

Results: The hydroalcoholic extract of Yarrow herb significantly decreased the levels of CA-15-3 and CEA ($P\text{-value}=0.008$ and $P\text{-value}=0.018$, respectively). In addition, hydroalcoholic extracts of Yarrow, Rose and Marjoram plants significantly reduced tumor size in comparison with the tumor group ($P\text{-value}<0.001$ for Yarrow, $P\text{-value}=0.004$ for Rose and Marjoram plants). Yarrow herb significantly had the highest effect on tumor size in comparison with Rose and Marjoram plants ($P\text{-value}=0.011$ for both the plants).

Conclusion: no significant differences were found among the groups treated with the plants in comparison with the tumor mice in term of SOD and total antioxidants ($P\text{-value}>0.05$). Our findings revealed that A. millefolium had the highest antitumor effects on mice with breast cancer in comparison with other herbs.

Keywords: Breast cancer, Hydroalcoholic extract, Herbal medicine, Marjoram, Rose, Yarrow

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The therapeutic potential of γ-Al 2 O 3 nanoparticle containing 5-fluorouracil in the treatment of colorectal cancer

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5-Fluorouracil (5-FU) is being used in the treatment of several malignancies, but side effects are often reported and include: diarrhea, vomiting, nausea, poor appetite, watery eyes, and photophobia. We have developed and tested the cytotoxic activity of nanocrystalline powder of γ-alumina (γ-Al2O3) containing 5-FU in two-dimensional and three-dimensional (3D) CRC cell culture. γ-Al2O3 was prepared using a facile sol-gel method. The physicochemical properties of nanoparticles were investigated by Fourier Transform Infrared (FTIR) analysis, Field Emission Scanning Electron Microscopy (FESEM), and Energy Dispersive X-ray Analysis (EDXA). Moreover, the particle size was monitored by Transmission Electron Microscopy (TEM). We used MTT and a scratch assay to assess the antiproliferative and anti-migratory of this agent. The effect of γ-Al2O3-5-FU on SOD, MDA, and total-thiols levels was evaluated. We assessed the expression of apoptotic markers in mRNA or proteins by RT-PCR and ELISA respectively. γ-Al2O3-5-FU inhibited cell growth in two-dimensional (2D) and three-dimensional (3D) cell culture and increased apoptosis as detected by DAPI staining via modulation of caspases, BAx, BCl2, and cyclinD1. γ-Al2O3-5-FU also reduced the migratory activity of CRC cells relative to untreated controls. γ-Al2O3-5-FU increased the level of MDA, while reducing the level of SOD and total-thiols as well as inflammatory markers (e.g., TNF-s and IL-6). Our study demonstrated that γ-Al2O3-5-FU inhibited cell growth and migration, indicating its potential value in the treatment of colorectal cancer.

Keywords: 5-FU, CRC, EDXA, FESEM, FTIR, γ-Al (2) O (3)-5-FU

A-10-1056-1

Fabrication of a three-dimensional fibrin gel model to evaluate anti-cancer effects of Astragalus hamosus plant extract on breast cancer cells

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Introduction: Breast Cancer (BC) is a malignancy with high mortality among women. Recently, scaffold-based three-dimensional (3D) models have been developed for anti-cancer drug research. The present study aimed to investigate the anti-proliferative effects of Astragalus hamosus (A. hamosus) in 3D fibrin gel against MCF-7 cell line. We have also evaluated anti-cancer effect of A. hamosus differences between 3D and 2D cultures.

Methods: The fibrin gel formulation was first optimized. Then the cytotoxic effect of A. hamosus extract was assessed on MCF-7 cells by MTT assay. Cell apoptosis, Cell cycle and proliferation were analyzed by flow cytometry.

Results: Flow cytometry analysis revealed that apoptosis increased after treatment with A. hamosus extract in 3D culture model compared to 2D culture. The A. hamosus extract arrested cell cycle in the S and G2/M phases in 3D model while in the 2D culture G0/G1 phase was affected. Treatment with A. hamosus extract led to downregulation of the Ki-67 in the 3D-culture compared with the 2D culture.

Conclusion: These results indicated that A. hamosus extract could be used as a therapeutic candidate for BC due to its anti-proliferative effects. Furthermore, 3D fibrin gel could be better than 2D-cultured cells in simulating important tumor characteristics in vivo, namely, anti-proliferative and anti-apoptotic features.

Keywords: Astragalus hamosus, Breast Cancer, Fibrin gel, three-dimension cell culture model

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Gas chromatography–mass spectrometry based untargeted metabolomics reveals metabolic perturbations in medullary thyroid carcinoma

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Introduction: Medullary thyroid cancer (MTC) is a rare tumor that arises from parafollicular cells within the thyroid gland. The molecular mechanism underlying MTC has not yet been fully understood. Here, we aimed to perform plasma metabolomics profiling of MTC patients to explore metabolic pathways perturbation contributing to MTC tumorigenesis.

Methods: Plasma samples from 20 MTC patients and 20 healthy subjects were obtained to carry out an untargeted metabolomics strategy by gas chromatography-mass spectrometry (GC-MS). Multivariate analyses, namely orthogonal partial least squares discriminant analysis and univariate analysis, including student t-test and volcano plot, were employed as diagnostic tools via MetaboAnalyst and SIMCA software.

Results: A total of 76 features were structurally annotated; among them, 13 metabolites were selected to be differentially expressed in MTC patients compared to controls ($P<0.05$). These metabolites were mainly associated with the biosynthesis of unsaturated fatty acids and metabolisms of amino acids, mostly leucine, glutamine, and glutamate metabolism, that are tightly responsible for energy production in tumor cells. Moreover, according to the receiver operating characteristic (ROC) curve analysis, metabolites with the area under the curve (AUC) value up to 0.90, including linoleic acid (AUC = 0.935), linolenic acid (AUC = 0.92), and leucine (AUC = 0.948) could discriminate MTC from healthy individuals.

Conclusion: The results of this preliminary work contribute to existing MTC metabolism knowledge by providing evidence of a distinctive metabolic profile in MTC patients relying on the metabolomics approach.

Keywords: medullary thyroid cancer, metabolomics, GC-MS, metabolites, metabolic pathways

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VEGFR3 suppression through miR-1236 inhibit proliferation and induce apoptosis in ovarian cancer via ERK1/2 and AKT signaling pathways

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Introduction: Vascular endothelial growth factor receptor 3 (VEGFR3) exerts critical role in cancer development and metastasis and is considered as an ideal target for cancer treatment. Although microRNAs serve key roles in modulating VEGFR signaling, the crosstalk between miR-1236 and VEGFR3 in cancer cells has remained unclear. Therefore, our study proposed to examine the potential role of miR-1236 in regulating the VEGFR3-mediated signaling in ovarian cancer cells.

Methods: Functional experiments including MTT, colony formation assay, wound healing, and flow cytometry were done to clarify the precise function of miR-1236 in ovarian cancer cell proliferation, survival, migration, and apoptosis, respectively. The interaction between miR-1236 and VEGFR3 were examined via real-time PCR and western blotting. Furthermore, VEGFR3 downstream signaling mediators ERK1/2 and AKT phosphorylation status were assessed with miR-1236 transfection using western blotting.

Results: We found that the mRNA and protein of VEGFR3 were expressed in the ovarian cancer cell lines, but down-regulated after miR-1236 transfection. The inhibition of VEGFR3, using miR-1236, significantly reduced cell proliferation, clonogenic survival, and migration ability in SKOV3 and OVCAR3 cells ($P < 0.01$). The flow cytometry results indicated that the rate of apoptotic cells in SKOV3 (38.65%) and OVCAR3 (41.95%) cells increased following VEGFR3 inhibition. Moreover, VEGFR3 stimulation (using specific ligand, VEGF-CS) significantly increased ERK1/2 and AKT phosphorylation ($P < 0.01$), whereas VEGFR3 suppression reduced p-ERK1/2 (67.94% in SKOV3 and 93.52% in OVCAR3) and p-AKT (59.56% in SKOV3 and 78.73% in OVCAR3) compared to the VEGF-CS treated group.

Conclusion: This finding demonstrated that miR-1236 may act as an endogenous regulator of ERK1/2 and AKT signaling by blocking upstream regulator of VEGFR3. Overall, we demonstrated the importance role of the miR-1236/VEGFR3 axis in ovarian cancer cell proliferation by regulating the ERK1/2 and AKT signaling that might be an effective strategy against ovarian cancer.

Keywords: MiR-1236, ovarian cancer, VEGFR3, ERK1/2, AKT.

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PEGylated Liposomal Encapsulation Improves the Antitumor Efficacy of Combretastatin A4 in Murine 4T1 Triple-Negative Breast Cancer Model

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Introduction: Combretastatin A4 (CA4), a vascular disrupting agent has been recently proposed as an anticancer agent. However, its low water solubility and low bioavailability limited its clinical efficacy. Overcoming this issue requires developing new delivery strategies to enhance its anticancer effects.

Methods: Here, we prepared various PEGylated liposomal formulations containing CA4 composed of different molar ratios of HSPC/DSPE-mPEG2000/Cholesterol/CA4 (F1: 80:5:10:5; F2: 75:5:15:5; F3: 70:5:20:5; F4: 60:5:30:5 and F5: 50:5:40:5) by the thin-film hydration method plus sonication and extrusion.

Results: All formulations had a particle diameter of 100-150 nm, a monomodal distribution with low polydispersity index and a negative zeta potential. Among the formulations only F1, F2, and F3 showed a high CA4 encapsulation efficiency; so their anticancer effects on triple-negative breast cancer (TNBC) were investigated in vitro and in vivo. The release study showed that F3 liposomes had significantly lower CA4 release compared to the F1 and F2 liposomes in different pH of 5.5, 6.5, and 7.4. We found that, CA4-loaded liposomes effectively inhibited both proliferation and migration of 4T1 and MDA-MB-231 TNBC cell lines by inducing cell cycle arrest at the G2/M phase and decreasing MMP-2 and MMP-9 expression and activity. In vivo studies revealed that F3 liposomes were highly accumulated at the tumor site and more effectively delayed tumor growth and prolonged the overall survival than other groups in 4T1 breast tumor-bearing mice.

Conclusion: Taken together, encapsulation of CA4 in F3 liposomes enhances its anti-tumor activity and may be serve as a promising approach for TNBC treatment and merits further investigation.

Keywords: Combretastatin A4, Vascular disrupting agent, Liposome, Triple-negative breast cancer.

17th National Congress of Biochemistry & 8th International Congress of Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

Page | 74

A-10-1123-1

The effect of heat-killed Lactobacillus Plantarum on oxidative stress and liver injury in experimental model of liver fibrosis in rats

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Introduction: Cholestasis is a pathologic condition due to an imparirment of the bile flow and can result in oxidative stress, hepatocellular injury and liver fibrosis. There is emerging evidence that probiotics have beneficial effects on ameliorating liver injury via regulation of immune responses, reduction of oxidative stress and impact on the intestinal barrier. This study was conducted to evaluate the hepatoprotective effects of heat-killed Lactobacillus plantarum against cholestatic liver injury in rats.

Methods: Thirty-two male Wistar rats wereb distributed into four groups(n=8). Rats in two groups underwent common bile duct ligation (BDL) to induced liver fibrosis. One BDL group received heat-killed L.plantarum and another one vehicle. Sham-operated and normal controls either received vehicle. This groups were administrated by gastric gavage once a day for 28 days. Finally, serum levels of ALT, AST, ALP, LDH and bilirubin were analyzed. Also, oxidant and antioxidant parameters including MDA, nitric oxide(NO), protein carbonyl content, total antioxidant) TAC), oxidant status (TOS) , GSH, Catalase(CAT) and SOD activity ,and the experssion of αSMA,TNFα, IL-6 and IL-10 genes in liver tissue were measured. Liver tissue were histologically assessed.

Result: After treatment with heat-killed L.plantarum liver enzymes activity and serum bilirubin levels were lower compared with the control group of BDL (P≤0.05). The amount of MDA, NO, TOS and carbonyl protein in the liver tissue were lower (P ≤0.001), but GSH, TAC and activity of both SOD and CAT enzymes were higher (P ≤0.001) .Forthermore the expression of αSMA, TNFα, and IL-6 genes were lower (P ≤ 0.001), but gene expression of IL-10 was higher (P ≤ 0.01). In liver tissue, fibrosis, inflammatory and necrosis cells were reduced (P ≤ 0.05). Also, bile duct hyperplasia was decreased (P ≤ 0.01).

Conclusion: Heat-killed L.plantarum has an protective effect against liver fibrosis progression.It improved liver functions via reduction oxidative stress and inflammation.

Keywords: Lactobacillus plantarum, Liver fibrosis, Bile duct ligation, Oxidative stress.

17th National Congress of Biochemistry & 8th International Congress of Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

Page | 75

A-10-1211-1

Effect of Kaempferol-Loaded Silica Nanoparticles on 5-Fluorouracil-induced Kidney toxicity in Rats

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Introduction: 5-Fluorouracil (5-FU), a chemotherapeutic drug, has adverse effects on kidney functions. Kaempferol (KPF) is a natural flavonoid present in fruits and vegetables possessing antioxidant, anticancer, and anti-inflammatory features. In this study, we used silica nanoparticles (SiNPs) to trap KPF and evaluate its protective effects on kidney toxicity induced by 5-FU in male wistar rats.

Methods: After the synthesis of KPF-loaded SiNPs (KPF-SiNPs) by ultrasound-assisted wet impregnation method, this process w:as characterized and approved by morphology, particle size, and drug content. Twenty-four rats were divided into 3 groups (control, 5-FU and KPF-SiNPs + 5-FU). Kidney toxicity was induced by intraperitoneal administration of 5-FU (100 mg/kg). After treatment with KPF-SiNPs (1 mg/kg/d), Blood Urea Nitrogen (BUN), Creatinine (Cr) and serum total protein as well as total antioxidant capacity (TAC), malondialdehyde (MDA) content, and expression of tumor necrosis factor α (TNF-α) gene in kidney tissues were determined. Hematoxylin-Eosin staining was performed to kidney tissue injury pathology analysis.

Results: Scanning electron microscope (SEM) data demonstrated that KPF-SiNPs have a spherical form, and dynamic light scattering (DLS) data showed that 85% of the produced NPs have a size of 212.5 nm. BUN, Cr, MDA levels, and TNF-α expression were significantly increased in the 5-FU group compared to the other groups. TAC was significantly lower in the 5-FU group compared with control group, and determined to be increased in KPF-SiNPs + 5-FU. Also, histopathological examination indicated a reduction in kidney damage (congestion, necrosis, and inflammation) in the groups treated with KPF-SiNPs + 5-FU compared to 5-FU group.

Conclusion: We indicated that KPF-SiNPs have protective effects on 5-FU-induced kidney toxicity.

Keywords: 5-Fluorouracil, Kaempferol, silica nanoparticles, kidney toxicity

A-10-1286-1

Effects of chitosan-quercetin complex on NF-κB pathway in male wistar rats with NASH

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Introduction: Non-alcoholic fatty liver disease includes excessive accumulation of fat in the liver. NF-κB activation due to the oxidative stress is involved in the disease pathogenesis. Quercetin, is an antioxidant and anti-inflammatory flavonoid with limited bioavailability. This study investigates the effect of chitosan-quercetin complex on the fatty acid composition and expression of selective genes in NF-κB pathway in the liver tissue of wistar rats with induced non-alcoholic steatohepatitis.

Methods: Thirty-seven male Wistar rats were fed a normal or high-fat diet, high in palmitic acid and cholesterol for three months. The Rats were randomly divided into normal control (N-ctrl/ normal salin), fatty liver control (FL-C/ normal salin), quercetin (Que/ 33 mg/kg), chitosan (Chit/ 66 mg/kg) and chitosan-quercetin nanoparticles (Ch-Q NP/ 100 mg/kg), treated via intra-gastric gavage over the last four weeks. The expression of selective genes of NF-κB pathway in the liver tissue and the serum levels of liver enzymes, triglyceride, total cholesterol, malondialdehyde and total antioxidant capacity were examined.

Results: A significant increase in the mRNA expression of TNFR-1, TRADD, IL-6, A20 and MKK7, was induced in the FL-C group ($P < 0.01$). Ch-Q NP treatment reduced the the gene expression level of IL-6 more effective than Que ($P < 0.05$), MKK7 than Chit ($P < 0.01$), TRADD and A20 than both Que and Chit groups ($P < 0.05$). Increase in linoleate and γ-linolenate ($P < 0.01$) and decrease in palmitate, stearate, pentadcanoate and heptadecanoate ($P < 0.05$) were observed in the Ch-Q NP group. Increases in TAC and decreases in AST, TG and T-chol ($P < 0.05$) occurred in all three treatment groups, although Ch-Q NP group performed best for lipid markers ($P < 0.001$) and TAC ($P < 0.01$). **Conclusion:** Treatment with quercetin and chitosan-quercetin nanoparticles may reduce the high-fat diet-induced liver damage, through the suppression of NF-κB.

Keywords: Non-alcoholic fatty liver, NASH, quercetin, chitosan, NF-κB

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Effect of Cineole on the Alleviation of Acute Kidney Injury and Renal Function Recovery Following Gentamicin Administration in Rats

Introduction: Gentamicin leads to the production of free radicals and renal impairment. Terpenoids like cineole, are compounds that have antioxidant properties. Antioxidants can play an effective role in preserving the oxidant-antioxidant balance. Hence, the present study investigated the effects of cineole on the acute kidney injury and renal function recovery following gentamicin administration in rats.

Methods: 36 male Wistar rats were randomly divided into 6 groups; healthy control, gentamicin, DMSO carriers, cineole 50, cineole 100, vitamin E. After 12 days of treatment, the animals were anesthetized with ketamine and xylazine. Serum and kidney samples were taken for biochemical and gene expression experiments. Finally, the data were analyzed using SPSS and $p < 0.05$ was considered significant.

Results: Cineole had no notable effect on biochemical factors such as serum MDA, GPX, NO, urea, and urine protein. It considerably decreased the gene expression of inflammatory factors such as TNF-α and IL-6. However, it remarkably increased the gene expression of kidney GPX antioxidant enzyme. Furthermore, improvement in histological changes was observed in the cineole-treated groups compared with the gentamicin group.

Conclusion: Cineole, due to its antioxidant properties, can be efficient in improving kidney impairment in some diseases and utilized as nephroprotective agent against kidney injury caused by nephrotoxins like gentamicin. However, more extensive studies with more experimental groups and longer follow-up are necessary to affirm the results of the present study.

Keywords: Gentamicin, nephrotoxicity, cineole, oxidative stress, rat

A-10-1649-1

Trimethylamine-N-oxide (TMAO), a new risk factor for non-alcoholic fatty liver disease correlates with the expression of miRNA-34a, miRNA-122 and miRNA-192; a dual in-vivo and in-vitro study

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Introduction: Non-alcoholic fatty liver disease (NAFLD) is a multifactorial disorder with complicated pathophysiology ranging from simple steatosis to steatohepatitis and liver fibrosis. Trimethylamine-N-oxide (TMAO) production has been thought to be correlated with choline deficiency. This study investigated the circulatory levels of TMAO and choline (as a lipotropic factor and the precursor of TMAO) as well as miRNA-34a, miRNA-122, and miRNA-192 in patients with NAFLD. These microRNAs were also evaluated in the fatty liver cell model treated with TMAO.

Methods: In 30 patients with confirmed fatty liver disease and 30 healthy individuals TMAO and choline were measured using the LC-MS/MS. A fatty liver cell model was developed by exposing HepG2 cells to a mixture of palmitate and oleate in a ratio of 1:2 at 1200 µM final concentration for 24 hours. The confirmed fatty liver cells were treated with 37.5, 75, 150, and 300 µM of TMAO for 24 hours. The expression of microRNAs was measured by RT-qPCR in both patients and cellular models.

Results: The plasma level of TMAO was higher in patients (P=0.030), while their choline was lower than in healthy individuals (P = 0.001). The expression of miRNA-34a and miRNA-192 was higher in the serum of patients (P=0.0024 and P=0.0001 respectively). The cellular expression of all microRNAs was significantly higher in untreated fatty liver cells compared to normal HepG2 cells (P<0.05). Only the 75 and 150 µM of TMAO significantly increased the expression of miRNA-34a and miRNA-122 compared to both fatty and normal control cells (P<0.05).

Conclusion: Our results provided documentation for high circulatory levels of TMAO and low concentration of choline in NAFLD patients to confirm the correlation of TMAO to the pathogenesis of the disease. The evaluation of microRNAs and their diagnostic values in patients highlights their potential mediating role in pathogenesis and as monitoring biomarkers.

Keywords: Trimethylamine-N-oxide, choline, Non-alcoholic fatty liver, miRNA-34a, miRNA-122, miRNA-192

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Crocetin, a saffron carotenoid, ameliorates the Aβ-induced toxicity in differentiated PC12 cells through AKT/GSK3β pathway

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Introduction: Neurodegenerative diseases are progressive chronic disorders accompanied with the physical and functional loss of neurons in some areas of the brain. The role of natural products, including saffron (Crocus sativus L.) has been shown in prevention of the progress of some neuronal disorders. Herein, we investigated the role of Crocetin (Crt), an active carotenoid of saffron stigma, in a cell model of Alzheimer's disease (AD). In this regard we focused on the Nrf2 upstream pathway mainly AKT/GSK-3β signaling pathway, which plays a critical role in regulating Nrf2 activity and the phosphorylation of Tau protein in AD.

Methods: PC12 cells were differentiated using nerve growth factor (NGF). Then, the cells were transfected by application of Aβ1-42 oligomers. The cell viability in the presence and absence of Crocetin (0.1-10 μM), before and after transfection (as preventive or therapeutic modalities) were evaluated at different time intervals. After obtaining the optimum Crt concentration and time, the expression of some important markers in the mentioned pathway was evaluated by Western blot and immunocytochemistry (ICC).

Results: The data indicated that Crt significantly decreased the Aβ toxicity against differentiated PC12 (dPC12) cells in both preventive and therapeutic modalities. Crt suppressed GSK-3β kinase in dPC12 cells and significantly reduced Tau phosphorylation (p-Thr231) levels. In addition, Crt significantly increased the expression level of NQO1, AKT phosphorylation, and inactive GSK3β by increasing its phosphorylation and Nrf2 translocation into the nucleus. All of these effects were time dependent.

Conclusion: Crt decreased Aβ-induced apoptosis in dPC12 cells. It showed a neuroprotective effect against Aβ1-42 infection of dPC12 cells in both preventive and therapeutic manners. This function was through AKT/GSK3β pathways.

Keywords: Neurodegenerative Disease, Prevention, Therapeutic, Apoptosis, Signaling Pathway.

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Serum vitamins E and A, immune response to heat shock protein 27 and systemic inflammation are associated with depression in adolescent girls

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Introduction: Studies showed that oxidative stress and inflammation play an important role in the etiopathogenesis of some psychological disorders. We aimed to investigate the potential association between haematological markers of inflammation, antibody titres to Hsp27 (anti-Hsp27) and serum fat-soluble vitamins (Vitamins E and A),) with mood disorders in adolescents girls.

Methods: A total of 563 adolescent girls were involved in this cross-sectional study. The presence and severity of insomnia, sleepiness and depression, were evaluated using validated questionnaires. Anti-Hsp27 antibody titres, serum vitamins A and E, neutrophil, lymphocyte, white blood cell, platelet counts, and red blood cell distribution width (RDW) were also measured. platelet to lymphocyte ratio (PLR), Neutrophil to lymphocyte ratio (NLR), and RDW to platelet ratio (RPR) were calculated.

Results: Serum anti-HSP27 antibody titers, RPR and PLR values were significantly higher in individuals with a high depression score compared to normal subjects ($p < 0.05$). However, there was no association between sleep disorders and serum inflammatory markers concentrations; although subjects with insomnia had a lower vitamin E/HDL ratio compared to healthy adolescents. multivariate logistic regression analyses showed that anti-HSP was an independent predictor of severe depression (OR = 5.0, 95% CI: 1.6–15.7, $p < 0.05$).

Conclusion: Our results revealed that serum anti-HSP27 antibody titres might be a valuable biological parameter in depressive patients. This finding may support the role of oxidative stress in the aetiology of depression, and targeting this pathway may be of value in the treatment of depression.

Keywords: Red cell distribution width, Neutrophil-lymphocyte ratio, Heat shock protein, Platelet-lymphocyte ratio

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In-vitro (2D and 3D cultures) and in-vivo cytotoxic properties of Zataria multiflora

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Introduction: Ethnopharmacological relevance: Zataria multiflora is an iranian valuable traditional plants, called Avishan Shirazi in Persian language used to reduce inflammation, spasm, pain, and cancer symptoms. Zataria essential oil (ZEO) is one of the essential oils possessing broad biological activities Aim of the study: The aim was to investigate the anticancer effects of ZEO both in-vitro and in vivo using mouse mammary carcinoma 4T1 cell line and mouse cervical cancer TC1 cell line.

Methods: The in-vitro effects of ZEO on the proliferation of these cell lines were considered in 2D and 3D culture by MTT assay. In the following, to indicate death mode, fluorescence staining, AnnexinV/PI flowcytometry and caspase-3 activity assay of monolayer cells treated with ZEO was done. In order to evaluate the antitumor activities of ZEO, tumor bearing BALB/c and C57BL/6 mice were eaintraperitoneally administered with ZEO and the immunomodulatory effects of ZEO were considered through cytokine assay. Additionally, hematobiochemical factors including aspartate aminotransferase and alanine aminotransferase were investigated to confirm the harmless effects of ZEO.

Results: The In-vitro results showed that treatment of cells with ZEO leads to significant inhibition of 4T1 and TC1 cell proliferation and apoptosis in monolayer cell culture (2D) and multicellular spheroids (3D). Based on In-vivo results, ZEO was effective in decreasing the tumor weight compared to the control. Furthermore, ZEO was effective in tilting the balance of cytokines in favor of T helper 1 through the increase in the secretion of TNF-α, IFN-γ, IL-2 and decrease in IL-4. During the treatment with ZEO, hematobiochemical factors of mice did not significantly change.

Conclusion: the present study demonstrated that the ZEO has potent antiproliferative, apoptosis inducing and immune system stimulant properties in breast and cervical cancer.

Keywords: spheroid, cervical cancer, breast cancer, apoptosis, cytokine

17th National Congress of Biochemistry & 8th International Congress of Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

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Paradoxical effect of Aβ on protein levels of ABCA1 in astrocytes, microglia, and neurons isolated from C57BL/6 mice: an in vitro and in silico study to elucidate the effect of Aβ on ABCA1 in the brain cells

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Introduction: Impaired cholesterol metabolism has been reported in Alzheimer's disease. Since ABCA1 is one of the main players in the brain's cholesterol homeostasis, here we used the in-vivo and in-silico experiments to investigate the effect of Aβ on ABCA1 protein levels in microglia, astrocytes, and neurons in mice.

Methods: microglia, astrocytes, and neurons were cultured and exposed to beta amyloid. ATP-binding cassette transporter A1 in cell lysates was determined by Western blotting (WB), and cholesterol efflux was measured in the conditioned media. Molecular docking and molecular dynamics (MD) simulations were conducted to gain a better understanding of the effects of Aβ on ABCA1.

Results: In response to Aβ, the protein levels of ABCA1 increase significantly in microglia, astrocytes, and neurons; however, its ability to enhance cholesterol efflux is diminished. Aβ inhibited the function of ABCA1 by obstructing the extracellular tunnel that transports lipids outside the cell, as determined by molecular docking. MD simulation analyses validated these findings.

Conclusion: Our results demonstrated that Aβ could increase ABCA1 protein levels in various brain cells, regardless of cell type. Molecular docking and molecular dynamics simulation studies indicate that Aβ has a significant effect on the structural conformation of ABCA1, possibly interfering with its function. We believe that the conformational changes of ABCA1 will inhibit its ability to subsequently release cellular cholesterol. Aβ may obstruct the extracellular tunnel of ABCA1, rendering it less accessible to proteases such as the calpain family, which may explain the increase in ABCA1 levels but decrease in its function.

Keywords: Keywords: Brain cholesterol homeostasis, ABCA1, Molecular docking

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PT-Gliadin Induce Phenotypic and Functional Maturation of DCs Derived from Peripheral Blood Mononuclear Cells of Celiac Disease

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Introduction: Celiac disease (CD) is a chronic immune-mediated small intestinal enteropathy with accumulation of dendritic cells induced by gluten in genetically susceptible subjects. Dendritic cells (DC) are anticipated to be crucial in determining the immunological response. The direction of the immune response toward immunity or tolerance depends on the stage of maturation and the functional properties of the DC. DC become fully functional APC upon maturation in response to diverse stimuli. The aim of this study is to investigated the effect of Peptic-Tryptic digest of gliadin on the phenotypic and functional maturation of DCs derived from peripheral blood mononuclear cells of celiac disease.

Method: peptic-tryptic fragment of gliadin was prepared using the pepsin-trypsin enzyme. Peripheral Blood Mononuclear Cells isolated by Ficoll-Hypaque gradient separation of buffy coats obtained from celiac disease donors. The adherent monocytes incubated in the presence of human GMCSF (100 ng/ml) and human IL-4 (50 ng/ml) for 5 days. The DC generated (CD11c+, CD14-) were harvested and seeded at a concentration of 0.5×10^6 cells/ml in 24-well plates. PT-gliadin (100, 200 or 500 µg/ml) and LPS (1µg/ml) were added to cells for 24 and 48 h to induce DC maturation. The expression of DC surface markers and cytokines secretion in response PT-gliadin were investigated by Flow Cytometry and Real Time PCR.

Results: the effect of PT-gliadin was dose dependent. The treatment of monocyte-derived immature DC from celiac disease with PT-gliadin (500µg/ml) for 48 h led to enhanced expression of maturation markers, including CD83 (68.2%), CD86 (95.5%) and inflammatory cytokines IL-12(4.3 folds) and TNF-α (1.3 folds).

Conclusion: In conclusion, our results demonstrate that PT-gliadin have an ability to promote phenotypic and functional maturation of human DC. Moreover, PT-gliadin stimulates monocyte-derived immature DC from celiac disease to produce inflammatory cytokines and maturation markers similar to that induced by LPS.

Keywords: Celiac Disease, gliadin, Dendritic cells

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Microfluidic paper based device for enhanced colorimetric detection of glycine extended gastrin using phage displaying antibodies

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Introduction: Applying phage displaying antibodies and single monoclonal antibodies in biosensors is an amazing approach alternating with whole antibodies benefiting from their stability, easy and cost effective produce. Implementing these biorecognition elements along Microfluidic paper based analytical devices(µPADs) is a breakthrough beyond patient bed for a fast and efficient diagnosis.

Methodes: Here we developed a wax patterned µPAD with enhanced sensitivity by using phage displaying antibodies coated with AuNPs as detection elements. Moreover, we compared two types of capturing reagents, single antibody fragments and phage displaying antibody fragments in this device. Paper surface in a simply and one step procedure was modified with chitosan for an electrostatic physical absorption of capturing elements because of their opposite charges. Results were imaged with iPhone12 and analyzed both qualitatively with naked eye and quantitatively with MATLAB software. Glycin extended Gasterin (G17-Gly) as a previously declared biomarker of colorectal related cancers was used as a target element in this sandwich immunoassay detection test.

Results: Results indicated phage displaying VL antibodies compared to single VL antibodies with limit of detection(LOD) 0.96 Picomolar work better in capturing process on the muicrofluidic Paper based device. Furthermore Phage displaying scFv antibodies conjugated with gold nanoparticles(AuNP) can enhance the signal intensity to have a faster and better detection.

Conclusion: Thus, obtained results suggest, for the first time, the potential of phage displayed antibodies to sandwich immunoassay on microfluidic paper-based device.

Keywords: Microfluidic paper based diagnostic device) µPAD, Phage displayed antibodies, Gold nanoparticles, Sandwich immunoassay

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The effects of progesterone nanoparticles on parameters affecting fertility in men

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Low motility is one of the causes of male infertility. In this study, the effects of progesterone solid lipid nanoparticles (SLNs) on sperm capacitation, acrosome reaction, oxidative stress and expression of SPACA1 and MAPK way genes were investigated. Progesterone SLNs were synthesized using the solvent emulsification evaporation method. Twenty asthenozoospermia samples were selected, and sperm and acrosome membrane integrity, acrosome reaction, sperm motility, viability, total antioxidant capacity (TAC), total oxidative status tests and PKA, PTK, P38MAPK and SPACA1 gene expressions were assessed. The synthesized nanoparticles were prepared with the size (187.6 nm), PDI (0.184), EE (85.82%), LP (3.43%) and ZP (-23.5mV). Progesterone SLNs increased sperm and acrosome membrane integrity and TAC ($p < .05$). Also, the expression of P38MAPK, PKA, PTK, and SPACA1 genes in this group showed a significant increase ($p < .001$). Progesterone SLNs increased acrosome reaction, sperm capacitation and TAC. Also, it increased the expression of PTK PKA, SPACA1 and P38MAPK genes.

Keywords: acrosome reaction, asthenozoospermia, progesterone nanoparticles, sperm capacitation, total oxidative status.

A -10-1586-1

Application of two novel anionic peroxidases from Raphanus sativus L. var niger roots in labeling antibodies and developing an enzyme-linked immunosorbent assay

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Introduction: We previously reported the purification and characterization of two anionic peroxidases from Raphanus sativus L. var niger (black radish) roots. Here, we evaluated the applicability of these two novel peroxidases as alternatives to the traditional horseradish peroxidase (HRP) in labeling antibodies and enzyme-linked immunosorbent assay (ELISA).

Method: Two novel peroxidases (BRP-A and BRP-B) and HRP were conjugated to IgY polyclonal antibodies using the periodate and cyanuric chloride methods. The applicability of BRP-A and BRP-B in immunoassays was investigated by comparing the intensity of the signal generated by these novel peroxidases with HRP conjugates in ELISA. Additionally, the limit of detection (LOD) was calculated for BRP-A, BRP-B, and HRP conjugates in a direct ELISA using diphtheria toxoid (DTx) as antigen. Finally, the thermal stability of conjugates at 37 and 4 °C was compared.

Results: The peroxidase-antibody conjugates prepared by the periodate method generated a much stronger signal than those prepared by the cyanuric chloride method. The signal obtained by BRP-A and BRP-B conjugates was much lower compared to a commercial HRP enzyme. The limit of detection was found to be 385.71 and 213.75, and 43.60 ng/well for BRP-A, BRP-B, and HRP conjugates prepared by the periodate method, respectively. However, for conjugates prepared by the cyanuric chloride method, the limit of detection could only be estimated for HRP since BRP-A and BRP-B gave an extremely low signal-to-noise ratio. All conjugates prepared by the periodate method showed comparable thermally stable at 37 and 4 °C.

Conclusion: The periodate method seems to be more efficient for conjugation of the novel peroxidases to IgY polyclonal antibodies. As the novel peroxidases had a much higher LOD, they seem to be less suitable than HRP for labeling antibodies and developing immunoassays.

Keywords: Peroxidase, Raphanus sativus L. var niger, black radish, bioconjugation, immunoassay

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HNMR based metabolome profiling in COVID-19 patients

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Introduction: COVID-19 is an infectious respiratory disease that can cause post infection symptoms resulting in different organ dysfunctions within human body. There is limited information about pathogenesis and targeted treatment strategies. Fast spreading of the virus is the main challenge, but gathering of data about pathogenesis should be acknowledged because of its importance in diagnosis and therapy. Recently, the importance of metabolomics in pathogenesis, prognosis, diagnosis, and therapy of several diseases has been documented. Immunologic responses within host after exposure to coronavirus, could be led to metabolite changes determining clinical outcomes. In this study, COVID-19 patients with different outcomes were selected and their metabolite profile investigated using HNMR.

Methods: In this study, serum samples of 61 covid-19 severe ICU hospitalized patients and 20 healthy controls were collected with an ethics number of 1400/D/13/14453 then, HNMR used for collection of metabolites spectral data. The potential raw data were analyzed by different data pretreatment methods, i.e. binning, alignment, centering, autoscaling, pareto scaling, range scaling, vast scaling, and level scaling, were tested on a real-life metabolomics data set. For data analysis PLSDA, PCA statistical methods were used.

Results: Pretreatment data analysis showed significantly effects on the consequence of the data analysis, thus the rank of metabolites pathways, from a biological point of view, should be considered. Metabolic pathway changes including Glycine, serine and threonine metabolism, Pyrimidine metabolism, Histidine metabolism, Aminoacyl-tRNA biosynthesis, Pantothenate and CoA biosynthesis, Amino sugar and nucleotide sugar metabolism, Ascorbate and aldarate metabolism were observed.

Conclusion: Changes in metabolites in COVID-19 patients are consistent with disease progression, which could provide valuable information discovering COVID19 plasma markers. In addition, selecting a suitable data pretreatment method is a fundamental step in the analysis of metabolomics data that significantly affects on the determined metabolites.

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Exogenous expression of Beclin 1 leads to greater survival of mice infected with wild rabies virus

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Introduction: Rabies is an important zoonotic deadly disease and it is natural for researchers to look for ways to increase the life expectancy of rabies patients. Autophagy is a way for reducing the damage to the cell and its organelles. It is a process that maintains homeostasis and can be used as an innate defense mechanism against viruses. Apoptosis is the programmed cell death induced by physiological and pathological conditions. The crosstalk of autophagy and apoptosis plays a key role in rabies disease process.

Methods: The proper functioning of the Beclin1 gene in the brains of normal mice was first evaluated in vitro and then in vivo. Then pIRES2-EGFP- Beclin1 vector for the test group, rapamycin (as positive control), trimethyl adenine (as negative control) and buffer (as sham group) were injected in the brains of normal mice via cannula. Clinical signs of rabies were closely monitored and evaluated in all groups, samples were taken from the brains of each dead mouse and FAT test was performed to determine whether the dead mouse was rabid or not. Tunnel assay performed to evaluate the type of cell death and to ensure the occurrence of autophagy, pathological slides were prepared and stained with anti-LC3 antibody. Also, for more assurance, the activation of autophagy-related genes in different experimental groups was examined by Real-time PCR technique.

Results: Activation of autophagy-related genes (Atg5, Map1lc3, and Beclin1) observed in the brain cells of the test group. The study of pathological slides showed that expression of exogenous Beclin1 protein (pIRES2-EGFP- Beclin1 vector transfection into the mouse brain) affects rabies virus pathogenesis in the brain and will lead to longer survival of rabies-infected animals (compared to controls).

Conclusion: This research could pave the way for the use of methods that delay death from rabies infection.

Keywords: Beclin1, Life expectancy, Street rabies virus, Autophagy, Real time-PCR, Immunohistochemistry, Tunnel assay.

A-10-1816-1

Comparison of the Plasma Proteome Pattern of Migraines Patients with Healthy Subjects

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Introduction: Background: Migraine is a common neurovascular disability worldwide. There is no comprehensive diagnosis or treatment method for migraine as a disabling disease since the evolutionary pathophysiology of migraine has not been fully understood. Therefore, there is a need for new diagnostic markers and target candidates for migraine treatment. Many factors such as differences in protein expression may be involved in the unknown evolutionary pathophysiology of migraines. This study examines plasma proteome in migraineurs to look for the pattern of protein expression with the potential to diagnose or target migraine headaches.

Methods: In this case-control study, 97 volunteers were assigned to groups: 68 migraine patients and 29 healthy participants without migraine symptoms. Blood samples were collected after 12-hour fasting. Two-dimensional gel electrophoresis (2-DE) was performed on the proteins extracted from plasma samples. Based on the analyzed gels, we focused on protein spots with a significant change, >two times between groups. The possible corresponding proteins for these spots were predicted by the 2-DE gels of the EXPASY databases.

Results: Several spots were identified using 2-DE gels and detection software. However, only some have significant expression changes and were subjected to the following analysis. These spots belonged to the haptoglobin, clusterin, fibrinogen alpha chain, fibrinogen beta chain, complement c3, transthyretin, α1-microglobulin, and retinol-binding protein 4.

Conclusion: There are differences in the expression levels of some plasma proteins between groups. Most of them are related to inflammatory conditions, oxidative stress, immune defence, and neuroprotective effects that may be considered as the potential biomarkers of this disease in the future. Nevertheless, more proteomic research is needed to introduce new protein biomarkers to prevent or treat migraines.

Keywords: Migraine Headache, Episodic, Chronic, Proteomics, Two-Dimensional Electrophoresis

17th National Congress of Biochemistry & 8th International Congress of Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

Page | 90

Mini-Oral Presentations

A-10-1000-1

Design and Application of a Loop-Mediated Isothermal Amplification (LAMP) Assay to Detect of Bacillus anthracis

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Introduction: Anthrax is an important zoonotic disease worldwide that is caused by Bacillus anthracis, a spore-forming pathogenic bacterium. Presumptive diagnosis in a hospital microbiology laboratory is based on a direct Gram's stained smear of samples, demonstrating encapsulated, large Gram positive bacilli (box car shaped) in short chains. The purpose of the present work was to design of a loop mediated isothermal amplification (LAMP) assay to detect pXO2 (Cap) gene as a protective gene for anthrax.

Methods: The LAMP was developed using specific primers designed based on the sequence of the pXO2 (Cap) gene of B. anthracis. Analytical specificity and sensitivity of the Cap-LAMP were evaluated.

Results: The LAMP reaction was performed at 65°C for 45 minutes. The amplification obtained with the Cap-LAMP was detected by visual inspection of turbidity and fluorescent color change and confirmed by gel electrophoresis. The LAMP assay was highly specific and no amplification products were observed from the non- B. anthracis organisms.

Conclusion: The Cap-LAMP was developed as a rapid and sensitive method for detecting B. anthracis, which could be important for anthrax risk management and control in animal cases to address public health issues in laboratory or field.

Keywords: Bacillus anthracis, Anthrax, LAMP, Cap, pXO2

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MEDICAL SCIENCES

A-10-1005-2

Page | 92

Effects of SLC22A3 rs543159 and rs1317652 variants on Therapeutic Response to metformin in Individuals with Type 2 Diabetes Mellitus: 6-Months Follow-Up Study

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Introduction: Despite the existence of various anti diabetic drugs, metformin has been verified to be the first-line treatment for type 2 diabetes mellitus (T2DM). However, not all patients respond well to metformin. It has been suggested that Genetic variations, particularly within genes related to pharmacokinetics and pharmacodynamics of metformin (e.g., SLC22A3), are responsible for this variability in response. Organic cation transporter 3 plays an important role in the hepatic uptake of metformin. This study was designed to examine the association of rs543159 and rs1317652 variants in the SLC22A3 gene with response to metformin monotherapy in newly diagnosed individuals with Type 2 Diabetes Mellitus.

Methods: The study population consisted of 200 T2DM patients who received metformin monotherapy for six months. The patients were divided into two groups according to their HbA1c values: the responders (decrease in HbA1c levels by at least 1% after six months of treatment with metformin) and non-responders (less than 1% decrease in HbA1c levels after six months of treatment with metformin). Tetra ARMS-PCR method was used to determine genotypes of the variants.

Results: Our result revealed that under the dominant model, CA and AA genotypes of rs543159 were more frequent in responders as compared to non-responders (OR= 2.48; 95% CI =1.28-4.78, P-value=0.0057). For rs1317652, CC and CT genotypes were more frequent in responder group as compared to non-responders (OR= 2.49; 95% CI= 1.32-4.70, P-value= 0.0043) under the dominant model. Fasting blood sugar (FBS), HbA1c, and total cholesterol (TC) levels were significantly reduced in responder group after six months of metformin monotherapy.

Conclusion: Based on our findings, it seems that rs543159 and rs1317652 in the SLC22A3 gene might be associated with observed differences in response to metformin monotherapy in individuals with Type 2 Diabetes Mellitus.

Keywords: Pharmacogenetics, Metformin, Type 2 diabetes mellitus, HbA1c, SLC22A3

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Breast cancer presenting with palpable axillary lymphadenopathy and breast mass in a 45 -year-old woman and role of RA & TNFα in Presentation

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The findings from our patient's case should increase awareness that patients presented with palpable axillary lymphadenopathy and breast mass, have the potential to develop lymphoma, which in turn increases the risk of developing other primary tumors, so that in rare cases a patient may have concurrent tumors.

Keywords: Breast cancer, Lymphoma, R-CHOP, Rheumatoid Arthritis, TNFα

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Bioinformatics study to find common genes and molecular pathways in hepatocellular carcinoma and hepatitis B

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Introduction: Globally, hepatocellular carcinoma (HCC) is known as the leading type of liver cancer, accounting for ~75% of all liver cancer. It has a poor prognosis in all regions of the world. Also, the Hepatitis B virus (HBV) induces chronic necroinflammatory disease that promotes mutations in liver cells and ultimately leads to HCC. Recently, in silico studies provide valuable information regarding aberrant gene expression profiling and introducing novel biomarkers.
Method: We used R programming to analyze the GSE58208 dataset containing the gene expression data of peripheral blood mononuclear cell (PBMC) samples from healthy individuals and patients with chronic hepatitis B carriers and HCC. Afterward, the aberrant gene expression (p-value <0.001, adj. p-value <0.05, and log Fc = 1) between two groups, chronic hepatitis B carriers and HCC, were recognized. Subsequently, the overlapped genes between the two groups were recognized through Venn Diagram. In the next step, we used R programming to examine the system biology of overlapped genes. Eventually, the Cytoscape software was used to construct the interaction network, and the top ten genes) ranked by Degree method (were found using the cytoHubba plugin.
Results: The result of the Venn Diagram represented 484 overlapped genes between chronic hepatitis B carriers and HCC. Based on the system biology, Insulin signaling pathway was selected as the most crucial pathway. In addition, protein serine/threonine kinase activity, cellular response to insulin stimulus, and actin filament were the most significant Molecular Function (MF), Biological Process (BP), and Cellular Component (CC), respectively. Finally, AKT1, STAT3, SF3B1, SOCS3, PPP1CA, DHX9, GTF2F1, HNRNPL, UBE2S, SOCS1 were selected as top ten genes in network string interactions, including 143 nodes and 660 edges.
Conclusion: This study set out to better understand chronic hepatitis B and HCC pathogenesis. Moreover, the hub genes could be considered as possible prognostic/diagnostic biomarkers.

Keywords: Hepatocellular Carcinoma (HCC), Hepatitis B, Bioinformatics study, System Biology

17th National Congress of Biochemistry & 8th International Congress of Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

TEHRAN UNIVERSITY OF MEDICAL SCIENCES

Page | 95

A-10-1256-2

A systematic review of immunity biomarkers in COVID-19

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Introduction: Coronavirus disease 2019 (COVID-19) is a clinical syndrome caused by the coronavirus 2 (SARS-CoV-2) that causes a severe acute respiratory syndrome. Patients may be asymptomatic or have respiratory and gastrointestinal symptoms, including multiple organ failure that can lead to death. The balance between an effective antiviral response and a dysregulated immune response is a key determining the severity of progression of COVID-19.

Methods: A systematic review was conducted using the NCBI PubMed database and found articles related to COVID-19 immunity and inflammatory response published between December 1, 2019 and April 15, 2020. Haematological, immunological and biochemical parameters were extracted and related to disease severity, age and presence of co-morbidities. Twelve articles with different parameters were analyzed.

Results: The total number of lymphocyte and levels of CD3+ and CD4+ T cells were decreased in severe cases. Neutrophilia has been observed in patients who have progressed to acute respiratory distress syndrome (ARDS). Interleukin-6 (IL-6) is elevated in mild and severe patients, regardless of comorbidity. Erythrocyte sedimentation rate (ESR) and the number and level of C-reactive protein (CRP) increased regardless of disease severity or presence of comorbidity. Elevated levels of D-dimers and lactate dehydrogenase are present in diabetics and in patients with ARDS. The level of Procalcitonin increased to different degrees in severe and critical patients.

Conclusion: The total lymphocyte, CD3+ and CD4+ T cells are low, especially in severe and critical COVID-19 patients; ESR, CRP and IL-6 are all increased regardless of the severity of disease. Understanding the inflammatory response of patients with COVID-19 is necessary to develop better treatment.

Keywords: COVID-19, SARS-CoV-2, immunity, inflammatory response

17th National Congress of Biochemistry & 8th International Congress of Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

TEHRAN UNIVERSITY
OF
MEDICAL SCIENCES

Page | 96

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Periplasmic Production of Brain Derived Neurotrophic Factor

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Introduction: Brain Derived Neurotrophic Factor (BDNF) is one of the several neurotrophins in the human brain. Any disruption in synthesis, maturation, and binding of BDNF to its receptor can lead to the different diseases such as epilepsy, depression and Alzheimer's disease.

Methods: In order to produce this protein as a medicinal protein on a large scale, the optimized sequence of the BDNF coding gene was synthesized and cloned in the expression vector; pET-26b(+). The BDNF gene was located after PelB sequence and before His-Tag. This vector has a kanamycin resistance gene, which made it possible to easily confirm the presence of the vector in the bacterial hosts, during next steps. This vector was extracted from DH5-Alpha E. coli cells with plasmid extraction kit and it was transformed to E. coli BL21. IPTG was added to the bacterial cell culture for protein expression induction and after 6, 12 and 18 hours the concentration of proteins were determined in periplasmic space.

Results: Polymerase Chain Reaction (PCR) with 5'- CCATGGATCACTCTGACCCG-3' (forward primer) and 5'- CTCGAGACGACCACGTTG -3' (reverse primer) and the PCR product size (about 400bp) confirmed the chemical transformation of the vector. E. coli BL21 produced acceptable amounts of BDNF and its expression was better on the 18th hours after incubation with IPTG. Finally, SDS- PAGE analysis showed that the concentration of this recombinant protein was higher in periplasmic space, because of the PelB signal sequence in the expression vector. **Conclusion:** In this study BDNF produced efficiently in a simple bacterial host; E.Coli. In addition secretion of this recombinant protein to the periplasmic space facilitated downstream processing and next purification steps. It seems that this recombinant system is an appropriate factory to access enough recombinant stable and soluble BDNF as a pharmaceutical protein to treat or control of a wide range of diseases.

Keywords: BDNF, BL21, periplasmic space.

A-10-1065-3

Genetic Association of VDR Apa1 Polymorphism with Scleroderma in an Iranian Population

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Introduction: Accumulating evidence indicates that aberrant vitamin D status could contribute to the risk of autoimmune diseases such as scleroderma (SSc). As this contribution is mediated through binding to vitamin D receptor (VDR), considering the genotype and allele frequencies of VDR gene polymorphisms may help to clarify the etiology of SSc. The aim of this study was to investigate the possible association of VDR gene ApaI variant with susceptibility to SSc in an Iranian population.

Methods: The study was conducted on 50 patients with scleroderma and 50 healthy controls. VDR ApaI polymorphism was genotyped using polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) technique. The difference of genotype distribution between the groups was analyzed using Chi-square test and logistic regression analysis.

Results: The allelic frequency of VDR gene Apa1 variant was in the Hardy-Weinberg equilibrium both in whole population and also in studied groups. No significant difference was found for the allelic and genotype distributions of ApaI polymorphism between SSc patients and healthy controls neither in the crud state nor after adjustment for age and gender (OR=0.88: 95% CI=0.50-1.54, p=0.651).

Conclusion: The present study suggested that ApaI polymorphism may not contribute in the development of SSc in an Iranian population. As the association between ApaI polymorphism and SSc varies across different ethnic population, further large cohort studies are necessary to confirm the results.

Keywords: Keywords: Systemic sclerosis, Vitamin D receptor, Polymorphism, ApaI

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Association of inflammatory and oxidative stress markers with the severity of stenosis in patients with coronary artery disease

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Introduction: In several investigation, evaluation of oxidative stress and inflammatory markers in coronary artery disease (CAD) patients were done, but the relationship of these two parameters with the severity of stenosis has been less studied. The aim of the present work was to study the association of oxidative stress [malondialdehyde (A) and total antioxidant capacity (TAC)] and inflammatory markers (CRP) with the severity of stenosis in CAD subjects.

Methods: According to the angiography reports participants (n=190) were classified into two groups of non-CAD (n=80, subjects without any coronary artery stenosis) and CAD patients (n=110, subjects with more than 50% stenosis in at least one major coronary artery). Additionally, subjects were classified based on Gensini Score. Serum levels of A, TAC and CRP were determined using tiobarbitoric acid, FRAP colorimetric method and immunoturbidometric assay, respectively.

Result: Serum levels of CRP, A, and TAC were higher in CAD than non-CAD subjects, but the significant difference was noted just for CRP level. Classification of subjects according to Gensini Score show that CRP, A and TAC were not statistically different between patient with mild or sever stenosis and those with no stenosis. There was a significantly positive correlation between serum level of A and age and triglyceride. Additionally, a positive correlation of CRP with A and TAC was noted (p< 0.05). Regression analysis showed that older age, high BMI, history of dyslipidemia and high CRP level increase the risk of CAD significantly.

Conclusion: Serum levels of CRP significantly higher in CAD patients in compared to non-CAD group. No significant association was noted between inflammatory and oxidative stress markers and the severity of stenosis in CAD subjects. More research with larger sample size is require confirming our findings.

Keywords: oxidative stress, cardiovascular disease, inflammatory markers

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A2B adenosine receptor induces cell cycle arrest in esophageal cancer cells

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Introduction: A2B adenosine receptor is an important receptor in cancer. Many study indicated that A2B adenosine receptor have various function in biology of cancer such as cell proliferation, metastasis, cell cycle and apoptosis. At present the role of this receptor on cell cycle in esophagus cancer has not been elucidate. The aim of this study is evaluation the effect of A2B adenosine receptor agonist on cell cycle in esophagus cancer .

Methods Esophagus cancer cell lines YM-1 and KYSE-30 were used in this study. BAY 606583 was used as agonist A2B adenosine receptor. The effect of Bay 606583 on cell viability and cell cycle was evaluated by MTT and PI assay respectively.

Results: A2B adenosine receptor agonist inhibited cell viability in a dose dependent manner in esophagus cancer YM-1 and KYSE30. This data also demonstrated that A2B adenosine receptor agonist induced G1 cell cycle arrest in esophagus cancer YM-1 and KYSE30.

Conclusion: Our data showed A2B adenosine receptor agonist induces cell cycle arrest in esophagus cancer and in future studies, its mechanism of action should be determined in esophagus cancer.

Keywords: Esophageal cancer, A2B Adenosine Receptor, Cell cycle

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Adenosine induces apoptosis in esophageal cancer cells

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Introduction: Esophageal cancer is the eighth most common type of cancer around the world and constitutes the 6th death cause of cancer [1]. Adenosine is a major signaling in the body that has many function in the body[2]. It has been reported that adenosine induces apoptosis in various cancer cells [3]; but the role of it in induction of apoptosis in esophagus cancer has not been explored. This study evaluated the effect of adenosine on esophageal cancer cell lines YM1 and KYSE-30.

Methods: For this study, we used YM1 and Kyse-30 esophagus cancer cell lines. The cells were cultured in DMEM–F12 supplemented with 10% heat-inactivated fetal bovine serum, in a humidified environment of 5% CO_2 and 95% at 37 °C. Cell viability was evaluated with MTT assay and apoptosis was evaluated with Annexin V and propidium iodide using flow cytometry. **Results** :Adenosine induced cell death in a dose dependent manner in esophagus cancer cell lines in YM-1 and KYSE-30 esophagus cancer cells. Our data also indicated adenosine in concentration of 100 induces cell apoptosis in YM-1 and KYSE-30 esophagus cancer cells. this data also indicated the effect of adenosine on cell death and apoptosis in KYSE-30 was more than YM-1. **Conclusion:** Our data indicated adenosine induces apoptosis in esophagus cancer and it could be considered as a treatment for esophageal cancer.

Keywords: Esophageal cancer, Adenosine, Apoptosis

Hypoxia upregulates the expression of FASN and SREBP-1c in the human gastric adenocarcinoma AGS cell line

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Introduction: Lipid metabolic alterations play pivotal roles in the tumorigenesis and progression of gastric adenocarcinoma (GA), a very aggressive and life-threatening tumor. This study aimed to identify the possible effect of Hypoxia-inducible factor-1α (HIF-1α) on fatty acid synthase (FASN) and sterol regulatory element-binding protein-1c (SREBP-1c) regulation in human gastric adenocarcinoma cell line AGS.

Methods: To investigate the hypoxia effects on the expression of HIF-1α, FASN and SREBP-1c genes, we cultured the human gastric adenocarcinoma AGS cell line under hypoxic or normoxic conditions. To generate hypoxic condition, AGS cells were incubated in a chamber sustained at 1% O_2, 5% CO_2, and balanced with N_2 at 37 °C. AGS cells were cultured 24 h for mRNA expression analysis and 48 h for protein expression. HIF-1α, FASN and SREBP-1c gene and protein expression were analyzed by qRT-PCR and western blot, respectively.

Results: In vitro findings indicate the upregulation of HIF-1α, FASN and SREBP-1c genes in hypoxic culture of AGS cells compared to normoxia. Similarly, protein expression of HIF-1α, FASN and SREBP-1c were increased in the AGS cell line under hypoxic condition. In addition, our in vitro studies provide evidence that the overexpression of HIF-1α was consistent with enhanced FASN and SREBP-1c gene and protein expression in human gastric adenocarcinoma AGS cell line in hypoxic condition.

Conclusion: Consequently, HIF-1α induction accompanied with FASN and SREBP-1c upregulation seems to be a survival approach of GA cells in hypoxic condition, indicating that SREBP-1c and FASN genes could be subject to the same regulatory mechanisms in the human GA progression.

Keywords: Gastric adenocarcinoma, Hypoxia, HIF-1α, FASN, SREBP-1c

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MEDICAL SCIENCES

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Evaluation of the relationship between smoking and type of nutrition on two liver enzymes alanine aminotransferase and aspartate aminotransferase in smokers compared with the control group

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Introduction: A healthy diet provides the body with essential nutrition that includes fluids, macronutrients, and micronutrients and calories. The liver is one of the most important organs in the body that has the function of detoxification and cleansing, and smoking causes an additional burden for the detoxification function of the liver, which can lead to inflammation and fatty liver. This study was designed to investigate the effects of smoking on liver function.

Methods: This is a cross-sectional descriptive analytical study in which the relationship between smoking and the type of nutrition of liver enzymes in healthy people and people who smoke was investigated in Zabol. In this study, 150 people were selected who were divided into two groups of healthy people without smoking (75 people) and people with smoking with liver problems (75 people). A questionnaire containing items such as gender, age, weight, smoking, water, fruit and vegetable, rice consumption, meat and soda consumption that the validity and reliability of this questionnaire was confirmed for each participant in this study Their data were collected.

Results: In this study, there was no statistical relationship between age and levels of AST and ALT liver enzymes ($P > 0.05$), but there was a relationship between weight and levels of liver enzymes AST and ALT. Hepatitis also increased ($P < 0.05$). There was a statistical relationship between alcohol consumption with AST and ALT liver enzymes, ie the more alcohol consumption, the higher the amount of liver enzymes ($P < 0.05$). There was no statistically significant relationship between fruit and vegetable consumption, rice consumption, meat consumption and water consumption ($P > 0.05$).

Conclusion: This relationship is positive and direct, in other words, the higher the consumption of tobacco, the higher the activity of liver enzymes ALT and AST.

Keywords: Smoking, Liver Enzymes, type of nutrition, alanine aminotransferase, aspartate aminotransferase

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Clinical significance of TRIM44 expression in patients with Gastric cancer

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Introduction: Although tripartite motif-containing 44 (TRIM44) has been reported to be overexpression in multiple aggressive malignant tumor, the possible association between the gene expression and clinico-pathological features in gastric cancer (GC) remain unclear. The aim of this study was to explore the clinical significance of TRIM44 expression and the prognosis in GC patients.

Methods: Fresh frozen samples and adjacent normal tissues were collected from 40 GC patients using real-time quantitative PCR method to examine TRIM44 expression, and β-catenin. The Kaplan–Meier method, pearson's correlation test, and Cox proportional-hazards regression were used to evaluate the correlation between TRIM44 expression and clinical significance and the patients' overall survival (OS).

Results: Our results showed a remarkably overexpression of TRIM44 and β-catenin in GC tissues compared with their normal tissues (Fold change=1.71, p=0.004). Subgroup analysis were performed and based on the TRIM44 expression, pateints with high level of TRIM44 showed worse OS (HR = 1.46, 95% CI: 1.07-1.98, p=0.016). Overexpression of TRIM44 was also associated with high level of β-catenin in GC, indicating that TRIM44 might exert its oncogenic activities probably via the β-catenin axis.

Conclusion: This study demonstrated that TRIM44 may serve as an independent prognostic factor in GC patients and shed light on association between this tripartite motif-containing protein and β-catenin. However, further studies, especially with a larger sample size, are needed to identify the effect of TRIM44 in GC.

Keywords: Keywords: Gastric cancer, TRIM44, β-catenin, overall survival, prognosis.

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MEDICAL SCIENCES

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Study on different biomarkers for diagnosis COVID-19: A systemic review

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Introduction: As of the 28th April 2020, the COVID-19 pandemic has spread to more than 200 countries and affected more than three million people. We examine various biomarkers to assess their ability to predict clinical outcomes and are associated with the severity of COVID-19 disease.

Methods: A systematic literature review was conducted to identify related articles using six different databases. The keywords used to refine the search contained 'COVID-19', 'SARS-CoV2', 'Biomarkers', among others. Only studies that reported data for predefined outcomes were included. Key findings: This review describes different classes of biomarkers- immunological, inflammatory, coagulation, hematological, cardiac, and biochemical, in terms of pathophysiological evidence, followed by current evidence.

Result: Thirty-four related articles were identified and examined for the following biomarkers: C-reactive protein, serum amyloid A, interleukin-6, lactate dehydrogenase, neutrophil-to-lymphocyte ratio, D-dimer, cardiac troponin, renal biomarkers, lymphocytes and platelet count. All but two of these displayed significantly higher levels in patients with serious complications of COVID-19 infection compared to non-serious patients. Lymphocytes and platelet count displayed remarkably lower levels in serious patients compared to non-serious patients.

Conclusion: the research to date shows there is clear evidence that biomarker levels can vary depending on the severity of COVID-19 infection. It can be used as an adjunct to clinical practice to guide the treatment and hospitalization of the ICU. This improves prognosis and minimizes mortality. However, since we are in the infancy stages of understanding the pathology of this infectious disease, we call for more research worldwide to better understand the changes mentioned in this review.

Keywords: SARS-CoV-2, COVID-19, Biomarkers, Lymphocytes

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MEDICAL SCIENCES

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Effect of pretreatment silymarin on ethanol-induced apoptosis in rat

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Page | 105

Introduction: For a long time silymarin, as the main ingredient of the plant milk thistle, has been used for the treatment of gastrointestinal and nervous system disorders. Moreover, it has been shown that ethanol impairs nervous system function and causes apoptosis. The aim of present study was to investigate the effect of pretreatment silymarin on the ethanol-induced apoptosis in rat.

Methods: Twenty-eight rats (n= 7 in each group) was used in four groups (saline, silymarin, ethanol. and silymarin+ethanol). Silymarin (200 mg/kg was administered using gavage for 30 consecutive days. Ethanol (2mg/kg/i.p.) was injected for 30 days. Bcl2, Bax and caspase were used as apoptotic markers were measured using Western blotting.

Results: Bcl2/Bax ratio was increased and decreased in silymarin and ethanol group, respectively, compared to control group ($p<0.001$ and $p<0.001$), however, caspase was decreased and increased in silymarin. and ethanol group, respectively, compared to ethanol group ($p<0.001$). Moreover, Bcl2/Bax ratio in silymarin+ ethanol co-administered group was increased compared to ethanol group ($p<0.01$), Moreover, caspase in silymarin + ethanol co-administered group was decreased compared to ethanol group ($p<0.001$). Data analyses were made using one-way analysis of variance at the significant level of $p<0.5$.

Conclusion: Pretreatment silymarin prevents ethanol-induced apoptosis in rat and demonstrates anti-apoptoic properties.

Keywords: Silymarin, Alcohol, Apoptosis, Rat

Investigation of DNA disorders on sperm morphology and infertility in men

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Abstract: Infertility is a problem that affects an increasing number of couples in the world, and since sperm morphology is the most relevant parameter in routine semen analysis to predict fertilization potential and has a potential impact on sperm function, in particular, the factors affecting it are necessary. One of the factors that can affect sperm morphology is DNA damage. Although the exact relationship between DNA fragmentation and sperm morphology has not yet been determined, but research has shown that abnormal sperm morphology is associated with a decrease in normal semen parameters as well as symptoms of sperm damage such as DNA fragmentation.

Method: About 20 articles from PubMed, Open Knowledge Map and Google Scholar sources were analyzed in detail. Result it showed avery significant difference in the telomere distribution pattern of the sperm nucleus of control and infertile groups. globozoospermia without acrosome and with low density chromatin has a positive correlation with the occurrence of small halo and high DFI in SCD test. A strong interaction between sperm chromatin quality and DNA damage has been shown.

Conclusion: The number of telomere signals in the sperm nucleus of infertile men is increased compared to normal men, which causes increased DNA damage and increased nuclear vacuoles, and finally causes abnormal morphology. It was also observed in patients with varicocele that SDF increased in them, which causes a decrease in progressive motility and an increase in sperm concentration. DNA fragmentation is associated with apoptosis, mitochondrial membrane dysfunction, or failure to repair DNA double-strand breaks, which Finally, high DFI in sperm caused by endogenous and exogenous factors includes decreasing the quality of motility - decreasing the number and viability and finally decreasing the normal morphology of sperm. Above, increased DNA damage causes changes in sperm morphology and ultimately infertility.

Keywords: sperm, infertility, DNA damage, oxygen radicals

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Downregulation of miR-1236 predicts poor survival in ovarian cancer patients and correlates with lymphangiogenesis and its corresponding mediators

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Page | 107

Introduction: Lymphangiogenesis is a critical component in cancer progression and miR-1236 have been reported to be implicated in this process. However, the prognostic importance of miR-1236 and its clinical relevance with lymphangiogenesis in ovarian cancer (OC) remains unclear.

Methods: Tumor tissue of 52 patients with OC and 28 normal ovary tissues were analysed for miR-1236, VEGFR3, VEGF-C, LYVE–1 and PROX1 expression by Real-time PCR. VEGFR3 protein expression and lymphatic vessel density (LVD) was also examined using IHC technique. Overall survival (OS) was analysed by Kaplan-Meier method.

Results: MiR-1236 expression was significantly decreased in ovarian tumors compared to normal tissues (P < 0.001) and correlated with advanced clinical stage, lymph node metastasis, distant metastasis, and patient's survival (All P < 0.05). Moreover, in ovarian tumors, LVD (P = 0.007) as well as VEGFR3 (P = 0.029), VEGF-C (P = 0.001), and LYVE–1 (P = 0.013) gene expression, but not PROX1 (P = 0.368), were found to be remarkably higher compared with normal tissues. We also observed that the proportion of tissues which stained strongly for VEGFR3 was significantly higher in OC tissues than normal tissues (P = 0.040). Furthermore, our results demonstrated an inverse association between miR-1236 expression with LVD, VEGFR3, LYVE-1, and PROX1 expression in OC tissues. The receiver operating characteristic curve analysis revealed that miR-1236 has the potential to be used as prognostic biomarker in OC. Survival analysis further verified a lowered OS rate in patients with low miR-1236 expression, and we indicated that miR-1236 was an independent predictor of poor prognosis in OC patients.

Conclusion: Our results provide evidence for translational involvement of miR-1236 in lymphangiogenesis of OC by regulating lymphangiogenesis-related mediators and support the clinical importance of miR-1236 as a new diagnostic and prognostic biomarker for OC.

Keywords: Ovarian cancer, lymphangiogenesis, miR-1236, VEGFR3, VEGF-C.

A-10-1026-1

Evaluation and comparing of hepatic enzymes activities and inflammatory biomarkers levels in COVID-19 patients

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Introduction: COVID-19 is a threat to public health and a pandemic outbreak of acute disease over the world. COVID-19 may induce various degrees of liver injury. Liver function tests contained alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP) and total bilirubin (TBili). C Reactive Protein (CRP) and Interleukin (IL-6) are inflammatory biomarkers that indicate infection with pathogen. In this study, we assessed the hepatic enzyme activities in patients with COVID-19 positive tests for knowing more about the pathogenesis of liver disease and to better control liver damage in patients with COVID-19.
Method: The present study comprised 120 patients diagnosed with COVID-19 with PCR positive tests. Some patients had symptoms including, fever, cough, sore throat, and shortness of breath. Serums were collected from patients, liver enzyme tests (LFT) including (ALT), (AST), alkaline phosphatase (ALP), and (TBIL) and also and inflammatory tests including CRP and IL- 6were analyzed in these patients. For comparing patients with normal and abnormal serum hepatic enzyme activities, we use statistical evaluations. P-value of<0.05 was considered to show statistical significance.
Results: To study the status of patients with abnormal LFT according to inflammatory markers level, we compared CRP and IL-6 in abnormal and normal LFT. The levels of CRP and IL-6 were elevated in patients, but, the levels of CRP and IL-6 in patients with abnormal LFT were significantly higher than those of normal LFT P-value < 0.05.
Conclusion: Our results showed that, TBili is most common and less common ALT and AST and least common ALP abnormality respectively. The levels of inflammatory biomarkers in serums are effectively show disease severity. In summary, abnormal hepatic enzymes are common among COVID-19 patients. Liver damage may be caused by COVID-19 However, we should consider the effect of drugs and duration of receiving drugs on hepatic enzyme activities.

Keywords: COVID-19, Liver function tests, inflammatory biomarkersers

A-10-1809-1

Short- and long-term effect of niosome hesperidin on locomotor activity and muscle strength in depression rats.

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Page | 109

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Introduction: Depression disorder is known as a debilitating condition in the world. Depression can affect locomotor activity function. Hesperidin is a natural antioxidant and Niosome hesperidin is new in Nano ug delivery. This study aims to analyze the short- and long-term effect of niosome hesperidin on locomotor activity in depression rats

Methods: In this study, we used 44 adult male rats. The animals were divided into six groups. The control group received saline for 14 days. The depressed group received reserpine (0.5 mg/kg) for 14 days to induce depression. The treatment group with hesperidin first received reserpine for 14 days to induce depression and then received the antioxidant hesperidin (20 mg/kg) for 14 days. The hesperidin group received hesperidin (20 mg/kg) for 14 days. The niosome hesperidin group received niosome hesperidin (20 mg/kg) for 7 days. The treatment group with niosome first received reserpine for 14 days to induce depression and then received niosome hesperidin (20 mg/kg) for 7 days. The Behavioral tests included the Rota rod test and the Grip strength test was performed on days 7 and 14 to assess locomotor activity and muscle strength.

Result: The results show a significant difference between the groups in both tests so that in the Rota rod test, the amount of locomotor activity in the treatment group with niosome hesperidin group was significantly increased compared to the hesperidin group ($p < 0.05$). In the Grip strength test the muscle strength in the treatment group with niosome hesperidin group was significantly increased compared to the depression group and treatment with hesperidin ($p < 0.05$)

Conclusion: it seems niosome hesperidin treatment in the depressed rats has a positive effect on the neuromuscular junction. Niosome hesperidin as a safe nano carrier can improve the balance and the force of contraction in depressed animals.

Keywords: Key words: Niosome ug delivery, Depression, locomotion, muscle strength

A-10-1802-1

Cytotoxic evaluation of chitosan-coated Fe3O4 nanocarriers in conjugation with opium alkaloids

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Introduction: Magnetic nanoparticles (MNPs) especially Superparamagnetic Iron Oxide Nanoparticles (SPIONs) known as nano theranostics have been widely used for therapeutic and diagnostic applications. Modification of the MNP surface with polymeric materials such as chitosan not only prevents from oxidation but also provides a site for ug linkage which render them as a great ug carrier. This study was conducted to evaluate the cytotoxic activity of papaverine/noscapine (non-narcotic opium alkaloids) nanocarriers against 4T1 murine breast cancer cells

Methods: In our preliminary study, we synthesized and characterized noscapine/papaverine loaded on chitosan functionalized SPIONs. The nanoformulations with acceptable pharmaceutical properties were considered for further evaluation. To study the cytotoxicity of the developed formulations, MTT and colony-forming assays were applied. Flowcytometric analysis (Annexin V/PI double staining and ROS production) was performed to get a deeper insight into the mechanism of inhibitory activity.

Results: Our result showed that the delivery system was in favor of papaverine and could effectively augment its anticancer activity against 4T1 breast cancer cells in comparison with the free ug. Notably, its cytotoxicity was around 12 folds more potent relative to non-malignant L929 cells. However, noscapine-MNPs were prone to agglomeration in serum-containing medium resulting in low cellular uptake. In the long-term cytotoxicity assay, both tested formulations were able to attenuate the colony numbers. Moreover, late apoptotic/necrotic cell death was most likely induced by ROS generation.

Conclusion: Our results propose papaverine-MNPs as a biocompatible nanotherapeutic carrier to control metastatic breast cancer cells.

Keywords: Breast cancer, Cytotoxicity, ug delivery, Noscapine, Papaverine, Magnetic nanoparticles

A-10-1976-1

Designing a Humanized Immunotoxin Based on HER2 Specific scFv and DFF40 Toxin Against Breast Cancer: An in-Silico Study

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Page | 111

Introduction: Breast cancer is the most frequent cancer in women worldwide. Human epidermal growth factor receptor 2 (HER2) is a receptor that is overexpressed in breast cancer cells. Targeting this receptor could be a key factor in the treatment of breast cancer patients. Herceptin is an antibody that can bind to the HER2 receptors, in addition, Herceptin-derived single chain fragment V(scFv) can be used in designing immunotoxins for targeting HER2 positive cancer cells. DFF40 is a nuclease activated by caspase-3 and is responsible for genomic DNA fragmentation during apoptosis.

Methods: In this study, we used bioinformatics tools to design an immunotoxin containing HER2-specific scFv and DFF40 toxin. An immunotoxin construct was designed by linking scFv and DFF40 amino acids sequence via a peptide linker. The secondary structure, physicochemical features, solubility, and allergenicity of the construct were predicted. The tertiary structure was built, refined, and evaluated. Protein-protein docking and molecular dynamics studies were carried out to evaluation of immunotoxin-receptor binding, and the stability of the immunotoxin, respectively.

Results: The results indicated that the designed construct could be a stable protein with appropriate solubility, which is not an allergen and has a suitable structure that can bind to HER2 appropriately.

Conclusion: This construct could be a promising candidate for producing a HER2 targeting immunotoxin. However, different in vitro and in vivo immunological assays should be performed to confirm the efficacy of the designed construct.

Keywords: Breast cancer · Bioinformatics · Her2 · Immunotoxin · DFF40 · Herceptin

A-10-1085-1

Effects of Hydroxytyrosol on the expression of miR-21, MMP-2 and MMP-9 in HepG2 cell line

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Introduction: Hepatocellular carcinoma (HCC), one of the most common types of cancer in the world, accounts for almost 90% of all primary liver malignancies. Most cancer-related deaths are affected by the invasion and migration of cancer cells to other organs. Hydroxytyrosol (HT) is a natural polyphenol compound that has numerous activities, such as the ability to inhibit metastasis by the regulation of microRNAs and the genes associated with the invasion of cancer cells. Therefore, this study aimed to investigate the effect of HT on the expression of microRNA-21 (miR-21) and matrix metalloproteinase-2, 9 (MMP-2, 9), in HepG2 cells.

Methods: In the current study, the human hepatocellular carcinoma cell line HepG2 was treated with different concentrations (50, 100, and 150 µM) of HT for 24 hours. The expression levels of miR-21, MMP-2, and MMP-9 were determined by RT-qPCR. Additionally, Pearson's correlation test examined the correlations between gene expressions.

Results: The results showed that HT significantly downregulated miR-21, MMP-2, and MMP-9, in different treatment groups than the control group. Pearson's correlation analysis showed that the expression of miR-21 was directly related to the expression of MMP-2.

Conclusion: Our findings suggested that HT probably plays a critical role in the inhibition of HCC metastasis by downregulating miR-21, MMP-2, and MMP-9. So, we concluded that hydroxytyrosol could be helpful in preventing the proliferation of cancer cells.

Keywords: Hepatocellular Carcinoma, Metastasis, hydroxytyrosol, microRNA-21, Matrix Metalloproteinase

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In vitro evidence for Anti-proliferative and proapoptotic effects of postbiotics from Lactobacillus spp. on colorectal cancer cells: A systematic review

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Introduction: As is well known, colorectal cancer (CRC) is considered a leading cause of cancer death globally. Postbiotics are microbial metabolites with beneficial activities. Research in the field of postbiotics has gained more attention due to their antiproliferative and proapoptotic effects on cancerous cells which can be accounted as a promising strategy for dealing with the problems of patients with CRC.

Methods: In the current systematic review, Medline (PubMed), ScienceDirect, Scopus, and Google Scholar databases were examined for the English language articles until April 2022 using "postbiotics", "Lactobacillus", "colorectal cancer", "anti-proliferative", "cell free supernatant", "parabiotic" and "apoptosis" keywords. The inclusion criteria were in vitro investigations utilizing Caco-2, HT-29, HCT-116, DLD-1, HRT-18, SW-480, and RKO cell lines aiming to highlight the anti-proliferative and proapoptotic effects of postbiotics from lactobacillus strains.

Results: In total, 28 articles were included. The results of these works revealed that postbiotics (including cell-free supernatant or CFS, sonicated-cell suspension, heat-killed cells, inactivated cells, cell-wall protein, short-chain fatty acids, and exopolysaccharide) derived from Lactobacillus spp. (including L. casei, L. rhamnosus, L. paracasei, L. acidophilus, L. plantarum, L. fermentum, L. ruteri, L. brevis, L. pentosus, L. lactis and L. delbrueckii) could significantly inhibit the growth of colorectal cancer cells by inactivation of wnt/β-catenin signaling pathway, redusing matrix metalloproteinase (MMP)-9 and downregulagion of NF-kB-dependent genes. They can also induce cell cycle arrest (G0/G1 phase) and apoptosis by increasing the expression of proapoptotic genes (Bax, Bak and Caspase-3) and decreasing the expression of anti-apoptotic genes (Bcl-2, Bcl-xL and Survivin) in CRC cell lines.

Conclusion: Overall, postbiotics derived from Lactobacillus spp. can be used as promising tools in supportive therapy and improving the treatment efficiency of CRC patients, due to their efficacy in inhibition of proliferation in colorectal cancer cells.

Keywords: Postbiotics, Lactobacillus, Colorectal cancer, Apoptosis, Proliferation, Cancer therapy

A-10-1121-2

Single nucleotide polymorphism of PERK gene is associated with colorectal cancer

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Introduction: Single nucleotide polymorphisms (SNPs) are one of the critical genetic factors that involve in cancer initiation and progression. Several studies have examined their association with numerous human cancer types. The present study examined one SNP of PERK gene related to the UPR-signaling, one of the most critical pathways in cancer. The primary aim of this study was to investigate the association of rs13045 with colorectal cancer (CRC) risk.

Methods: In the present study, 64 patients (34 men and 30 women) with colorectal cancer as a case group, and 60 patients (31 men and 29 women) as a control group were included. Following DNA extraction and quantitative and qualitative control by the Nanodrop method and Real-time PCR, respectively, the genotypes of the samples were analyzed using high resolution melting (HRM). Finally, all the data were statistically analyzed with SPSS.

Results: Our results and statistical analysis showed a significant relationship between the T/T genotype of PERK rs13045 and susceptibility to CRC. This genotype may protect against CRC. Meanwhile, the frequency of T/C genotypes of PERK rs13045 varied significantly among the two groups. As a significant risk factor, this genotype may positively affect the incidence of CRC based on their odds ratio of over one.

Conclusion: Based on the findings of this study, the T/T genotype of PERK may be associated with a reduced risk of CRC. Contrary to this genotype, the T/C genotype of PERK seems to be related to an increased risk of CRC.

Keywords: Colorectal cancer, SNP, ER stress, UPR signaling, PERK, HRM

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Cloning and Purification of RBD and Fusion Protein of GFP/RBD in Prokaryotic Host

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Introduction: The COVID-19 has outspread all over the world as a serious pandemic which is caused by SARS-CoV-2. The expression of RBD in E. coli, which has four disulfide bounds, is an effective approach to find anti-covid therapeutics due to its economic efficiency and applicability.
Methods: The DNA coding of the 6xHis-tag-RBD fusion protein and GFP were cloned into Pet28a. Both constructs were transformed into competent cells. LB broth media were prepared and 0.2 mL of the stocks and kanamycin were added to it and was grown at 38 °C for 16 h. The culture was added to 50 mL fresh 2xyt media . Then IPTG was added. The culture was cooled on ice for 15 min and centrifugated. The cell pellet from each 50 ml culture was resuspended in 0.5 ml of lysis buffer. The suspended pellet was sonicated then centrifuge. Pellet and supernatant were run on acrylamide gel. The Pellet portion after the last centrifugation resuspended in lysis buffer and then urea added to it.
Results: The construct evaluation performs with sanger sequencing and enzymatic digestion. GFP was cloned at the N-terminal of RBD and both constructs had His-tag at their N-terminals. Constructs were transformed into BL21 competent cells. Expression induction was accomplished at the final IPTG concentration. Expression evaluation was performed with SDS PAGE and protein bands was seen on gel at 31 kDa for RBD and 52 kDa for fusion protein.
Conclusion: Founding better solutions for bacterial expression in E. coli with higher yield and correct conformation is an important issue for further studies on covid-19 treatments. In this research, we try to express and purified RBD and fusion of GFP/RBD for future investigations. Our aim is selection of a peptide that can interact with RBD and inhibit interaction between RBD and ACE2

Keywords: SARS-CoV-2, E. coli, RBD, Chromatography, IPTG

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Evaluation of serum levels of lactate dehydrogenase (LDH) and creatine phosphokinase (CPK) in patients with COVID19

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Page | 116

Introduction: Coronavirus is one of the viruses that play an important role in causing respiratory diseases. Covid disease is one of the most important viral diseases in the current decade, which has created a widespread pandemic in the world. This disease was first reported on December 8, 2017 in Wuhan, China, from patients with severe pneumonia. On January 8, 2017, the Centers for Disease Control and Prevention in China identified the virus.

Methods: The present study is a descriptive cross-sectional study. In this study, the initial diagnosis of COVID19 was first made by the treating physicians and after the final diagnosis, they were selected for the present study. A total of 500 patients were studied. The present study was a blood serum that was prepared immediately after blood sampling using a centrifuge. A biochemical autoanalyzer was used to perform the present study.

Results: In the present study, 323 cases (64.6%) increased lactate dehydrogenase and 254 (50.8%) increased creatine phosphokinase was observed.

Conclusion: The results of the present study show that COVID19 virus with its effect on various tissues and organs can increase the serum level of some metabolites and enzymes in the body, so further study on the pathogenic mechanism of this virus is necessary

Keywords: Pathogenicity, virus, lactate dehydrogenase, creatine phosphokinase

A-10-1185-1

Crocin and Metastasis Prevention

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Introduction: Crocus sativusL. (saffron), a spice and food colorant, was prescribe as a remedy for various maladies four millennia ago. In the last three decades, it has been discovered that the anti-primary tumor propertiesof crocin, the main carotenoid of saffron, are associated with induction of apoptosis by enhancing the Bax/Bcl-2 ratio and blocking the G2/M and G1 phases of the cell cycle. Despite the fact that metastasis is the leading cause of deaths in cancer patients, the anti-metastatic potential of crocin has been surveyed only this decade. We aim to evaluate the anti-metastatic property of crocin and the mechanisms underlying these effects.

Methods: Researches were identified through a systematic review of the literature published in English. We included all cell and animal studies that assessed the effect of crocin on different types of cancers. We tested the main hypothesis that crocin therapyis associated with lower chance of metastasis and the secondary hypothesis that crocin exerts its effect on various cancersvia different mechanisms.

Results: Investigations on breast, gastric, prostate, colorectal, melanoma and osteosarcoma cancers revealed the anti-migratory, anti-invasion, anti-angiogenic potentials of crocin treatment, as well as its effects suppressing cell-ECM adhesion and enhancing cell-cell attachment. Crocin exertsits impact through different mechanisms such as reduction of CD34 and suppression of Wnt/β-catenin, Ras/ERK, DCLK1, EMT, matrix metalloproteinases and urokinases, and enhancement of cleaved caspase-3 and caspase-8. Crocin displayed more effective anti-metastatic potency, in comparison with saffron extract and crocetin.

Conclusion: The bioaccessibility/bioavailability, nontoxicity on noncancerous cells, confirmed anti-tumor efficacy and the recent evidence on the anti-metastatic potential of crocin, nominatesit as a propitious multipotent herbal component.

Keywords: Crocin, Anti-invasion, Anti-migration, Anti-angiogenesis, Mechanism

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A-10-1026-2

The relationships of inflammation markers and antibody levels in COVID-19 positive patients requiring hospitalization, as compared to those not requiring hospitalization patients

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Introduction: COVID-19 has caused a pandemic of respiratory illness and rising the mortality of death. In most patient with positive test of COVID-19 regardless of signs of disease, changing in serum inflammatory markers including interleukin-6(IL-6), ESR, hs-C reactive protein hs-CRP, ferritin, and also immunoglobulin G (IgG), and immunoglobulin M (IgM) are seen. our aim was to compare these markers in healthy, not equiring hospitalization, and hospitalized subjects.
Methods: Three group were selected: healthy, not requiring hospitalization, and hospitalized patient. The level markers of (IL-6), ESR, hs-CRP, ferritin, and also (IgG), and (IgM) were measured. For comparing the markers in three groups, we use statistical evaluations. P value of<0.05 was considered to show statistical significance.
Results: Median IL-6, hs-CRP, ESR, ferritin (IgG), and (IgM) levels in not requiring hospitalization were increased but not significantly compare to control. the markers levels in hospitalized pateint were significantly higher than control group and also significantly higher than not requiring hospitalization.
Conclusion: Our goal of our studies was to search about the relationships of inflammation markers and antibody levels in COVID-19 positive patients requiring hospitalization, as compared to such subjects not requiring hospitalization, in order to develop a risk algorithm for need for hospitalization. The highest median inflammatory marker hs-CRP, IL-6, ferritin, ESR levels, and the highest median IgG, IgM, levels were noted in hospitalized COVID-19 patients. We also noted a high degree of variability in IgG response. The inflammatory markers are associated with an exaggerated immune response along with markedly elevated blood levels of white blood cells associated with a high COVID-19 mortality. According to obtained data, the levels of inflammatory biomarkers in serums are effectively show disease severity. Antibody testing may be useful for documenting exposure and potential immunity, as well as for case finding in family and exposed individuals

Keywords: COVID-19, inflammation markers, antibody

A-10-1025-1

Pharmaceutical induction of Beta cell regeneration in Type 1 diabetes, an alternative or a supportive treatment for pancreas transplantation

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Page | 119

Introduction: type 1 diabetes (T1D) is a result of autoimmune-mediated destruction of beta cells Insulin therapy; pancreas transplantation and beta cell regeneration are some of the treatment strategies. In transplant or regenerated beta cells strategies, protecting replaced beta cells from the immune system could be one of the contingent challenges.

Methods: in this study, normal and Streptozotocin-induced diabetic mice (n=20) were treated with magainin (Mag). Fasting blood sugar (FBS) and glucose tolerance test (GTT) were measured. The pancreases of mice were then removed for western blot and histopathology experiments to evaluate beta cell regeneration and differentiation.

Results: in this treatment, the islet size and cell counts were increased in both normal and diabetic Mag treated (N-Mag, D-Mag) mice. FBS and GTT results, and also the no. of insulin + cells per islet among treated mice, were improved. These data were accompanied by 143% and 221% higher expressions of paired box 4 (PAX4), one of the main factors for α to β cell trans-differentiation among N-Mag and D-Mag mice, respectively. Also among D-Mag mice, the expression of P-ERK and P-S6 respectively increased by 162% and 245%. Interestingly total immune T and B cells (CD3+ and CD19+ pixel count) were reduced by more than 33 percent in D-Mag mice.

Conclusion: if Mag's effects on beta cell regeneration and suppressing the immune system could be potentiated by Mag, it could be considered as an alternative treatment for pancreas transplantation or insulin therapy pending extension of the study to the clinical level.

Keywords: β-cell regeneration, trans-differentiation, proliferation, immune system

A-10-1168-1

Investigating the Association of LncRNA HULC Gene G^A rs17144343 Polymorphism with Susceptibility to Recurrent Spontaneous Miscarriage in Eastern Azerbaijan of Iran

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Introduction: Abortion refers to the termination of pregnancy before the twentieth week, which is the most common complication in the first and second trimesters of pregnancy. Women who experience more than two miscarriages suffer from Recurrent Spontaneous Abortion. The incidence of RPL is about 1% to 5% among couples. The LncRNA-HULC gene with a length of 1638 pb on chromosome 6p24.3 was first discovered in 2007 as a non-coding RNA with very important settings in Hepatocellular carcinoma. This study investigates the association of single nucleotide polymorphism of rs17144343 G>A in HULC gene with susceptibility to recurrent miscarriages.

Methods: In this case-control study, 150 patients and 150 healthy individuals were genotyped. DNA was extracted from the peripheral blood of individuals by salting-out method and the polymorphism of rs17144343 in HULC gene was assessed by TETRA-ARMS-PCR. Finally, the genotyping data were statistically analyzed using the software package javastat online statistics (www.statpages .info/ctab2x2.html) and SPSS version 23.

Results: The genotypic distribution of rs17144343 Single-nucleotide polymorphism in cases was 24.7% and 75.3% for GA and GG genotypes, respectively. In the control group, 2% and 98% of individuals showed GA and GG genotypes, respectively. The frequency of allele A in controls was 1% and in case individuals was 12.4%. Statistical analysis of the genotyping results, showed a significant relationship between the risk of recurrent miscarriage and rs17144343 polymorphism of HULC gene (P=0.000). Also, investigating the relationship between rs17144343 polymorphism and some clinical and pathological characteristics has revealed a significant relationship between genotypes and the familial relationship of the couple's parents (P=0.003).

Conclusion: The results obtained in his study suggests that HULC might have a role in susceptibility to recurrent spontaneous abortion, but larger sample studies are needed to verify this finding further.

Keywords: Recurrent Spontaneous Abortion, LncRNA, HULC gene, rs17144343 Single-nucleotide polymorphism.

A-10-1209-1

Synthesis of a novel nanocomposite containing chitosan as a three-dimensional printed wound dressing technique: Emphasis on gene expression

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Introduction: Ahighly porous three-dimensional (3D) -printed wound healing core / shell scaffold fabricated using poly-lactic acid (PLA). The core of scaffold was composed of hyaluronic acid (HA), copper carbon dots (Cu-CDs), rosmarinic acid, and chitosan hydrogel.

Methods: Carbonate-copper, poly lactic acid, hyaluronic acid/chitosan, rosemary acid scaffolds were prepared and tests such as FE-SEM EDSMAP, DLS, FTIR, and XPS were fabricated for bionanocomposite fabrication. Antibacterial effect, biocompatibility and scaffold wound healing efficiency using MIC and DDM test, MTT assay, tissueanalysis and Real-Time PCR to determine the relative expression of PDGF, TGF-β and MMP-1genes.

Results: Formulation containing 1 mg ml – 1concentration of Cu-CDs showed an excellent antibacterial activity against gram bacteria. At 0.25 mg ml – 1 of Cu-CDs concentration, scaffold had a good biocompatibility as confirmed by cytotoxicity assay on L929 fibroblast stem cells. In vivo wound healing experiments on groups of rats revealed that after 15 days of treatment, the optimal formulation of composite scaffold significantly improves the wound healing process compared to the PLA scaffold. This finding was confirmed by histological analysis and the relative expression of PDGF, TGF-β, and MMP-1 genes.

Conclusion: Rosemary acid, Chitosan, Hyaluronic Acid, Polylactic Acid,Cu. Cund scaffold that greatlDs Nanocomposite is a biocompatible antibacterial woy accelerates the skin regeneration process

Keywords: Dot-copper carbon, Chitosan, 3D printing, Wound healing, , Polylactic acid, Gene expression

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A-10-1256-3

Physicochemical Properties of Polyomaviruses

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Introduction: Members of the Polyomaviridae family share the same general genomic composition as similar virion structures. Virions of polyomaviruses are nonenveloped, icosahedral particles composed of 360 copies of the predominant structural protein, VP1, and 30–60 copies of the minor structural proteins, VP2 and VP3. Virions of polyomaviruses are nonenveloped, icosahedral particles composed of 360 copies of the predominant structural protein, VP1, and 30–60 copies of the minor structural proteins, VP2 and VP3. These molecules form 72 pentamer capsomeres arranged in a distorted (T = 7d) lattice. Each capsomere consists of five copies of VP1 and one copy of VP2 or VP3, each added to an internal cavity formed by the binding of five VP1 molecules.

Methods: During virion assembly, errors sometimes occur and unstable capsid structures (such as hollow particles, microcapsules, and tubular structures) are produced. When the VP1 DNA sequence of human polyomavirus (JCV) or BK virus (BKV) is inserted into a baculovirus plasmid vector and expressed in insect cells as a recombinant gene, the pentamers form capsomeres like virions.

Results: When these pentameric capsomere-like structures are purified and placed in a solution of physiological pH and ionic strength including Ca2 + ions, direct self-assembly of the pentamer to the genome-free virion happens. The formed capsids, called virion-like particles (VLPs), have the size of native virions, icosahedron symmetry, and antigenicity. VLP production has been put into practical use. JCV or BKVVLP have been used in enzyme immunoassays (EIA) to measure the titers of JCV or BKV-specific antibodies induced by infection with these viruses.

Conclusion: Due to the high sensitivity, specificity, and safety of these genome-free VLPs, their use in EIA has largely replaced the hemagglutination assay as the preferred method for measuring levels of JCV or BKV-specific antibodies.

Keywords: Polyomaviridae, polyomaviruses, capsomere, virion-like particles (VLPs)

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The Effect of Hydroalcoholic Extract of Ferulago angulata on Liver Function Parameters and Antioxidant Status in Alloxan-Induced Diabetic Rats

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Page | 123

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Introduction: The aim of this study was to evaluate the hepatoprotective and antioxidant activities of Ferulago angulata Extract (FAE) in experimental diabetic rats.

Methods: 54 adult male Wistar rats divided into 6 groups (n=9). Diabetes was induced in all animals except those in group 1 by the daily intraperitoneal injection of 120 mg/kg. alloxan monohydrate for 3 consecutive days. Experimental diabetic rats in groups 3-5 were orally administered with FAE (200,400, and 800 mg/kg/day, respectively). Group 6 was treated with 150 mg/kg of metformin. At the end of week 4, the rats were anesthetized and then sacrificed by cardiac puncture. Then, the levels of liver markers, malondialdehyde (MDA), and antioxidant enzymes capacity were evaluated in each group.

Results: Treatment with FAE resulted in a significant reduction in aspartate transaminase (AST) and alanine transaminase (ALT) activities as well as in the serum and liver tissue contents of MDA in comparison to the diabetic control group (P<0.001). The FAE-treated diabetic rats showed a significant increase in catalase, glutathione peroxidase (GPx), and super oxide dismutase (SOD) activities of the liver (P-values were dose-dependent). Furthermore, the extract has an ameliorative effect on the histopathological changes of the liver in alloxan induced diabetes.

Conclusions: These findings suggest that FAE can reduce the complications of diabetes, prevent oxidative stress, and improve antioxidant status in diabetic rats.

Keywords: Keywords: Ferulago angulata, antioxidant, oxidative stress, diabetes mellitus.

A-10-1065-2

Association between the VDR Taq1 polymorphism and susceptibility to systemic sclerosis

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Page | 124

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Introduction: Vitamin D with its immunomodulatory effect has newly been proposed as an important factor in the pathogenesis of systemic sclerosis (SSc). This immunomodulatory function is mediated through binding to vitamin D receptor (VDR). Therefore, genetic variations in VDR gene may play a role in etiology of SSc. The aim of this study was to explore the association between VDR Taq1 polymorphism and the risk of SSc disease in an Iranian population.

Methods: The polymerase chain reaction and restriction fragment length polymorphism (PCR-RFLP) was used to detect the genotype of VDR Taq1 variant in 51 SSc patients and 50 healthy controls. The difference of genotype distribution between two groups was analyzed using Chi-square test. Logistic regression analysis was also performed to calculate the genotypes odds ratios (ORs) as a measure of association with the presence of SSc.

Results: The allelic frequency of VDR gene Taq1 variant in whole population and also in studied groups was in the Hardy-Weinberg equilibrium. The genotype and allele frequencies of the Taq1 polymorphism exhibited no significant differences between SSc patients and healthy controls neither in the crud state nor after adjustment for age and gender (odds ratio: 1.09 (CI = 0.91–1.32), P = 0.313).

Conclusion: Results of the present study suggested that TaqI polymorphism may not contribute in the development of SSc in an Iranian population. However, regarding the controversial reports for Taq1 association with the risk of SSc in different ethnic population, further large cohort studies are necessary to confirm the results.

Keywords: Keywords: Systemic sclerosis, Vitamin D receptor, Polymorphism, Taq1

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MiRNA125b regulate sphingosine 1 phosphate lyase 1 expression in human lung fibroblast cells

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Page | 125

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Introduction: Remodeling of fibroblasts into myofibroblasts is a phenomenon that play important role in bronchial disease such as asthma. It seems that sphingosine 1 phosphate (S1P) has prominent role in the pathogenesis of bronchial disease, by stimulation of the alpha-smooth muscle actin (SMA) expression in a human lung fibroblast cells which has important role in remodeling of fibroblasts. It has been demonstrated that interaction of miRNAs and target genes, involved in S1P synthesis, regulate S1P metabolism pathway. In present study the effect of micro RNA 125b in regulation of S1P metabolism pathway in human lung fibroblast cell line evaluated.

Methods: At the first human lung fibroblast cell line (CIRC-HLF), C580 was obtained and cultured in 6 well plate and then transfection of the fibroblast cells was carried out using transfection agent, Lipofectamine 2000 kit with lentiviruses containing miR 125b vectors. The expression level of miR125b and its target gene sphingosine-1-phosphate lyase 1(SGPL1) were then evaluated in transfected cells against scramble, as negative control, using reverse transcription-quantitative polymerase chain reaction (qPCR) method.

Result: These techniques revealed that the miRNA125b significantly overexpressed in transfected cells against scramble ($p < 0.05$). Furthermore, it was showed that miRNAs targeted gene, SGPL1, expression significantly downregulated in transfected fibroblast cells against scramble as negative control ($p < 0.05$).

Conclusion: These data provided strong evidence that miR 125b may be involved in the S1P metabolism pathway in lung fibroblast cell by down-regulating SGPL1 gene.

Keywords: fibroblast, micro RNA, sphingosine 1 phosphate, SMA, SGPL1

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A-10-1745-1

A protocol for DNA extraction from first void urine sample and the effect of the preservative buffer on urine sample

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Page | 126

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Introduction: Urine is a useful source of cfDNA which is used for biomarker discovery and diagnose a few illnesses such as colorectal cancer. As a result, scientists are eager to make use of urine to detect illnesses. A major limitation of urine samples is that they are only stable for 2-6 hours at room temperature and urine sample commonly turns cloudy when it left at room temperature without preservatives. The aim of this study is to design a buffer that preserves urine sample for a long time, for the first time in Iran.

Methods: This case-control study was performed at Hamava Innovation Factory in Tehran, Iran. First void urine samples were collected from 10 healthy volunteers, 5 men and 5 women, in a completely clean (sterile) container. The next step is to added as a ratio of 1-part buffer to 2 parts urine sample and storage samples at room temperature for three time periods (1, 2, 7 days). Then based on four preservative buffers, urine samples were analyzed and DNA yield determined. These four preservative buffers contain EDTA, amphotericin B, vancomycin, penicillin streptomycin, and gentamicin.

Result: Following the storage of the samples in special buffers for a week, the culture and staining tests on these samples showed no bacteria or fungi present in them. Also, we found a significant difference in the quantity of DNA isolated in urine samples with or without preservative buffer.

Conclusion: Growing the stability of the samples with these buffers has led to the conservation of urine sample, which provide rapid viral detection and describe methodology that allows urine to be collected by patients at home and then posted to a laboratory for analysis.

Keywords: cfDNA, colorectal cancer, urine preservatory buffer, EDTA.

A-10-1238-1

In Silico evaluation of Allicin (diallylthiosulfinate) as potential COVID-19 main protease inhibitor

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Introduction: Allicin (diallylthiosulfinate) is one of the main active compounds derived from garlic. It may help prevent certain cancers and may help lower blood sugar, cholesterol, and blood pressure. COVID-19 main protease (Mpro) is a key enzyme of coronaviruses and has a pivotal role in mediating viral replication and transcription, making it an attractive drug target for COVID-19. The purpose of this research was to investigate inhibitory effect of Allicin, on the α-glucosidase activity using in silico tools.

Methods: the in silico molecular docking approach was carried out for Allicin against the active site region of COVID-19 Main Protease. The docking study was carried out by using the AutoDock 4.2 program. A dataset of the target compound was sketched using ChemDraw Ultra 7.0, then converted to pdb format using DS Visualizer 3.5. The X-ray crystal structures of the target enzymes were retrieved from the PDB Data Bank. In addition, the energy of the compound was minimized by using HyperChem Professional program. the resulting docking poses were analyzed in AutoDockTools, DS Visualizer 3.5 and GaussView 5.0 software.

Results: Allicin binds to the amino acid HIS163 with the result of 95 conformations in cluster 1. Appropriate interaction has been observed between the amino acids: GLY143, GLU166, THR190, GLN189, PHE140 & HIS164 in the active site of the enzyme and the cocrystal.

Conclusion: Nowadays, molecular docking as an in silico method is very popular in drug discovery researchers, because of its ability to illustrate the interactions between the ligand and its biological targets. Antiviral drugs are the most studied drugs. We hope that with the use of more models in research, plant-based antiviral drugs will be discovered for effective COVID-19 treatment.

Keywords: Allicin, inhibition, COVID-19, Docking, diallylthiosulfinate, Main Protease

A-10-1237-2

Computational studies of the interaction of squalene synthase with tangeretin in order to control cardiovascular disease

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Introduction: Cardiovascular disease is usually associated with a build-up of fatty deposits inside the arteries and an increased risk of blood clots. Squalene synthase is a critical enzyme in the cholesterol biosynthesis pathway. Molecular docking protocols are widely used for predicting the binding affinities for drug design. In current work, our aim was to Computational studies of the interaction of squalene synthase with tangeretin in order to control cardiovascular disease.
Methods: the chemical structures of tangeretin wase designed by HyperChem software and the protein X-ray crystal structure was received from https://www.rcsb.org. For the in silico protein–ligand docking simulation, Auto Dock 4.2 was used. The grid box size was set at 40, 40, and 40 Å for x, y, and z, respectively. The spacing between the grid points was 1.0 Å. The grid centre was set at 17.711, -4.411, and 56.122 Å for x, y, and z, respectively. The Lamarckian Genetic Algorithm (LGA) was chosen to search for the best conformers. During the docking process, a maximum of 100 conformers was considered for ligand. At the end of docking, AutoDockTools, DS Visualizer 3.5 and Ligplot softwares were used to analyze the data.
Results: the studied compound is able to bind to the active site of the enzyme by hydrogen bonding with amino acid Tyr73 and also by hydrophobic bonding with amino acids Tyr73, Phe54, Ser51, Phe288, Met207, Pro292, Cys289, Leu211. Interaction with amino acids Tyr73, Phe54, Leu211, Cys289, Phe288, Pro292 was also observed in the active site of the enzyme with the cocrystal molecule.
Conclusion: the docking study showed that this compound is able to bind the active site of the enzyme. Therefore, these results can be used for further invitro and invivo studies.

Keywords: cardiovascular, inhibition, molecular Docking, squalene synthase, interaction

A-10-1231-1

Molecular docking simulation of anti-diabetic properties of the main active ingredient of turmeric in the inhibition of Alpha-glucosidase

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Page | 129

Introduction: α-D-glucoside glucohydrolase (EC 3.2.1.20) is an exoenzyme. In humans, these enzymes aid digestion of dietary carbohydrates and starches to produce glucose for intestinal absorption, which in turn, leads to increase in blood glucose levels. In this study, the main active ingredient of turmeric, Curcumin, was evaluated as Alpha-glucosidase inhibitor (AGI). Alpha-glucosidase has long been known as an attractive target for antidiabetic drugs.

Methods: Molecular docking is a frequently used method in structure-based rational drug design. In order to investigate the mode of interaction of the compound with Alpha-glucosidase active site, the chemical structures of Curcumin wase designed and optimized using HyperChem Professional program. the protein X-ray crystal structure of Alpha-glucosidase with 3A4A code and Xray diffraction at 1.60 Å resolution was received from the Protein Data Bank and was used as the receptor starting structure. Docking study was performed by AutoDock 4.2 program and the resulting docking poses were analyzed in AutoDockTools, DS Visualizer 3.5 and GaussView 5.0 software.

Results: Binding model and the best docked pose of Curcumin showed 4 hydrogen bonds by ASN350 ASP215 ، APS352 and GLU411 with active site. The favorable interactions with the key amino acid residues at the active site of the enzyme with Crystal are ARG213, AGR442, GLU277, HIS351, APS352, ASP69, HIS112 and ASP215.

Conclusion: The in silico molecular docking study revealed that Curcumin, occupied the same space as Cocrystal with a similar binding mode. These insilico results can thus serve as a template for further studies invitro and invivo.

Keywords: anti-diabetic, inhibition, molecular Docking, Alpha-glucosidase

A-10-1170-2

Palmitate-increased SPHK1 and S1PR1 genes expression ameliorated by chicoric acid in the PBMCs of patients with type 2 diabetes

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Introduction: Type 2 diabetes (T2D) is one of the major public healthcare problems in the world. Sphingosine 1-phosphate (S1P) signaling pathway recognized as a vital regulator of many pathological processes such as T2D. Therefore, targeting S1P signaling pathway could be one of the possible therapeutic approaches for T2D. To this end, the aim of present study was to explore the effects of palmitate and chicoric acid (CA) on S1P signaling pathway genes expression including sphingosine kinase 1 (SPHK1) and sphingosine 1-phosphate receptor 1 (S1PR1) in peripheral blood mononuclear cells (PBMCs) from newly diagnosed patients with T2D.

Methods: Twenty newly diagnosed patients with T2D, aged 40-60 years, were enrolled in the study. Blood samples of all subjects were obtained and PBMCs were isolated. After that, BMCs were treated as follows: control group (untreated, treated with BSA 1 % for 12 h), CA group (treated with 50 μM CA for 6 h), palmitate group (treated with 500 μM palmitate for 12 h), palmitate + CA group (treated with 500 μM palmitate for 12 h and then treated with 50 μM CA for 6 h). Finally, the PBMCs were harvested for evaluation of SPHK1 and S1PR1 genes expression by real-time PCR.

Results: SPHK1 and S1PR1 genes expression significantly increased in palmitate-treated cells ($p < 0.001$). Compared to untreated cells, SPHK1 and S1PR1 genes expression were strongly decreased in PBMCs exposed to CA by 0.24 and 0.68 fold, respectively ($p < 0.001$). Palmitate-increased SPHK1 gene expression is reversely regulated by CA from 2.78 fold to 1.54 ($p < 0.001$). Moreover, increased S1PR1 gene expression induced by palmitate significantly has been restored via CA from 1.80 fold to 1.51 ($p < 0.05$).

Conclusions: These finding reveal that CA would be considered as a potential S1P signaling pathway inhibitor through down regulation of SPHK1 and S1PR1.

Keywords: Type 2 diabetes (T2D), Palmitate, Chicoric acid (CA), Sphingosine kinase 1 (SPHK1), Sphingosine 1-phosphate receptor 1 (S1PR1).

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Increased expression of legumain in peripheral blood mononuclear cells of patients with coronary artery disease and its relationship with severity of coronary artery stenosis

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Introduction: Overexpression of legumain in the peripheral blood mononuclear cells (PBMCs) may be contributed in early stages of atherosclerosis in patients with coronary artery disease (CAD), such as recruitment and activation of monocyte in the vascular lesion.

Methods: The studied population consisted of 100 Iranian individuals who underwent coronary angiography at the Hajar Hospital, affiliated to the Shahrekord University of Medical Sciences, Chaharmahal and Bakhtiari province, Iran. The mRNA level of legumain was measured with Real-time PCR. Student's t-test was carried out to compare the continuous data between the two groups. All data were expressed as mean±standard deviation (SD). $p \leq 0.05$ was considered significant.

Results: Gene expression of legumain was significantly augmented in PBMCs of CAD subjects as compared with NON-CAD subjects ($p \leq 0.05$). As well as, overexpression of legumain was correlated with severity of stenosis of LAD and LM arteries.

Conclusion: Our data indicated the involvement of legumain in the pathogenesis of atherosclerosis. As well as, deregulation of legumain may be contributed in artery stenosis.

Keywords: Legumain, Coronary Artery Disease, Peripheral Blood Mononuclear Cells

A-10-1096-1

Beneficial effects of Biochanin-A on nephropathy in the Kidneys of Type 1 Diabetic Rats

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Page | 132

Introduction: Diabetic nephropathy (DN) is one of the most prevalent complication of long term diabetes. Biochanin-A (BCA) as a phytochemical has beneficial effects on human health due to its antioxidant, anti-inflammatory. Therefore, this study designed to assess anti-diabetic and antioxidant properties of BCA and investigate its impact on gene expression of TLR4 and MCP-1 in the kidneys of type 1 diabetic rats.

Methods: 24 Wistar rats were divided into 4 groups as follows: control group, diabetic control group, diabetic group which received 10 mg/kg bw and diabetic groups which received 15 mg/kg bw of the BCA. STZ was used to induce diabetes. The expression of TLR4 and MCP-1 genes was assessed by real-time and enzymatic kits were used to measure biochemical parameters.

Results: Diabetic control rats in comparison to control group showed a significant elevation in serum level of FBG, urea, creatinine, malondialdehyde (MDA) and expression of TLR4 and MCP-1 in the kidney tissue ($P<0.05$). Also, the level of albumin and superoxide dismutase (SOD) in kidney tissue of diabetic control group significantly reduced compared to the control group ($p <0.05$). Remarkable disorder in lipid profile of the diabetic control group compared to the control group was observed ($P<0.05$). The results showed that all defective parameters in diabetic group were improved after supplementation of BCA in a dose dependent manner ($P<0.05$).

Conclusions: Our findings suggest that BCA has anti-diabetic effects and can prevent its complication. So BCA can be a potential phytochemical therapy for diabetes and diabetic nephropathy.

Keywords: Biochanin-A, Diabetic rats, TLR4, MCP-1

A-10-1163-1

Structure-based virtual screening of natural compounds library with clinical validation in COVID-19-related ARDS relief

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Introduction: SARS-CoV-2 infection effects on the lung can be classified in the combination of two-state, viral pneumonia with mild coagulation of hyaline, and ARDS. ARDS causes severe hyaline membrane formation in the alveoli, and this is followed by interstitial widening and by edema and then hypoxia requiring intensive care to avoid thrombosis, other organ injuries, and death. Herein, we introduce a cytokine storm and bradykinin inhibition method to relieve ARDS and lung failure for SARS-CoV-2 patients.

Methods: A library of the 200 natural supplements prepared cognizing on the SARS-CoV-2 infection affected signal transduction, and available information on the virus life cycle. VINA 1.1.2 docking and GROMACS 5.1.4 dynamic simulation package used to screen the. In clinic, non-hospitalized and hospitalized patients randomly assigned in a controlled phase 3 trial. The symptoms defined in X-ray Computed Tomography, blood factors examination, and ordinal elimination of the signs with R 4.0.3 program statistical assessing the results.

Results: Computation analysis indicated that supplements can deal with the virus plugin to the cell surface, inhibition of the viral Nsp12 (RdRp) and Nsp5 (3Cl Mpro). In the trial, the blood oxygen level, CT scan results for lung cleansing, amount of Lymphocytes, Neutrophil, LDH, PLTs, ESR, and WBC of the intervention patients were effectively improved than control patients and one of the hospitalized control patients died. The comparison of symptoms demonstrated a significant elimination in the prevalence of fever, sore throat, and chest pain, for intervention patients (5.40±1.80 hospitalization days; 3.84±0.8 treatment days) rather than in the control group (13.25±8.96 hospitalization days; 8.80±3.51 treatment days).

Conclusion: Analysis present that the method is useful for lung clearance, blood factors, and immunity enhancement to overcome the infection as well as to avoid viral seeding and dispersion.

Keywords: Keywords: SARS-CoV-2, Bradykinin, ARDS, Cytokine, Docking, MD Simulation.

A-10-1351-1

Lubiprostone alleviates cholestasis-associated hepatic injury via improving liver injury markers in adult male rats

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Introduction: Weakening of the intestinal epithelial barrier function in multiple pathological states results in liver damage and inflammation, which progresses to fibrosis and liver cancer. Particularly, intestinal barrier dysfunction has been robustly observed in cholestatic liver disease. Previous studies have reported that targeted activation of chloride channels can improve intestinal barrier function. Hence, in the present study, we investigated the effect of lubiprostone, an activator of chloride channels (ClC-2), on enzymatic markers of liver injury induced by bile duct ligation (BDL) in adult male rats.

Methods: Thirty-two male Wistar rats (230± 10 g) were used and divided into control, laparotomy sham, BDL, and BDL + lubiprostone groups. Rats subjected to BDL were treated with lubiprostone (10 μg /kg) twice daily for 14 consecutive days. Enzymatic markers of liver injury, alanine aminotransferase (ALT) and aspartate aminotransferase (AST), alkaline phosphatase (ALP) and bilirubin (total/direct) concentration were assessed in lubiprostone-treated and untreated rats with cholestasis.

Results: Significant increases in serum level of ALT, AST, ALP and total bilirubin were detected in rats subjected to BDL. Comparing assay of the liver enzymes and total bilirubin concentration showed a significant reduction in ALT, AST, and total bilirubin in lubiprostone-treated rats compared to BDL cholestatic rats. Furthermore, an insignificant decrease in serum ALP level was observed in lubiprostone-treated rats compared to BDL cholestatic rats.

Conclusions: The positive effect of lubiprostone on the indices of hepatic function may be a critical factor contributing to protection against cholestasis-associated liver injury. These findings raise the possibility of targeting intestinal ClC-2 channels for the treatment of cholestasis.

Keywords: Bilirubin, Cholestasis, Liver injury, Lubiprostone, ALT, AST, ALP, Rat

A-10-1131-2

The role and function of long non-coding RNAs in osteoarthritis

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Introduction: Osteoarthiritis (OA) is the most prevalent disease of articulating joints in human that frequently results in joint pain, movement limitations, inflammation, and progressive degradation of articular cartilage. The etiology of OA is not completely clear and there is no full treatment for this disease. Molecular investigations have revealed the involvement of non-coding RNAs such as Long non-coding RNAs (lncRNAs) in OA pathogenesis. LncRNAs play roles in multiple cellular and biological processes. In this review, we underlie the increasing evidence for the critical role of lncRNAs in OA pathogenesis reviewing the latest researches.

Methods: This review of clinical studies was conducted to evaluate lncRNAs in osteoarthritis studies. The studies were identified by searching the PubMed/MEDLINE, Google Scholar, and Sciencedirect databases for peer-reviewed journal articles that were published by September 2019.

Results: Several lncRNAs have now been detected as being either differentially expressed in diseased joint tissue or as candidate central regulators of inflammatory pathways relevant to joint pathology. A major challenge of all of these approaches is to accomplish target specific delivery. Recently, several novel delivery strategies have been developed to reduce offtarget effects, especially nanoparticles that are characteristic by improved stability, extremely small size, biocompatibility and self-assembly.

Conclusion: Some dysregulated lncRNAs may be used as valuable diagnostic biomarkers and therapeutic targets. future studies to determine the functional role and mode of action of these disease-associated lncRNAs will be insightful, as will joint tissue expression profiling of lncRNAs for which functional roleswithin key inflammatory pathways have been determined.

Keywords: Osteoarthritis, Long non-coding, RNA lncRNA, Joint disease, OA

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Magnesium supplementation effect on the expression of p53 and endothelial nitic oxide synthase genes in patients with atherosclerosis: a clinical trial study

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Page | 136

Introduction: Magnesium seems to play a role in improving cardiovascular function, but its exact mechanism is unknown. Aims: The aim of present study was to evaluate the effect of magnesium sulfate on the expression of p53 and endothelial nitric oxide synthase (eNOS) genes in patients with atherosclerosis.

Methods: This study was a placebo-controlled double-blind randomized clinical trial on 56 patients with angiographically proven atherosclerosis. Participants were randomly divided into two groups receiving 300 mg/day magnesium sulfate (n = 29) and placebo (n = 27) for three months. Fasting blood samples were taken before and after the intervention and total RNA was extracted and used to evaluate the expression level of p53 and eNOS genes by Real Time PCR.

Results: The expression of eNOS gene was significantly increased (P <0.0001) and the expression of p53 gene was decreased (P = 0.02) in the magnesium sulfate group compared to the placebo group.

Conclusion: Our findings demonstrate that magnesium sulfate supplementation may have protective role against the progression of atherosclerosis through upregulation of eNOS and downregulation of p53 gene.

Keywords: Magnesium, Atherosclerosis, p53, eNOS

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Expression analysis of noncoding RNAs LINC00460 and miR-539 in invasive breast carcinoma

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Introduction: Breast cancer, as one of the most common cancers in the world, is a heterogenic disease including distinct subgroups that are different in the diagnosis. Identifying noncoding RNAs as biomarker is a major challenge for cancer diagnosis.

Methods: This study was designed to investigate and identify the expression levels and the potential of biomarker for two non-protein coding genes, LINC00460 and miR-539. Two case and control groups set the foundation for this study. Total RNA was extracted from breast carcinoma samples and the cDNA were then synthesized. The LINC00460 and miR-539 were amplified by RTq-PCR in order to evaluate the level of expression.

Results: Evaluation of LINC00460 and miR-539 expression showed that LINC00460 expression in tumor samples was significantly higher than normal samples ($*P < 0.01$). In contrast, miR-539 expression level in tumor samples was less than normal controls ($*P < 0.01$). In addition, LINC00460 and miRNA-539 have exclusively upregulation and down-regulation in HER-2 positive and Stage III of breast cancer cases, respectively. According to the results of ROC Curve to check the biomarker potential out for the LINC00460 and miRNA-539 reducing significant expression up to 0.86 in the AUC index for miR-539, as well as vice versa by mention the increase LINC00460 expression level with AUC index 0.78 in all cancer stages.

Conclusion: We found that the LINC00460 and miR-539 expression were associated with the clinical characteristics of patients and the biomarker potential for both ncRNAs is recommended.

Keywords: Key words: Breast cancer, MicroRNA, lncRNA, miR-539, LINC00460

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Inhibition of SARS-CoV-2 binding on ACE2 bearing cells following neutralizing antibodies produced against truncated spike protein

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Introduction: Spike glycoprotein of SARS-CoV-2, especially RBD binds the ACE2 surface receptor containing host cell, resulting in entering the viral genome and replication of viral particle which damages the host cells. Therefore, RBD plays a key role in initiating and spreading viral infection in host cells. Hence this protein may be used as a target for vaccine production to inhibit SARS-CoV-2 to ACE2 receptor binding. The aim of this study was to investigate the binding of recombinant RBD (rRBD) to ACE2 and the effect of the neutralizing antibodies against rRBD on this binding.

Method: Both bioinformatics and in vitro methods were used. Molecular docking of rRBD-ACE2 was performed by Auto Dock. rRBD gene was cloned, then the protein was expressed and injected into 4 groups of mice (BALB/c) to select the best dose-response. Stimulation of the humoral and cellular immune system was assessed by ELISA. Histological studies were performed to rule out complications of rRBD injection. The neutralizing property of antibodies produced against SARS-CoV-2 was evaluated by VNT. The binding of rRBD to ACE2 and effect of the neutralizing antibodies produced against rRBD on this binding were evaluated by flow cytometry.

Result: In molecular docking, binding of rRBD-ACE2 was confirmed. It was shown that the mice serum antibodies which produced against rRBD protein after injection, have ability to neutralize the SARS-CoV-2. The binding of rRBD protein to ACE2 cell surface receptors as well as the inhibitory effect of neutralizing antibodies on this binding were also confirmed. **Conclusion:** The protein has the ability to produce antibodies with virus-neutralizing properties inhibiting binding of the virus to the ACE2 receptor. Therefore, due to the neutralizing properties of antibodies against SARS-CoV-2, this protein was shown to have potentials to be used as recombinant vaccine based on spike protein.

Keywords: SARS-CoV-2, Spike protein, ACE2, neutralizing antibodies, vaccine

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Anticancer Activity of the Quinoline Alkaloids of Cinchona Bark: A Systematic Review

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Page | 139

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Introduction: Cinchona bark contains quinine and related alkaloids. Quinine has been used for centuries in the prevention and therapy of malaria.

Methods: At the beginning common search engines, for example Cochrane Library were searched for systematic review articles about the effect of major components of cinchona bark on cancer cells. There weren't any systematic review study in this field until May, 2022. Then, PubMed, Science Direct and Google Scholar search engines, were searched to find all of the articles which contained "Cinchona" with "cancer" or "tumor" or "anticancer" or "antitumor".

Results: After searching by two reviewers and removing duplicate and inappropriate articles or articles without abstract, 14 original papers were remained. During 45 years evaluation of quinoline alkaloids of cinchona bark, as anticancer agents have been reported for different cell lines. They include HeLa cells, MCF-7 breast cancer cells, A-549 lung adenocarcinoma cells, human hepatocellular carcinoma HepG2 Cells, glioblastoma U-87, neuroblastoma SH-SY5Y, PC3 prostatic cancer cells, and human colon cancer LoVo cells.

Conclusion: Quinoline alkaloids have shown anticancer activities for a wide range of cancer cells, in different reports with in silico, In vitro, and In vivo studies. It seems that cinchona bark extract and its major components can be useful in the treatment of different cancers.

Keywords: quinoline alkaloids, cancer, cinchona

Umbilical coiling index and VEGF expression

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Introduction: This study investigated the impact of the postnatal umbilical coiling index (UCI) and gestational diabetes mellitus (GDM) on vascular endothelial growth factor expression. **Methods:** The postnatal UCI measurements of 57 neonates of GDM and normal parturients were prospectively studied within 24 hours after delivery. The expression level of VEGFA and VEGFR genes were evaluated using Real-time PCR assays. The nonparametric test for comparing the medians and the Chi-squared test were used to compare the continuous and discrete variables between the groups, respectively.

Results: In this study, 57 singleton parturients were enrolled, comprised of 29 GDM and 28 normal pregnancies. The median (IQR) of maternal age was 31 (28-34) and 29(24.5-32) in these groups respectively (p-value=0.082). The median of VEGFA and VEGFR expressions did not significantly differ between GDM and normal groups. The expression levels of VEGFA and VEGFR significantly differed between the five strata (P-values=0.001 and 0.002, respectively). Abnormal coiling status may induce VEGFA down-regulated pattern. **Conclusions:** GDM status may not influence the expression level of VEGFA and VEGFR. However, the abnormal coiling pattern appears to make difference in their expression and may cause VEGFA down-regulated pattern.

Keywords: Gestational diabetes mellitus, Umbilical coiling, VEGF expression

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Evaluation of serum concentrations of zinc and copper in multiple sclerosis and neuromyelitis optica patients

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Page | 141

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Introduction: Multiple sclerosis (MS) and Neuromyelitis Optica (NMO) are autoimmune diseases of the central nervous system that have distinct immunological and pathological features. The aim of this study was the evaluation of serum concentrations of zinc and copper in multiple sclerosis and neuromyelitis optica patients.

Method: This study was performed on 30 patients with MS and 24 patients with NMO and 30 healthy control individuals. We used ICP-OES technique to measure serum levels of zinc and copper in study population.

Results: Our results indicate that zinc serum levels in the MS and NMO patients were significantly decreased in comparison with the healthy control group. The level of copper was significantly higher in NMO group than in MS and control groups and also higher in the MS group than in the control group.

Conclusion: Alterations of trace elements may have a significant role in the pathogenesis of MS and NMO diseases. It is suggested that the body status of trace elements might be significantly correlated with the therapeutic effects and complications of MS and NMO diseases. It can be concluded that zinc supplementation in these patients both compensates for the decrease of serum levels of this important element and also leads to modulates the concentration of body copper levels.

Keywords: Multiple sclerosis, Neuromyelitis optica, Zinc, Copper

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MicroRNA regulatory network encoded in POU5F1 gene

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Introduction: MicroRNAs are small non-coding RNAs of 18-25 nucleotides that regulate gene expression at the post-transcriptional level by binding to the 3'-UTR of mRNAs. Each microRNA alone can affect the expression of thousands of mRNAs. MicroRNAs may function as either oncogenes or tumor suppressors under certain conditions. The dysregulated miRNAs have been shown to affect the hallmarks of cancer, including sustaining proliferative signaling, evading growth suppressors, resisting cell death, activating invasion and metastasis, and inducing angiogenesis.

Methods: Using machine learning and bioinformatics tools we predict the target genes of microRNA encoded in POU5F1 gene. Functional annotation and involvement of the miRNA target genes in cellular signaling pathways were analyzed using Kegg database. Biological interactions of the target genes were analyzed using STRING website.

Results: Machine learning and bioinformatics analysis revealed mTOR as one of the target genes of POU5F1-hosted microRNA. Functional annotations revealed that mTOR is a serine-threonine protein kinase involved in the mTOR signaling pathway and plays an essential role in regulating protein synthesis, cell growth, proliferation, actin cytoskeleton regulator and the promoter of cell survival and cell cycle. Functional enrichment analysis demonstrate that mTOR gene interacts with various important protein which involve in mTOR signaling pathway.

Conclusion: Considering the role of microRNA as an expression suppressor, it could be concluded that the effect of the microRNA transcribed from POU5F1 gene can negatively regulate the cell growth and proliferation. It could have a tumor suppressor role in cancer biogenesis.

Keywords: OCT4, pluripotency gene, stem cell.

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Genome-wide transcriptome profiling of safflower (Carthamus tinctorious L.) by RNA-Seq analysis

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High-throughput methods of transcriptome profiling, such as RNA sequencing, can quantify the expression of all transcripts/genes in an organism at the level of RNA between two contrasting genotypes or in response to stress conditions versus normal physiological conditions (Chen et al., 2012). Safflower (Carthamus tinctorius L.) is an important medicinal plant, which is commercially cultivated for vegetable oil extracted from the seeds. Due to the high importance of this plant, it seems necessary to study the transcriptome and identify the function of its genes, activity pathways and important proteins. Iran is considered as one of the major cultivation centers of safflower in the old world (Golkar 2014). Due to increasing water deficiency, farmers need crops with high tolerance and resistance to drought and salt stresses to feed the world increasing population. One of the best candidates is safflower with natural tolerance to abiotic stresses such as drought. For this purpose, safflower seeds were grown under field conditions and leaf sampling was done with six replications. After RNA extraction, cDNA libraries were sequenced through Novaseq6000 using paired method. Due to the lack of reference genome, de novo assembly method was used to reconstruct the transcriptome. According to the results of gene ontology, most safflower genes involve in cellular and metabolic processes and response to stimuli. In addition, our identified genes were involved in different pathways, including the two important pathways: the biosynthesis pathway of linoleic acid and biosynthesis of secondary metabolites, producing important yellow carthamidin and flavonoids compounds in this plant. More important protein classes enriched for contigs were transcription factors (TFs) and kinases, all or some of which play vital roles in cell cycle, differentiation and tissue/organ growth and development. Our results shed light on the systems biology of safflower cell, particularly the active biological pathways and gene modules.

Keywords: RNA-Seq, Biological process, Systems biology, Gene ontology

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The anti-diabetic effects of L-lysine and Lysulin in STZ+NA-induced diabetic rats.

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Introduction: Type 2 diabetes mellitus (TDM2) is known as a chronic and widespread disease. In previous studies the effect of L-lysine, vitamin C and Zinc have been shown to prevent the diabetic progression in type 1 diabetes. This study aimed to compare the anti-diabetic effects of Lysine and Lysulin (a combination of vitamin C, Zinc and L-lysine) in streptozotocin + nicotinamide (STZ+NA) induced type 2 diabetes in rats.

Methods: Sixty adult male Wistar rats was divided into six groups: CL (Control-Lysine), CS (control-Lysulin), CN (control with no more treatment), DL (diabetics received L-Lysine), DS (diabetics received Lysulin), DN (diabetics with no more treatment). Induction of TDM2 was performed by injection of STZ+NA (50 mg/Kg body weight STZ and 110 mg/Kg body weight NA). One week after induction of diabetes, treatment with Lysine and Lysulin dissolved in drinking water was started and continued for 8 weeks. The blood samples were collected from the retro obituary of animals at 4th and 8th weeks. At the end, animals were sacrificed and whole blood samples were collected from heart. Serum glucose and ferric reducing ability of plasma (FRAP) were measured by spectrophotometry assay and HbA1c was measured by enzymatic assay.

Results: The treatment of Lysine and Lysulin could significantly decrease serum glucose and HbA1c in DL and DS group compared with DN group after 8 weeks. In addition, losing weight in DL and DS was lower than DN. FRAP, as an antioxidant marker, was measured in plasma, after 4 and 8 weeks. FRAP significantly increased in DL and DS groups. But, Lysulin was more effective than Lysine after 8 weeks.

Conclusion: Our study suggests that both Lysine and Lysulin can ameliorate serum glucose and glycation of proteins and improve antioxidant power of plasma; and Lysulin has more effective in controlling diabetes complication than Lysine.

Keywords: diabetic, Lysine, Lysuline, FRAP, HbA1c, serum glucose.

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Targeting and manipulation of SARS-CoV-2 cell fusion mechanisms through molecular modeling methods

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As the newly emerged coronavirus (SARS-CoV-2) that causes a respiratory system involving disease called Covid -19, developed some new strategies to expose the public health to grave danger, researchers have been targeting the pathogenic approaches, especially virulence factors of the virus, as known as the Spikes, surface proteins containing two main subunits, S1 and S2 which are responsible for cell entry mechanisms. Regarding the cascade interactions between potential receptor ACE2 of the somatic cells and the RBD segment of the S1 subunit, the formation of helical bundle structure of six integrated HR1 and HR2 domains and insertion of fusion peptides into the cell membrane, many therapeutic, biochemical, and genetic approaches have been introduced to block every component of this pathway. In the current study, the potential therapeutic agents were investigated by molecular docking and dynamic simulation methods based on the interactions among S protein subunits and the specific ACE2 receptor. For this purpose, some FDA-approved drugs that can bind to Spike of the virus were selected and evaluated, considering the conformational alterations made to the Spike structure. The required inhibitory effect can take place through the binding of ligands possessing high affinity to the S protein. Since the inhibition of the fusion process is the key to preventing the virus from the entry into the cells, the Covid can be treated in the preliminary levels of infection with these potential drugs. Based on the results, Conivaptan and Cefpiramide were the most prominent two candidates with preferable characteristics and parameters, including low binding energy and high affinity to the fusion core of the virus. These two drugs could effectively manipulate HR segments of the S2 subunit and can be used in curative management of the SARS-CoV-2 pandemic.

Keywords: SARS-CoV-2, cell fusion, cefpiramide, conivaptan, S protein

A-10-1370-1

Methylation-mediated silencing of miR-125a-5p facilitates breast cancer progression by inducing autophagy

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Introduction: microRNA-125a-5p (miR-125a) is a tumor suppressor gene whose role in autophagy remains poorly understood. In the current study, we aimed to investigate the methylation status of miR-125a, its transfection into SK-BR3 cells, and its effects on autophagy. **Methods:** Sixty samples of tumor and non-tumor adjacent tissue were collected and the methylation status of miR-125a was evaluated by methylation-specifc PCR (MSP). The effect of 5-Aza-dC on miR-125a expression was investigated in the SK-BR3 cells. Cells were also transfected with miR-125a mimic/antimiR. The expression of miR-125a and its target genes was evaluated by Real-Time PCR. Protein levels of ATG5 and LC3 were assessed by Western blotting. HER2 expression was investigated by immunocytochemistry (ICC).

Results: The data showed that the miR-125a promoter CpG Island was signifcantly hypermethylated in breast cancer tissues ($p<0.01$) and in SK-BR3 cells. The 5-Aza-dC could significantly increase miR-125a expression by decreasing its methylation ($p<0.05$). In addition, Western blot analysis indicated the expression of ATG5 and LC3 II/ LC3I, as autophagy biomarkers, was signifcantly reduced in SK-BR3 cells transfected with miR-125a ($p<0.05$).

Conclusions: Our data showed miR-125a expression was signifcantly decreased in tumor tissues due to its promoter hypermethylation. Overexpression of miR-125a was associated with a reduction in autophagy, which could provide a new therapeutic avenue for advanced-stage breast cancer treatment.

Keywords: Breast cancer · Autophagy · Methylation · microRNA-125a

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In vitro effect of butanol extracts of Crocus Sativus on butyrylcholinesterase purified from human plasma

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Page | 147

Introduction: Alzheimer's disease (AD) is recognized as a principle basis of cognitive impairment in the elderly. Discovery alternative and multi-targeted therapeutic approaches like natural compounds are sought. Crocus sativus(saffron) is one of this medicinal plant which distinguished with a wide range of biological and pharmacological belongings, exclusively clearance of amyloid-beta aggregation and cholinergic enzyme inhibition. Butyrylcholinesterase (BuChE) predominates in the healthy brain and considered to be a legitimate therapeutic targets for declining the cholinergic deficit. Experimental evidence from the use of agents with enhanced selectivity for BuChE, indicates potential therapeutic benefits of inhibiting BuChE in AD. The development of new natural BuChE inhibitors like Crocus Sativus will lead to a wider variety of potent treatment options.

Methods: For fractionation of a crude extract, appropriate solvents, n-hexane, ethyl acetate, methanol and water for solvent partitioning in VLC set up together with silica gel, C 18. After the stamen of plants was isolated, they are subjected to separation by HPLC. For structure elucidation, NMR is used. Butyrylcholinesterase activity was measured using the Ellman spectrophotometric method and human blood as the enzyme source. Molecular modeling studies were obtained by docking method with Auto dock.

Results: Butanolic sub-fractions (40% ethyl acetate/60% hexane and 50% water/methanol 50%) had the highest ability. A methanolic sub-fraction obtained from 100% methanol has the same positive effect on BuChE. Name of Compound was identified and the its enzymatic inhibitory activity was approved. The molecular docking results of this compound with the active site of the BuChE also showed high inhibitory potency of phenolic structure.

Conclusion: The IC50 recorded for the selected compounds was very close to the IC50 of rivastigmine. Any possible clinical side effects of this herb could be similar to the side effects of rivastigmine and galantamine which needs further investigation.

Keywords: Alzheimer's diseases, Crocus sativus, Butyrylcholinesterase, Rivastigmine, Galantamine, Natural Products

A-10-1498-1

Qualitative investigation of the effect of Heracleum Persicum root extract active ingredients on the osteogenic differentiation of adipose mesenchymal stem cells

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Introduction: Mesenchymal stem cells are very noteworthy in tissue engineering. Because of its ability to differentiate into skeletal lines and its high proliferative capacity, these cells can play an important role in the treatment of bone and cartilage lesions. Studies have shown that plant extracts have been effective in the proliferation and differentiation of stem cells. Plants availability and fewer associate side effects compared to the chemichal ugs, make plants and their corresponding extracts noted resources. Heracleum Persicum is an endemic plant with antioxidant properties that are found throughout Iran. Pimpinlin and isopimpinlin are furanocoumarins extracted from Heracleum persicum.

Methods In this study, the roots of ied plants were ground up, then using hexane solvent its extract was obtained. The extract's nanoemulsion was prepared. The nanoparticle sizes were determined by DLS. Subsequently, the optimal concentration of the extract and its active ingredients was determined through a toxicity test (MTT). During the two-week experiment, the osteogenic differentiation was assessed in the presence of optimal concentrations of inducers in the culture medium.

Results The results showed that the nanoparticle sizes were 36 nm. The optimum concentrations of the extract and its active ingredients measured at 1 and 0.75 µM, respectively. Acridine Orange staining was used to qualitatively examine the morphology and proliferation of differentiated cells and primary mesenchymal cells, the results of which were consistent with MTT assay. Alizarin red and von Kossa staining were used as qualitative tests to show calcium deposition and confirm osteoblastic differentiation, which indicated significant bone differentiation. By measuring the activity of the catalase enzyme, an increase in the enzyme level was observed.

Conclusion: In the case of patients with bone injuries such as misplaced bone fusion or complete bone loss due to tumors that are not easily treatable, cell therapy can offer a more effective treatment.

Keywords: Key words: Differentiation, Heracleum Persicum, Mesenchymal, Osteogenic

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Co-administration of 5FU and propolis on AOM/DSS induced colorectal cancer in BALB-c mice

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Introduction: Currently, the main problems with chemotherapy are its side effects, toxicity, and drug resistance. Propolis has biological activities, such as anti-inflammatory and anti-cancer properties. This study aims to examine the combined effects of 5-fluorouracil (5FU) and propolis on colorectal cancer (CRC) in mouse models.

Methods: The chemical composition of ethanolic extract of propolis was determined by gas chromatography– mass spectrometry (GC–MS). In this study, 49 male Balb/c mice (16–20 g) were divided in seven groups as a control group and experimental groups (treated and untreated CRC model [azoxymethane + dextran sodium sulfate]). This study was conducted in 8 weeks. To examine the anti-cancer effects of propolis, the number of aberrant crypt foci (ACF) was counted and the pathological lesions in the distal colonic epithelial tissue were diagnosed. In this study, the expression of beta-catenin (β-catenin), induced nitric oxide synthase (iNOS) and cyclooxygenase-2 (Cox-2) proteins, which play a major role in the incidence and progression of cancer, were determined.

Results: GC–MS analysis of propolis showed the presence of hydrocarbons, alcohols, ketones, terpenes, phenols, and flavonoids. Administering propolis in combination with 5FU reduced the number of ACFs and pathological lesions in comparison with cancer control groups ($p < 0.0001$) and 5FU-alone treatment ($p < 0.05$). The propolis combined with 5FU reduced the expression of Cox-2, iNOS, and β-catenin proteins.

Conclusion: The results showed that propolis increased the efficiency of 5FU and could be taken into account as the adjunct therapy for colorectal cancer.

Keywords: Propolis ‹Azoxymethane ‹Catenins ‹Nitric oxide synthase type II. Colorectal neoplasms. Fluorouracil. Mice

Ameliorative effect of silymarin on oxidative and histopathological changes in 1, 2 dimethylhydrazine-induced mice colon cancer

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Page | 150

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Introduction: Background Colorectal cancer (CRC), the third most common cancer worldwide, is a leading cause of cancer mortality. Flavonoids have been studied broadly for their antioxidant, anti-inflammatory, and anti-carcinogenic properties. Among all, silymarin (SMN) is well-known for its anti-inflammatory, hepatoprotective, and anti-tumor effects. We aimed to investigate the effects of SMN on oxidative and histopathological changes in mice colon cancer Materials and

Methods: Twenty-four BALB/c male mice (25-30 g) were divided into three groups with eight mice per group (control, DMH, SMN+DMH). Colorectal cancer(CRC) was induced in twenty-four BALB/c male mice (25-30 g) through intraperitoneal injection of DMH at the dose of 20 mg/kg b.w. once a week for ten consecutive weeks. SMN (2500 ppm) was added to the diet of the theSMN+DMH group daily for eight weeks post CRC induction. At the end of 18th week, colons were dissected out, washed in chilled saline, and cut longitudinally immediately after cardiac blood sample collection and euthanasia. Malondialdehyde (MDA), and NO levels were determined in colon samples preserved at -70 oC. Also, serum levels of lactate dehydrogenase (LDH), Superoxide dismutase (SOD), and inflammatory cytokines (CRP, TNF-α) were examined. H&E staining was performed for pathology analysis of the colon samples.

Results: DMH administration resulted in a significant increase in the serum levels of LDH, SOD, CRP, and TNF-α as well as the MDA and NO levels in colonic homogenates ($p<0.05$). SMN-supplemented diet could significantly decrease these indices in comparison with the DMH group ($p<0.05$). Histopathological evaluation showed that DMH could induce hyperplastic/dysplastic changes in colonic mucosa, goblet cell depletion, and lymphoid aggregation. SMN supplementation could significantly ameliorate the carcinogenic effects of DMH on colon tissues ($p<0.05$).

Conclusion: SMN supplementation could efficiently reduce the inflammatory and histopathological changes of colon cancer in mice. Thus, it could be considered as an anti-colorectal herbal remedy besides chemotherapy regimens.

Keywords: Colorectal cancer, Silymarin, DMH

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Expression and Purification of Terminal Deoxynucleotidyl Transferase (TdT) Enzyme

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Introduction: Terminal deoxynucleotidyl transferase (TdT) is a nuclear polymerase enzyme as it can catalyze the stepwise addition of nucleotides randomly to single-stranded DNA without the need for a DNA template. In the present study, we want to perform heterologous expression in E. coli, then purify it by affinity chromatography.

Methods: The nucleotide sequence of the TDT was optimized, synthesized, and cloned into an expression vector, pET-28b (+), then inserted between the two restriction sites of ndeI and BamHI. The recombinant vector was transformed into E. coli strain BL21 (DE3) and its expression were examined in different conditions. The protein was expressed in LB medium for 18h, 20h, 24h at 18 °C, 20 °C, and 22 °C after inducing by 4mM of Lactose, 8mM of Lactose, and 4mM of Lactose combined with 0.1 mM of Isopropyl β-D-1-thiogalactopyranoside (IPTG). Sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) was used to determine the optimal expression condition. After confirmed expression, the pellet of cells was sonicated. Then, the supernatant was purified by his-tag affinity chromatography. Also, SDS-PAGE was used to assess the enzyme purity.

Results: The constructed expression vector, pET28 – TDT, was transformed into E. coli BL21 (DE3). A soluble enzyme was obtained after expressing it in different conditions. SDS-PAGE analysis revealed a strong band for the recombinant enzyme near the 50 kDa marker agreeing with the predicted molecular mass of 46 kDa. The recombinant protein was purified by his-tag affinity chromatography. The purity of the enzyme was approved via the presence of a single band in SDS-PAGE.

Conclusion: In this study, we first cloned and then expressed the recombinant TDT enzyme using the pET-28 expressing system. The product obtained in this process was soluble. This protein can be used in enzymatic DNA synthesis in the future. After purification, the recombinant enzyme will be characterized.

Keywords: DNA synthesis, Tdt, E. coli, Expression, solubility

A-10-1267-1

Overexpression of MMP-9 in peripheral blood mononuclear cells of patients with coronary artery disease and its correlation with severity of coronary artery stenosis

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Introduction: Overexpression of matrix metalloproteinase-9 (MMP-9) in the peripheral blood mononuclear cells (PBMCs) may be involved in early stages of atherosclerosis in patients with coronary artery disease (CAD), such as recruitment and activation of monocyte in the vascular lesion.

Methods: The study population consisted of 115 Iranian individuals who underwent coronary angiography at the Hajar Hospital, affiliated to the Shahrekord University of Medical Sciences, Chaharmahal and Bakhtiari province, Iran. The mRNA level of MMP-9 was measured with Real-time PCR. Student's t-test was carried out to compare the continuous data between the two groups. All data were expressed as mean±standard deviation (SD). $p \leq 0.05$ was considered significant.

Results: Gene expression of MMP-9 was significantly elevated in PBMCs of CAD subjects as compared with NON-CAD subjects ($p \leq 0.05$). As well as, overexpression of MMP-9 was correlated with severity of stenosis of LCX, LAD, RCA and OM arteries.

Conclusion: Our data indicated the contribution of MMP-9 in the progression of atherosclerosis. As well as, alteration of gene expression of MMP-9 may be associated with coronary artery stenosis.

Keywords: MMP-9, Coronary Artery Disease, Peripheral Blood Mononuclear Cells

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Age and sex-specific reference intervals for fasting blood glucose and lipid profile in Iranian infants

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Page | 153

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Introduction: Accurate clinical diagnosis requires specific reference intervals (RIs) defined for different age ranges, the pediatric population in particular. However, there is limited available neonatal data for laboratory parameters. This study is focused to determine age- and sex-specific RIs for several metabolic markers in healthy Iranian infants from birth to 30 months, for the first time.

Methods: A cross-sectional study including 344 participants (186 girls and 158 boys) between the ages of 3 days to 30 months (mean age: 12.91±7.15 months) was conducted. The participants were recruited from January to March 2021. The serum concentration of five major metabolic markers including triglyceride (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and fasting serum glucose (FSG), were measured using an Alpha classic-AT plus auto-analyzer and conventional analytical methods. Age- and sex-specific IRs were established as per CLSI Ep28-A3 guidelines with a 90% confidence interval. **Results:** It was found that age partitioning is necessary for serum TG and FSG but not for TC, HDL-C, and LDL-C. Furthermore, serum concentrations of TC, HDLC, and LDL-C remained comparatively constant for the entire age range, while serum levels of TG and FSG decreased with age. The results showed that sex partitioning is not required for all lower and upper limits of metabolic markers.

Conclusion: The findings presented herein provide a better understanding of reference values for metabolic markers in infancy and early childhood. The critical gaps in population RIs for metabolic markers addressed in this study can improve complex processes in clinical interpretation and diagnosis of a wide range of diseases in infants.

Keywords: Keywords: pediatric population, Reference intervals, Metabolic markers

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Designing Artificial Neural Network to Evaluate the Biochemical Parameters Relating to Fasting Blood Glucose, Lipid Profile and Liver Enzymes

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Page | 154

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Introduction: The main aim of this study is to emphasis on the importance of artificial neural network (ANN) in clinical biochemistry with emphasis on carbohydrate and lipid metabolism.
Methods: One hundred and twenty-four plasma samples were analyzed for biochemical indices according to standard assay methods. To design ANN models, 11 biochemical parameters were chosen as independent parameters. Total cholesterol, fasting blood glucose (FBS), HDL-cholesterol, LDL-cholesterol, alanine transaminase (ALT) and aspartate transaminase (AST) were considered as dependent parameter in different ANN analyses. Activation functions in hidden and output layers were hyperbolic tangent and identify, respectively. Rescaling of the independent and dependent parameters was done by standardized method, with hyperbolic tangent and identity as the activation functions, respectively.
Results: Our designed ANN models showed sum of squares errors (0.001-0.304) and relative errors (0.048-0.630) in testing steps. Predicted by observed charts demonstrated a precise positive linear correlation in the concentration of total cholesterol (y=18.44+0.9x, R2=0.946), FBS (y=3.63+0.96x, R2=0.985), HDL-cholesterol (y=0.79+0.99x, R2=0.958), LDL-cholesterol (y=0.86+0.99x, R2=0.996), ALT (y=0.18+0.98x, R2=0.994) and AST (y=2.66+0.82x, R2=0.922).
Conclusion: ANNs are useful tools to solve problems stochastically, by creating mathematical models by regression analysis. In this study we designed accurate ANN models to identify the most important biochemical parameters in relation to the concentration of glucose, lipids and liver enzymes in human plasma.

Keywords: Artificial Neural Network, Biochemical Parameters, Glucose, Lipid, Liver.

Cloning and expression of Galactose dehydrogenase (Gal DH) enzyme in E. coli BL21

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Introduction: Oxidoreductase consist of a large and important class of enzyme, which can be used in many biotechnological processes. Galactose Dehydrogenase (Gal DH) is a member of the dehydrogenases family that catalyzes the conversion of D-galactose to D-galactono-1,4-lactone and NADH in the presence of NAD+. This enzyme plays a vital role in screening neonatal blood serum in galactosemia by determining and measuring β-D-galactose and α-D-galactose. Galactosemia is a rare genetic disease of carbohydrate metabolism which can affect the body's ability to convert galactose to glucose. This research aims to prepare the recombinant form of Gal DH protein in E. coli BL21(DE3).

Methods: The nucleotide sequence of the galactose dehydrogenase was optimized for expression in the bacteria. The sequence was synthesized in the pET-28a (+) vector. The gene was located between the BamHI and XhoI restriction sites in the expression construct. Then, it was cloned into pET-28 a (+), and the vector was transformed to the E. coli. Finally, the expression of the interested gene was investigated in various concentrations of Isopropyl β-D-1-thiogalactopyranoside (IPTG), lactose, different temperature and time conditions with appropriate aeration to find optimal conditions for expression. Expression analysis was monitored by Sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE).

Results: The constructed expression vector, pET28a-galactose dehydrogenase, was transformed into E. coli BL21(DE3) strain. To observe the expression level of galactose dehydrogenase, the bacterial pellet and lysate from 2xYT medium were used to determine the recombinant protein. According to SDS-PAGE analysis, the galactose dehydrogenase was successfully expressed under the optimized condition (0.5 mM IPTG, OD600 = 0.5 at 37 °C and a post-induction time of 5 hours).

Conclusion: The pET28a-galactose dehydrogenase was successfully expressed in the E. coli in the optimize condition, but the result showed that more protein was insoluble.

Keywords: Galactose dehydrogenase, Expression, E. coli

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MicroRNA encoded in SOX2 gene and its regulatory network: a bioinformatics study

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Introduction: MicroRNAs are a small single-stranded non-coding RNA molecules that functions in RNA silencing and post-transcriptional regulation of gene expression. MicroRNAs are now recognized to play a pivotal role in the regulation of certain processes related to development in all eukaryotes and because of their potential role as agents controlling cell growth and differentiation, they have been proposed to be good candidates for cancer therapy.

Methods: Using machine learning and bioinformatics tools we predict the target genes of microRNA encoded in SOX2 gene. Functional annotation and involvement of the miRNA target genes in cellular signaling pathways were analyzed using Kegg database. Biological interactions of the target genes were analyzed using STRING website.

Results: Machine learning and bioinformatics analysis revealed TP53 as one of the target genes of SOX2-hosted microRNA. Functional annotations revealed that TP53 plays an essential role in regulating cell proliferation. Functional enrichment analysis demonstrate that TP53 gene is a tumor suppressor and interacts with various important protein which involve in cancers. It although responds to diverse cellular stresses to regulate expression of target genes, thereby inducing cell cycle arrest, apoptosis, senescence, DNA repair, or changes in metabolism.

Conclusion: Considering that the role of microRNA is to suppress transcription, it can be concluded that the effect of microRNA transcribed from SOX2 gene can affect the expression of TP53 protein and negatively regulate anti-cancer activities.

Keywords: SOX2, pluripotency gene, stem cell, signaling pathway.

A-10-1080-1

Association of rs1862513 polymorphism of resistin gene with HDL and body mass index in patients with non-alcoholic fatty liver

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Page | 157

Introduction: The prevalence of non-alcoholic fatty liver disease and its complications is increasing in adults. Risk factors for the disease, the link between unhealthy eating habits and the disease has been proven in various studies. Increased body mass index increases the chance of developing hepatic steatosis. People with visceral obesity are affected by plasma fats, which include elevated triglycerides and decreased levels of HDL (high-density lipoprotein) cholesterol and increased levels of low-density LDL cholesterol. The aim of this study was to investigate the relationship between rs1862513 polymorphism with HDL and body mass index in patients with non-alcoholic fatty liver.

Methods: In this study, 80 infected and 80 healthy individuals were evaluated by K proteinase desalination method. Amplification of the desired fragments was performed by PCR, enzymatic digestion with restriction enzyme, agarose gel electrophoresis and data were analyzed by SPSS software.

Results: This study shows the frequency distribution of subjects based on the presence or absence of disease that in terms of age (p=0.001), body mass index (p=0.001), gender (p=0.001). = 0.001) and HDL p=0.001) there is a significant difference between the patient and healthy groups. The correlation between resistin and variables showed that there is a significant relationship with resistin in terms of body mass index (p=0.001). Frequency distribution based on genotype showed that age (P=0.004), body mass index (P=0.006) were significantly different in genotypes. In terms of regression analysis of genotypes shows that the percentage of patients in CC and GC genotypes is significantly higher than healthy individuals.

Conclusion: It was stated that there is a relationship between patients with this disease and rs1862513 polymorphism of resistin gene with HDL and body mass index.

Keywords: Non-alcoholic fatty liver disease - Resistin - rs1862513 polymorphism - Body mass index - HDL

The regulatory network of microRNA encoded in NANOG gene

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Introduction: MicroRNAs (miRNAs) are small non-coding RNAs that function as the guide by base-pairing with target mRNA to negatively regulate its expression. MiRNAs are vital regulators of gene expression at all stages of development, and their crosstalk via developmental signaling pathways is essential for orchestrating regulatory control in processes such as proliferation, differentiation and apoptosis of cells.

Methods: Using machine learning and bioinformatics tools we predict the target genes of microRNA encoded in NANOG gene. Functional annotation and involvement of the miRNA target genes in cellular signaling pathways were analyzed using Kegg database. Biological interactions of the target genes were analyzed using STRING website.

Results: Machine learning and bioinformatics analysis revealed WNT5A as one of the target genes of NANOG-hosted microRNA. Functional annotations revealed that WNT5A plays an essential role in regulating developmental pathways during embryogenesis. Functional enrichment analysis demonstrate that WNT5A gene interacts with various important protein which involve in Wnt signaling pathway.

Conclusion: Considering that the role of microRNA as expression suppressor, it could be concluded that the microRNA transcribed from the NANOG gene can affect the expression of WNT5A protein and disrupt the Wnt signaling pathway and affects the embryogenesis stages. The effect of this microRNA on WNT5A protein is very important during embryonic development.

Keywords: NANOG, pluripotency gene, stem cell, signaling pathway.

A-10-1352-1

Testicular Localization and Potential Function of DDX4 during Spermatogonial Stem Cells Proliferation and Differentiation Stages

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Page | 159

Introduction: DDX4 is a member of the DEAD-box proteins and an RNA binding protein with an ATP-dependent RNA helicase. The DDX4 gene expression required for mice germ cell development may maintain spermatogonia stem cells and infertility.

Methods: Our work examines the expression of this spermatogonia stem cell marker gene in more detail; we used immunocytochemistry (ICC), immunohistochemistry (IHC), and in-silico models to examine the expression of DDX4.

Results: The IHC revealed that the DDX4 protein was expressed in germ cells in the neonate and adult testis seminiferous tubules. DDX4 was not found in DAZL positive spermatogonia stem cells, was expressed lowly in proliferating spermatogonia, and became abundant in spermatocytes and mature sperm. Counting DDX4-positive cells in the seminiferous tubules of the neonate and adult testis revealed that DDX4 expression in the adult testis was substantially greater ($P < 0.04$) than in the neonatal testis. After digesting the testis, SSC colonies were produced in vitro and characterized by ICC for DAZL. In contrast to the non-detectable in vivo, ICC demonstrated that the DDX4 protein was highly localized in the cytoplasm of both neonatal and adult mice spermatogonia stem cells in vitro. Enrichr and Shiny Gene Ontology databases were used for pathway enrichment analysis and gene ontology. STRING and Cytoscape online evaluation were applied to predict proteins' functional and molecular interactions and performed to recognize the master genes.

Conclusion: as a result, the DDX4 protein is a specific marker of spermatogonia stem cell differentiation in vivo, and it is mostly expressed in the adult testis in spermatocytes, sperm, and round spermatids. In spermatogonia, the IHC signal is very weak. In vivo, DAZL positive SSCs are negative for DDX4; however, once separated from the testicular niche, DDX4 is likewise strongly expressed in spermatogonia stem cells in vitro.

Keywords: DDX4, Proliferation, Seminiferous tubules, spermatogonia stem cell, RNA binding

A-10-1248-2

Interaction of Annexin A2 protein on Lung Cancer Stem Cells with AP-9R Specific Aptamer: A Molecular Dynamics Simulation Study

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Introduction: Lung cancer is known as one of the most common cause of mortality with a great worldwide concern. Annexin A2 as a membrane-binding protein is highly expressed in lung cancer cells, and involved in cancer stemness. Aptamers are short synthetic single-stranded oligomers with great binding affinity to different targets. This study investigated the interaction of Annexin A2 protein with the cancer stem cell-specific aptamer, AP-9R sequence, by molecular dynamics (MD) simulation.

Methods: RNA Composer web servers were applied to specify the 3D structure of the AP-9R aptamer. To achieve the equilibrium form of the aptamer in the aqueous, MD simulation was done in the TIP3P water for 50 ns. To investigate the aptamer interaction with its specific target (Annexin A2), MD simulation was done for 100 ns with both chains (A and B) of the protein. All simulations were performed with GROMACS 2018.4.

Results: The ligand-binding analysis specified that Lys, Arg, and Asp residues were participants in the aptamer interaction with both chains of Annexin A2. The Lys and Arg residues possessed the participation of 41.2% and 29.4% respectively for the interaction of the chain A of the protein with the aptamer. Also, it was a participation of 20% and 40% for the interaction of its chain B with the aptamer. The aptamer possessed more effective interaction with chain A of Annexin A2 than its chain B; however, the Rg and DSSP analyses indicated no significant structural changes between the two chains. The results highlighted hydrogen bonding and salt bridge as the dominant weak interactions in the aptamer-Annexin A2 complexation.

Conclusion: The MD simulation study clarified the binding sites of Annexin A2 with the AP-9R aptamer, including the Lys, Arg, and Asp residues. Besides, the hydrogen bonding and salt bridge were dominant in the aptamer interaction with Annexin A2.

Keywords: Lung cancer, Annexin A2, Aptamer, MD simulation, Binding site, Hydrogen bonding

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Molecular Docking of Some Quinoline Alkaloids for Possible PLK1 Inhibition

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Page | 161

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Introduction: Glioblastoma multiforme (GBM) is the most common primary brain tumor, with low survival rates, in many countries. The polo-like kinase 1 (PLK1) is required for the survival of GBM. PLK1 inhibition induce G2-M cell-cycle arrest and DNA damage, leading to caspase-mediated apoptosis in glioblastoma cells.

Methods: To assess herbal inhibitors of PLK1 as a treatment strategy for GBM we compared the affinity of two known inhibitors (volasertib and BI2536) to six quinolone alkaloids from the cinchona bark (cinchonine, cinchonidine, quinine, quinidine, dihyoquinine and dihyoquinidine) by an in silico experiment. First, the structures of compounds and PLK1 were obtained from PubChem and PDB databases, respectively. The structures of compounds saved in SDF format and were converted to PDB format using open babel converter. Then in each experiment, one of the ligands and PLK1 were prepared for molecular docking with AutoDockTools-1.5.7. Finally, open-source program AutoDock-Vina_1.2.3 was used for doing molecular docking.

Results: Quinine as the most abundant quinolone alkaloids in cinchona bark had similar affinity and negative energy to the suggested ug for different cancers like GBM; volasertib. The best values binding energies of enzyme– ligand complexes for quinine and volasertib were −8.8 and −8.9 kcal/mol, respectively.

Conclusion: The studied compounds of cinchona bark alkaloids showed good capability of inhibition, comparable with volasertib and BI2536. It seems that these alkaloids, like standard inhibitors, have proper localization and appropriate weak bonds in the active site of PLK1. As a result, after in vitro and in vivo studies of these alkaloids, it may be possible to use cinchona bark as a suitable herbal medicine to control or treat GBM.

Keywords: molecular docking, quinoline alkaloids, PLK1

A-10-1080-2

Association of rs1862513 polymorphism of resistin gene with liver enzymes and insulin resistance in women with non-alcoholic fatty liver disease in Iran

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Introduction: Fatty liver disease has been described as a hepatic manifestation of metabolic syndrome or insulin resistance, and its prevalence is increasing. Hepatic enzyme levels of adipokines increase in these patients. Due to the lack of effective drug treatment to reduce liver fat, its treatment is a targeted lifestyle, exercise and diet. The aim of this study was to investigate the association of rs1862513polymorphism of resistin gene with liver enzymes and insulin resistance in women with non-alcoholic fatty liver disease in Iran.

Methods: 80sick women and 80healthy women were evaluated by Salting out Proteinase K method. Amplification of fragments by PCR, enzymatic digestion with restriction enzyme, agarose gel electrophoresis and data were analyzed by SPSS software.

Results: This study on the frequency of women with healthy fatty liver shows that with increasing age and insulin, there is a significant difference between the two groups. There was a significant difference between the correlation of resistin with each of the variables (SGOT P=0.001) and (SGPT P=0.001). Frequency distribution of each genotype showed that there was a significant difference between insulin (P=0.001) and resistin (p=0.24) in each genotype. Genotype regression analysis The percentage of sick women in GG and CC genotypes is significantly higher than healthy women. In regression analysis of genotypes in insulin sensitive women, the percentage of insulin resistant women in GG genotype is higher than insulin sensitive women, but this difference is not significant.

Conclusion: There is a relationship between liver disease enzymes and insulin resistance between women with the disease and rs1862513 polymorphism

Keywords: Resistin - rs1862513 polymorphism - Insulin resistance - Liver enzymes

A-10-1399-1

Overexpression of receptor for advanced glycation end products (RAGE) in ovarian cancer

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Introduction: Ovarian cancer is one of the important challenges in the field of gynecologic oncology because of some problems in understanding its etiology and pathogenesis. Receptor for advanced glycation end products (RAGE) is a multiligand trans-membranous receptor which is upregulated in some human cancers. Mechanisms of RAGE involvement in carcinogenesis of ovarian cancer are unknown. OBJECTIVE: This study aimed to investigate the expression of RAGE in ovarian cancers and its association with clinicopathological characteristics.

METHODS: The RAGE expression level in ovarian cancer and corresponding noncancerous tissues were analyzed by real time quantitative RT-PCR and immunohistochemistry techniques.

RESULTS: Results indicated that RAGE gene was overexpressed in ovarian cancer tissue compared with adjacent noncancerous tissue ($p < 0.001$). A significant association between RAGE expression and tumor size ($p = 0.04$), depth of stromal invasion ($p = 0.031$), lymphovascular invasion ($p = 0.041$) and stage of cancer ($p = 0.041$) was observed. The receiver operating characteristic (ROC) analyses yielded the area under the curve (AUC) values of 0.86 for RAGE in discriminating ovarian cancer samples from non-cancer controls.

CONCLUSIONS: In conclusion overexpression of RAGE in ovarian cancer may be a useful biomarker to predict tumor progression.

Keywords: Carcinoma, ovarian cancer, receptor for advanced glycation end products, tumor

A-10-1391-1

Molecular docking investigation of oximinoarylsulfonamide as potential inhibitor of the main protease of coronavirus

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Introduction: Molecular docking investigation of oximinoarylsulfonamide as potential inhibitor of the main protease of coronavirus Kimia Mokhtari, Azizeh Asadzadeh Department of Biology, Faculty of Basic Sciences, NourdaneshInstitute of Higher Education, Meymeh, Isfahan, Iran Background: The SARS-CoV-2 has initiated in Wuhan city of China and then extend all around the world as a health emergency. For many viruses, the protease enzyme plays a critical role in viral protein maturation by cleaning proproteinsafter their translation into the host cell cytosol, as a result, SARS-CoV-2 proteases Mpro and PLpro are promising targets for antiviral drug development. Molecular docking is one of many computational tools that can be used in drug discovery. In this study, our aim was to molecular docking studies of the interaction of SARS-CoV-2 protease (Mpro) with Oximinoarylsulfonamide ($C_{34}H_{46}N_6O_6S_2$) in order to control Coronavirus disease.

Methods: The crystal structure of Mopar (PDBID: 6LU7) was obtained from the protein data bank. Oximinoarylsulfonamide structure (Compound CID: 9600417) was obtained from https://pubchem.ncbi.nlm.nih.gov and the energy of the compound was optimized by using HyperChem software. Finally, the docking study was carried out by using the AutoDock 4.2 software.

Results: GLN127, CYS128, ALA129, LYS137, ASN151 andALA129 in Mpro were the sites for hydrogen bonding interactions with Oximinoarylsulfonamide.

Conclusion: Oximinoarylsulfonamide was able to occupy the catalytic site of the SARS-CoV-2 protease (Mpro). We acknowledge that computational docking analysis has its limitations, and that further laboratory and clinical studies are needed to validate the inhibitory effects of this candidate against SARS-CoV-2 as potential drug for COVID-19. Key words: Mpro, Oximinoarylsulfonamide, molecular Docking, in silico, Coronavirus

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miR-1 and Endometriosis

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Background: Endometriosis is a painful disorder in which endometriotic tissue grows outside the uterine cavity. the underlying pathophysiology remains a mystery but There is evidence that proves microRNAs (miRNAs), posttranscriptional regulatory molecules, play a role in endometriotic lesion development. In this study, we investigated the role of mir-1 which can be a potential therapeutic target for treating this disease and There are no extensive studies on the expression of this miRNA in endometriosis.

Method: In This Case-Control research, we profiled the expression of miR-1 in 15 paired eutopic and ectopic endometrium of women suffering from endometriosis, who were referred to the Shahid Sadoughi yazd Hospital for treatment, and 15 normal endometrium of women without endometriosis, as the control group, using quantitative reverse transcription PCR (q-RT PCR). To compare the mean of the relative expression of miR-1 in three groups, SPSS software and ONE WAY ANOVA with post-hoc Tukey's HSD test were used.

Result: The relative expression of miR-1 in both ectopic and eutopic tissue pairs of patients with endometriosis showed a significant decrease compared to the samples of healthy individuals ($p < 0.0001$). However, no significant difference was observed between the relative expression of the miR-1 between the ectopic and eutopic groups ($p = 0.2231$).

Conclusion: Considering the different realetive expression of mir-1 between patients and healthy individuals, it seems that miR-1 can probably be used as a diagnostic and therapeutic biomarker for endometriosis.

Keywords: Endometriosis, microRNA expression, Micro-ribonucleic acid, miR-1

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Investigation of antioxidant activity of biosynthesized Copper Nanoparticles using aqueous extract of Artemisia annua

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Introduction: Green synthesis of Copper Nanoparticles (CuNPs) using medicinal plant extract has several benefits, including being simple, cost-effective, environment-friendly, and easily feasible for large-scale production. Artemisia annua, known for containing the anti-malarial phytochemical Artemisinin, is an important medicinal herb with various biological activities. In this study, the antioxidant activity of biosynthesized CuNPs has been investigated.

Methods: The CuNPs were synthesized using an aqueous extract, obtained from the Artemisia annua leaves. Antioxidant activity of different concentrations of CuNPs (12.5-125 µg/ml) and the standard reference compound, Ascorbic Acid (same concentrations as CuNPs), was measured using a 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging assay and the IC50 value was calculated using the plotted dose-response curve. Finally, the absorption of samples was measured at 517 nm.

Results: analyzing the final data from DPPH assay confirmed that with an increasing concentration of biosynthesized CuNPs, the free radical scavenging ability also increased. for an instance, The DPPH radical scavenging effect of the concentration 125 µg/mL of biosynthesized CuNPs was about 72.4%. Moreover, the IC50 value for biosynthesized CuNPs and ascorbic acid were 102.73 µg/ml and 71.83 µg/ml, respectively.

Conclusion: The results demonstrated that biosynthesized CuNPs exhibited promising antioxidant properties and could be utilized in the biomedical, cosmetic, food and pharmaceutical industries.

Keywords: Keywords: antioxidant activity, copper nanoparticles, Artemisia annua, DPPH method, green synthesis

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The H19 rs217727 Polymorphism Is Associated with Ovarian Cancer Susceptibility

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Introduction: Genetic aspects play the main role in the occurrence and development of ovarian cancer. Lack of protein-coding capacity is a main characteristic of long noncoding RNAs (lncRNAs) which, as molecular biomarkers, have found a novel pharmacological application in cancer and are reported to be important regulators of gene expression. H19 is reportedly involved in cancer progression and tumorigenesis. Among gynecologic cancers, ovarian malignancies are the main reason of death in developed countries.

Methods: The aim of the present study was to evaluate the correlation of ovarian cancer susceptibility with H19 gene in an Iranian population. We studied 150 Iranian patients and 150 controls. DNA genotyping was done by the tetra-primer ARMS-PCR method. The susceptibility of ovarian cancer and H19 rs217727 polymorphism was further analyzed.

Results: The H19 rs217727 T allele frequency was significantly higher in ovarian cancer cases ($P < 0.05$), and the polymorphism of H19 rs217727 was associated with ovarian cancer susceptibility in the codominant model.

Conclusion: This study showed that rs217727 and ovarian cancer susceptibility were statistically correlated in the Iranian population.

Keywords: ovarian cancer, protein-coding capacity, long noncoding RNAs (lncRNAs), H19

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Chlorogenic Acid Improves Anti-Lipogenic Activity of Metformin by Positive Regulating of AMPK Signaling in HepG2 cells

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Page | 168

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Introduction: Metformin improves lipid profile; however, combination therapy is developing to increase its effectiveness and reduce the deleterious effects of metformin. Chlorogenic acid (CGA) has exhibited lipid-lowering effects. This study aimed to investigate the combined effect of metformin and CGA on lipid accumulation, as well as to elucidate the engaged mechanism in HepG2 cells.

Methods: To find the non-lethal doses of metformin and CGA, MTT assay was performed. High Glucose (HG) at 33 mM was used to induce lipogenesis in HepG2 cells. Following treatment with different concentrations of metformin and CGA, total lipid content (Oil Red O-staining), triglyceride level, the genes expression of SREBP-1c and FAS, and phosphorylation of AMPK and ACC were measured.

Results: Both Metformin and CGA decreased HG-induced lipid accumulation individually, by decreasing total lipid content and triglyceride level. The lowest effective doses of metformin and CGA were 0.25 mM and 5µM, respectively, which significantly reduced SREBP-1c and FAS genes expression. The combination of these concentrations reinforced these effects. The phosphorylation of AMPK and ACC were more increased by metformin in combination with CGA than both individually.

Conclusion: Our findings suggest that CGA synergistically enhances metformin lipid reducing action via the regulating of involved factors in fatty acid synthesis. Therefore, co-administration of metformin with CGA may have further medical value in treating lipid metabolism disorders.

Keywords: AMP-Activated Protein Kinases, Combined Therapy, Chlorogenic Acid, Lipid metabolism, Metformin

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Maternal Zinc Supplementation prevents LPS-exposure Alterations in Inflammatory Markers Expression and Astrocyte Activation in an animal model of Maternal Immune Activation

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Introduction: Maternal Immune Activation (MIA) model is known to be associated with the pathophysiology of neuropsychiatric disorders such as Schizophrenia. Prenatal exposure to Lipopolysaccharide (LPS) is one of the several factors boosting the risk of schizophrenia in the next generation. In the present study, we investigated the deleterious effects of LPS during gestation on pro-inflammatory markers in the prefrontal cortex (PFC) of adult male offspring. Based on protective roles of zinc in brain function, we also utilized zinc supplementation during pregnancy to examine whether it could attenuate consequences caused by maternal LPS.

Methods: LPS was administered intraperitoneally (0.5mg/kg) on Gestational Day 15&16 and ZnSO4 supplementation (30mg/kg) was given via gavage during pregnancy. At post-natal day 60, the expression level of inflammatory markers such as IL-6, IL-1β, NF-κB was measured by qPCR. Furthermore, prefrontal cortex immunostained to evaluate the density of Astrocyte cells, in PFC.

Results: the present study showed significant upregulation of all inflammatory markers as well as increased density of Astrocyte cells caused by LPS. However, zinc treatment ameliorated the LPS-induced deficits in male offspring.

Conclusion: these findings indicated that zinc supplementation during gestational period could alleviate the deleterious effects of prenatal LPS in the next generation.

Keywords: Schizophrenia, Lipopolysaccharide, Zinc Supplementation, Astrocyte

Perspective of therapeutic and diagnostic capacity of nanobodies against SARS-CoV-2: A systematic review

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Introduction: The newly emerged coronavirus (SARS-CoV-2) continues to infect humans, and no effective treatment has yet been found. Antibody therapy is one way to control infection caused by COVID-19, but the use of classical antibodies has many disadvantages. Heavy chain antibodies (HCAbs) are single-domain antibodies derived from the Camelidae family. The variable part of these antibodies (Nanobodies or VHH) has interesting properties such as small size, identify criptic epitopes, stability in harsh conditions, good tissue permeability and cost-effective production causing nanobodies have become a good candidate in the treatment and diagnosis of viral infections.

Methods: Totally 157 records (up to November 10, 2021), were recognized to be reviewed in this study. 62 studies were removed after first step screening due to their deviation from inclusion criteria. The remaining 95 studies were reviewed in details. After removing articles that were not in the study area, 45 remaining studies met the inclusion criteria and were qualified to be included in the systematic review.

Results: In this systematic review, the application of nanobodies in the treatment and detection of COVID-19 infection was reviewed. The results of this study showed that extensive and sufficient studies have been performed in the field of production of nanobodies against SARS-CoV-2 virus and the obtained nanobodies have a great potential for use in patients infected with SARS-CoV-2 virus.

Conclusion: According to the obtained results, it was found that nanobodies can be used effectively in the treatment and diagnosis of SARS-CoV-2 virus.

Keywords: Nanobody, SARS-CoV-2, Therapeutic application, Diagnosis application, In-vivo, In-vitro

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The effect of varicocele condition on sperm parameters and heat-shock protein-A2 in male rats

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Introduction: Among all the different reasons for infertility, varicocele condition, an enlargement of the spermatic veins, with high incidence show a functional decrease in spermatogenesis and sperm production due to high level of heat stress and oxidative stress. Several studies showed the importance of heat shock proteins (HSPs) for sperm development and its association with heat stress condition. Therefore, we aimed to assess the influence of varicocele induction on sperm function, and heat shock protein (HSPA2).

Method: 20 male Wistar rats were divided into 3 groups: control, sham and varicocele induction. After 2 months of surgery, rats were sacrificed and left epididymis and testes were used for study parameters. After release of sperm from epididymis, sperm parameters, and chromatin status (DNA damage by acridin orang staining, and protamine deficiency by chromomycin A3) were assessed. Expression of testicular HSPA2 was evaluated by western blot and immunohistochemistry techniques. We analyzed study parameters ANOVA and independent t-test.

Results: Sperm concentration, motility and normal morphology were significantly lower in varicocele group compared with control and sham groups (P<0.05). In addition, we observed a significant increase in protamine deficient sperm, and DNA damage in varicocele group compared to control group and, sham group (P<0.05). Furthermore, a high significant expression in HSPA2 protein was observed in varicocele group compared with other groups (P<0.05). Immunohistochemical analysis showed expression of HSPA2 in the round spermatid and sperm.

Conclusion: Varicocele condition has a negative effect on decreased sperm quality. To deal with acute varicocele conditions in the rat model, the expression of HSPA2 protein is increased to overcome heat stress and oxidative stress. However, in the human model, due to chronic varicocele conditions, the expression of this protein is reduced. Both of these conditions can lead to low quality of sperm function.

Keywords: varicocele induction, sperm parameters, heat shock protein

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HDAC Inhibitors: Novel Therapies in advanced melanoma

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Introduction: Epigenetic dysregulations of histone deacetylases (HDAC) are directly associated with cancer cell's growth, so their inhibitors have been applied as promising therapeutic agent in advance and inoperable melanoma.

Methods: This review described a number of recent articles to investigate the novel melanoma therapy based on HDACIs and related mechanism from Google scholar and PubMed.

Results: The unique aspect of HDAC inhibitors is their selective cytotoxicity that lead to a range of immunologic changes such as increased expression of MHC I/II, CD40, CD80, CD86 and also pro-inflammatory surface indicators on melanoma cells. Moreover, HDAC inhibitors can diminish myeloid-derived suppressor cells. Taken together, increased T cell activation and improved immunogenicity of melanoma cells. Stoppage of cell growth and apoptosis-prompting effects of HDAC inhibitors was seen on A375 melanoma cells by producing ROS, inhibiting angiogenesis and increasing autophagy. Recent study has highlighted the role of HDAC inhibitors via TNF-related apoptosis-inducing ligand and its signaling death receptor 5 (TRAIL/DR5) pathway which sensitize apoptosis-resistant melanomas to Cytotoxic T Lymphocytes. Due to low-observed side effect in vivo, HDAC inhibitors are considered highly potential agent in combination therapy of melanoma. Co-targeting of HDAC inhibitors involved suberoylanilide hydroxamic acid (SAHA) and BRAF inhibitors destroy melanoma cells by inducing necrosis in a synergistic manner. Besides, in vivo and vitro evidence suggest that PD-L1 and, to a lesser extent, PD-L2 expression are upregulated by Class I HDAC inhibitors. Tucidinostat, as a selective HDAC inhibitor, when combine with immune checkpoint inhibitors (iCPI) in melanoma patients, intervenes in tumor microenvironment (TME) epigenetic modifications, result in increased efficiency of iCPI–anti-PD-L1 monoclonal antibodies- and present reasonable justification for combination therapies.

Conclusion: HDAC inhibitors are exciting novel anticancer agents that induce epigenetic reprogramming and immunomodulation. The increase in overall survival provide a valid reason for use it in combination with other effective treatments.

Keywords: Histone deacetylases inhibitors, Melanoma, Combination therapies.

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Association of FOXO3 rs2253310 polymorphism with risk of type 2 diabetes mellitus: A case-control study

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Introduction: Environmental and genetic factors interact to cause Type 2 diabetes mellitus (T2DM), a diverse and complicated condition. It has been established that Forkhead box class O (FOXO) transcription factors control the body's energy metabolism, skeletal muscle hypertrophy, and substrate switching, among other aspects of metabolism. This preliminary study is aimed at investigating if SNPs in Forkhead box O3 (FOXO3), a constituent of the insulin and insulin-like-growth-factor 1 signaling pathway, could affect the risk of developing T2DM development.
Methods: A total of 1000 age- and sex-matched subjects (including 500 controls and 500 patients clinically diagnosed with T2DM) were recruited from a southeast Iranian population. Genomic DNA was extracted from nucleated blood cells and genotyped for FOXO3 rs2253310 polymorphism using the polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) technique. Deviation from Hardy-Weinberg equilibrium (HWE) was calculated using the Chi-square test. Multiple logistic regression analysis was used to calculate odds ratios (ORs) with 95% confidence intervals (CIs).
Results: We observed no significant difference between cases and controls in terms of age (p=0.066) and gender (p=0.290). Our findings demonstrated that FOXO3 rs2253310 did not violate HWE in controls (p-value for HWE = 0.333). In addition, the studied variant was correlated with T2DM risk under codominant GG vs. CC [OR = 2.09, 95% CI (1.47-2.97), p <0.001], recessive GG vs. CC+CG [OR = 1.97, 95% CI (1.43-2.70), and allelic G vs. C [OR = 1.45, 95% CI (1.21-1.73), p <0.001] contrasted genetic models. Moreover, under the dominant model, subjects with the G allele (CG/GG) had higher susceptibility to T2DM than those with CC genotype [OR = 1.36, 95% CI (1.05-1.77), p = 0.018].
Conclusion: FOXO3 rs2253310 polymorphism may enhance the risk of T2DM by modifying multiple signaling pathways and can be considered a potential prognostic indicator in personalized medicine.

Keywords: FOXO3, Type 2 diabetes mellitus, single nucleotide polymorphisms, SNP

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The effect of resveratrol and gallic acid on SIRT1 mRNA expression in prostate cancer cell lines

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Introduction: Polyphenols are secondary metabolites of plants, extensively investigated for their potential benefits in health issues concerning various cancer. Polyphenols can exert an anti-cancer effect by targeting tumor-associated signaling pathways. SIRT1 is an NAD+ dependent histone deacetylase that plays a role in the epigenetic features of cells. SIRT1 also could deacetylate factors that are involved in tumor progression or suppression. Previous studies showed that SIRT1 expression is significantly induced in prostate cancer. On the other hand, SIRT1 depletion in prostate cancer cell lines leads to prostatic intraepithelial neoplasia (PIN) due to the suppression of the autophagy pathway. Gallic acid (Gal) and resveratrol (Res) are natural polyphenols belonging to phenolic acids and stilbenoid sub-groups, respectively. This study examined the effects of mentioned polyphenols on the SIRT1 mRNA expression in PC3 and DU145 cell lines. **Methods:** To determine the effect of Gal and Res on SIRT1 mRNA expression of DU145 and PC3 cell lines, the cells were treated with different concentrations of polyphenols for 72h (2.5, 5, 10, and 20μM). Then, the total RNA was isolated by an RNX-plus solution (Cinnagen, Tehran, Iran). Real-Time PCR was performed on the StepOne Real-Time PCR system (Applied Biosystems, USA).

Result: Our result showed that high concentration of Res and Gal significantly induces SIRT1 mRNA expression in PC3 and DU145.

Conclusion: SIRT1 interacts with several signaling pathways including PI3K/AKT pathway, autophagy, TGF-β signaling pathway, Wnt signaling pathway, etc. According to previous studies, Gal and Res inhibit cell proliferation of prostate cancer cell lines. SIRT 1 activity has been shown to suppress apoptosis and cell senescence. Hence, there is disagreement about the exact role of SIRT1 in extending or inhibiting cancer formation. The present findings suggest that Gal and Res may be considered as anti-neoplastic agents by affecting the expression of SIRT1 in prostate cancer cell lines.

Keywords: Resveratrol, Gallic acid, Prostate cancer, SIRT1

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The Relationship between Salivary Alpha Amylase Activity and mental health status in Patients with COVID-19

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Introduction: The symptoms of new coronavirus disease 2019 (COVID-19) can range from mild to severe. It has been shown that the spread of COVID-19 in addition to poor physical health can affect the mental health of people. The association between acute respiratory infections and psychological disorders has been evaluated in some studies. Therefore, this study was designed to evaluate the relationship between the level of active biomarker in stress, anxiety, and/or depression, and the severity of COVID-19 by measuring the salivary level of alpha-amylase.
Methods: This cross-sectional study was performed on 120 participants in three groups including healthy individuals (control), outpatients, and hospitalized patients with a definitive diagnosis of COVID-19. The standard questionnaire of Depression Anxiety Stress Scale-21 (DASS-21) was used to assess the mental health status. Assessment of salivary biomarker was performed according to the instructions of the assay kit.
Results: A significant increase in salivary levels of alpha-amylase and the DASS-21 score was observed in the group of hospitalized patients with SARS-CoV-2 compared to the outpatients and the control group. The results obtained from Pearson correlation analysis of the studied variables are as follows: a significant positive correlation was found between the salivary level of alpha-amylase and the DASS-21 score.
Conclusion: The results of this study showed a high level of psychological distress in patients with COVID-19 compared to the healthy control group and indicated a significant direct relationship between stress, anxiety, and/or depression and the severity of COVID-19.

Keywords: COVID19, salivary alpha-amylase, stress, DASS-21

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Investigating the role of Quercetin in increasing the rate of cisplatin-induced apoptosis via the NF-κB pathway in MG-63 cancer cells

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Introduction: Treatment of patients with osteosarcoma (OS) remains a major clinical challenge, which accounts for the second leading factor of tumor-related mortality in the pediatric age. Numerous studies suggest that the co-treatment of chemotherapeutic agents with flavonoids such as Quercetin (Que) may enhance tumor cells' susceptibility to these agents. Overall, we sought to evaluate the underlying mechanisms governing the phenomenon; wherein Que affects the cisplatin-induced apoptosis in OS cells, focusing on the Nuclear factor-kappa B (NF-κB) pathway.

Methods: The Que, Cisplatin, and their combination's general cytotoxicity effects were evaluated using a 3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay for 72 hrs. The protein expression levels of NF-κB were detected by an enzyme-linked immunosorbent assay (ELISA) Kit. Flow cytometry was used to evaluate cell apoptosis.

Results: Que considerably elevated the cytotoxicity of Cisplatin (P< 0.05). Que also dramatically down-regulated the expression levels of NF-κB in MG-63 cells compared to mono-treatment (P< 0.05). Besides, Que promotes cisplatin-induced apoptosis in MG-63 cells.

Conclusion: Our study's findings provide an exact point in the field of adjuvant therapy in osteosarcoma. In other words, this study could provide new insights into a better understanding of the role of Que in elevating cisplatin-induced apoptosis with NF-κB down-regulation.

Keywords: Osteosarcoma, Cisplatin, Quercetin, Apoptosis, NF-κB.

Naringenin induces intrinsic and extrinsic apoptotic signaling pathways in cancer cells: A systematic review and meta-analysis of in vitro and in vivo data

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Introduction: Various reports show the beneficial effect of naringenin on the development of cancer. We hypothesized that naringenin suppresses cancer cells by activating intrinsic and extrinsic apoptosis pathways. This systematic review and meta-analysis were performed to reveal the effect of naringenin on cancer inhibition in vitro and in vivo by altering apoptotic factors.
Method: Literature search was carried out using electronic databases including PubMed, Web of Science, Scopus, Google Scholar, and Embase up to February 2021. The heterogeneity test of the included studies was performed using the PRISMA checklist protocol and I2 statistic, respectively. Pooled standard mean difference (SMD) and effect size (ES) with 95% confident interval (CI) were used to evaluate each relationship.
Result: A total of 32 articles were enrolled in our final analysis. Meta-analysis of the pooled findings for apoptosis, viability percentage, and apoptotic factors determined that treatment with naringenin affects viability and apoptosis in cancer cells in vitro and in vivo. Moreover, the results of in vitro experiments showed that naringenin increases the activity of caspase-3 (ES: 5.04; 95% CI: [2.61 to 7.47]; I2= 99.9), caspase-9 (ES: 2.99; 95% CI: [2.47 to 3.51]; I2= 93.7%), caspase-8 (ES:2.86; 95% CI: [1.11 to 4.61]; I2= 99.7%), and Bax expression (ES: 2.73; 95% CI: [1.91 to 3.55]; I2= 99.4%) in cancer cells. It also increased the apoptotic rate and the activity of caspase-3 and caspase-9 in tumor-bearing animals.
Conclusion: Overall, our findings highlight the potential therapeutic effects of naringenin in cancer inhibition through caspases cascade.

Keywords: Naringenin, Apoptosis, Cancer, Caspase, Meta-analysis

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Insight of propolis activity in cancer cell line by cell cycle arrest; A systematic review

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Introduction: Cancer is the second cause of death worldwide. Due to various side effects of chemical ugs, researchers are inclined to assess natural products as effective supplements in the treatment and prevention of cancer. Propolis, the natural product of honeybee, presents a wide range of biological activities, especially anti-cancer properties. The association between the cell cycle and cancer was approved, and propolis can inhibit cancer progression by affecting the cell cycle. This systematic review aims to assess the original in vitro studies evaluating the inhibitory effect of propolis in the cell cycle in various cancer cell lines.

Methods: The search was conducted on the Google Scholar, PubMed, and ProQuest databases, using with terms "propolis," "Propolis and cancer," "Propolis and cell cycle," and simultaneous search for "propolis and cancer and cell cycle" were 1400 articles which 47 of them were original and in vitro articles that 10 of them were selected for review.

Results: Studies have shown that propolis at concentrations of 5 to 200 µg / ml causes the cycle to stop at its checkpoints by altering changes such as phosphorylation and inhibiting factors involved in cell cycle control. Propolis stops the cell cycle at G2 / M by inhibiting cyclin CDK2 / 4/6 and D and increasing the expression of p21 / p27 and p53. On the other hand, propolis can disrupt the E2F (a group of genes that encodes a family of transcription factors) complex by inhibiting Rb phosphorylation, which plays a crucial role in cell cycle control and prevents cell proliferation.

Conclusion: This systematic review showed the positive effect of propolis on cell cycle arresting, which is one of the most critical factors that increase the number of cancer cells. However, many clinical studies are needed to determine the positive effect of this natural product.

Keywords: propolis, cell cycle, cancer, cell line

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Designing a new aptasensor to identify the SARS-CoV-2

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Introduction: DNA has been extensively used for target recognition in biosensors because of its stability, cost effectiveness, and easy modification. Aside from complementary nucleic acids, DNA can also recognize other types of target molecules by using DNAzymes, and aptamers of DNA structure formed on non-canonical Hoogsteen-type base pairing. G-quauplex (G4) structures are DNA tetraplexes that Four guanine bases associate with each other through Hoogsteen hyogen bonds to form a guanine tetrad plane (G-quartet), and then two or more G-quartet planes stack on top of each other to form a G4 structure. Hemin/G-Quauplex DNAzyme can quickly detect molecular goals by the naked eyes which does not require complex instruments.In this research, an attempt has been made to introduce a new and easier method for identifying the corona virus by using SARS-CoV-2 Nucleocapsid Protein and aptasensor.

Methods: Using bioinformatics servers such as Mfold, the interference or non-interference between G-quauplex sequence and Nucleocapsid Protein-binding aptamer was checked. Fortunately, by placing the CCC spacer, the interference in folding was resolved and the functional lobes of each part of the aptosensor were folded well. G. quauplex GTGGGTAGGG CGGGTTGGGAptamer

GCAATGGTACGGTACTTCCGGATGCGGAAACTGGCTAATTGGTGAGGCTGGGGCGGT Full sequence GTGGGTAGGGCGGGTTGGGCCCGCAATGGTACGGTACTTCCGGATGCGGAAACTGGCTAATTGGTGAGGCTGGGGCGGT

Result: In this research, a new aptasensor was designed for the detection of theSARS-CoV-2 and due to the absence of disruption in the folding of G-quauplex and aptamer, we will theoretically conclude that this aptasensor can be used for the detection of the SARS-CoV-2.

Conclusion: the nucleocapsid (N) protein is one of the most crucial structural components of SARS-CoV-2.Due to its stability at high temperature and different concentration of salt concentration, the designed aptasensor can help in identifying theSARS-CoV-2 with a much lower cost and more easily.

Keywords: Aptasensor, SARS-CoV-2

Fabrication of chitosan/pectin nanoparticle containing 5-flurouracil

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Introduction: The aim of this study was the fabrication of nanoparticle for targeted ug delivery to the colon by chitosan and pectin. These biopolymers have advantages such as biocompatibility, non-toxicity, biodegradability, low price and mucoadhesive properties which make them interesting candidates for using in pharmaceutical and biomedical applications. 5-Fluorouracil (5-FU) is an effect antineoplastic and anti-metabolite material, prevents DNA and RNA synthesis which arrest cell growth and uses in the treatment of a range of cancers, including colorectal and breast cancers.

Methods: In this study, nanoparticle chitosan/pectin was made using ionic gelation method and blending technique. Then 5-fluorouracil was loaded into the prepared nanoparticles. The physical and chemical properties of nanoparticles were investigated by FTIR and DLS. Finally, in vitro ug release behavior was evaluated in different pHs at 37°c.

Result: The result of FTIR showed that there are chitosan, pectin and 5-flurouracil in the nanoparticle and the result of DLS demonstrated that the size of nanoparticle is about 660 nm. Also, the highest encapsulation efficiency (~97.0%) of the nanoparticle was observed. The ug release tests of the nanoparticle is underway.

Conclution: The obtained results showed that the nanoparticle containing 5-fu are suitable for ug delivery to the colon.

Keywords: Chitosan, Pectin, 5-fu, Blending, ug delivery, Cancer, Nanoparticle.

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Measurement of IL6 Serum Level in Individuals with Hypothyroidism and Hyperthyroidism and Investigation of these Serums on the Induction of Oxidative Stress in Cancer Cells

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Introduction: Hypothyroidism and hyperthyroidism are common disorders that are defined by disturbances in the synthesis and secretion of thyroid hormones. There is a link between thyroid hormones and cancer malignancies. Cancer, oxidative stress and inflammation are closely related. The occurrence of inflammation in the tumor microenvironment leads to an increase in pro-inflammatory cytokines interleukin-6 and reactive oxygen and nitrogen species. The present study aimed to measure the serum levels of thyroid hormones and IL6 in people with hypothyroidism and hyperthyroidism and study the effects of these sera on the induction of oxidative stress in MCF-7 cancer cells.

Methods: Thyroid hormones (T3, T4 and TSH) were measured in three groups of minimum 30 samples in normal, hypothyroid and hyperthyroid sera by quantitative luminescence immunoassay. Thereafter, ELISA test was conducted for IL6 measurement in the selected sera. Finally, one serum of each group was chosen to be added to MCF-7 cell culture microenvironment for 24h and 48h. Induced oxidative stress was measured by Griess test.

Results: The average level of IL6 production was seen to be increasing in the normal, hyperthyroid and hypothyroid sera, respectively. After 24h and 48h of exposure to specific-serum-containing media, generally, the level of nitric oxide production and induction of oxidative stress by MCF-7 cells were also highly proportional to the produced IL6 serum level.

Conclusion: Hypothyroidism and hyperthyroidism are associated with increased IL6 serum levels. Considering the relationship between thyroid hormones and cancer, and also considering that inflammation and oxidative stress are related processes, which are easily induced by each other; The results of this research showed that the presence of more inflammatory cytokine IL6 in the tumor microenvironment around the cells can generally lead to an increase in the production of more NO or reactive nitrogen species.

Keywords: Hypothyroidism, Hyperthyroidism, Oxidative Stress, Cancer

A-10-1624-1

Cytotoxic effect of iNOS agonist and antagonist and green tea polyphenols co-treatment on breast cancer stem-like cells

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Introduction: Breast cancer is one of the most prevalent cancers and the second leading cause of death in women under 40 worldwide. Cancer stem cells (CSCs) can initiate and proceed cancerous factors with self-renewal, metastatic, and treatment resistance potentiality, making them a suitable therapeutic target. The effects of Green Tea Polyphenols (GTP) have been proven in breast cancer comparing women, who consume green tea in their daily diet with women, who don't. In many tumors iNOS expression is high, however, the role of iNOS in breast cancer pathogenesis is complex and dual. Here, we evaluated the cytotoxic potential of agonist (sildenafil) and antagonist (L-NAME) of iNOS in combination with GTP on CD44+/CD24- CSC-Like cells (CSC-LCs), their parental cells (MCF-7) and A-MB-231.

Methods: Cytotoxic dosage of each single ug was determined by MTT assay. These concentrations have been used for combination therapy with GTP+Sildenafil and GTP+L-NAME. The synergistic combination dose has been confirmed by two software, Compusyn and Combenefit, which has been used for apoptosis, cell cycle, and ROS (reactive oxygen species) analysis.

Results: GTP+L-NAME had a synergistic effect on A-MB-231 and CSC-LC and no such effect was observed on MCF-7. GTP+Sildenafil induced considerable cytotoxicity on MCF-7, their CD44+/CD24+ stem-cells, and A-MB-231 at the same combination dose. Flowcytometric tests have shown more than 70% of A-MB-231 and MCF-7 cells underwent apoptosis and Sub-G1 arrest has been observed on MCF-7 cells along with a considerable decrease in ROS production of A-MB-231 cells with GTP+Sildenafil.

Conclusion: GTP and L-NAME are less likely to be cytotoxic for A-MB-231 and CSC-LC cells and more cytotoxic for MCF-7. A decrease in ROS production of A-MB-231 cells after treatment with GTP+Sildenafil can be considered an antiproliferative mechanism but the exactitude of this hypothesis needs further investigations. All together GTP+Sildenafil has shown more significant antiproliferative effects.

Keywords: Breast Cancer, GTP, CSC-LCs, Sildenafil, L-NAME, Combination Therapy

A-10-1634-1

Achillea Wilhelmsii C. Koch Hyoalcoholic Extract Induces Apoptosis and Alters LIN28B and p53 Gene Expression in Hela Cervical Cancer Cells

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Introduction: Inappropriate activation of the proto-oncogene LIN28B and inactivation of the p53 tumor suppressor, have been shown to have a critical role in tumorigenesis. Previousresearch has shown therapeutic potential for the use of herbal plants as an alternative strategy for cancer treatment. Achillae wilhelmsii C. Koch is a plant that has been traditionally used for its medicinal properties. The aim of this study was to investigate the cytotoxic and apoptosis-inducing effect of Achillea wilhelmsiiC. Koch hyoalcoholic extract (AWHE) on HeLa cervical cancer cells and its effect on LIN28B and p53 expression.

Methods: The cytotoxic activity of AWHE was evaluated on HeLa cells using a trypan blue exclusion assay. The Annexin V/PI double staining assay was used to evaluate the apoptosis-inducing effect of the extract. The expression of LIN28B and p53 mRNA was measured using the real-time-PCR method.

Results: Treatment with AWHE was shown to induce cytotoxicity in both time and concentration-dependent manners($P < 0.05$). The propositionof HeLa cells undergoing apoptosis increased with increasing concentrations of AWHE ($P < 0.05$). The mRNA levels of p53 increased following 12, 24, and 48 hours of AWHE treatment whereas the mRNA levels of LIN28B were significantly decreased after 4 to 12 hours of AWHE treatment ($p < 0.05$).

Conclusions: Our findings confirmed the pro-apoptotic function of AWHE on the cervical cancer HeLa cell line. This indicates that targeting the LIN28B signaling cascade may be a promising therapeutic strategy for cervical cancer. Further research is required to understand the therapeutic effects of AWHEin primary human cervical cancer cells and a pre-clinical cervical cancer model.

Keywords: Achillea, Apoptosis, Cervical cancer, LIN28B, p53.

A-10-1381-2

Comparative study of the effect Xanthotoxol and Aegle marmelos on S100P protein against breast cancer on the basis of bioinformatics analysis

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Introduction: Breast cancer (BC) is one of the biggest dilemmas in universal health affecting more than one million females per year. S100 calcium-binding protein P (S100P) is known to metastasis and mediate tumor growth in BC and several other cancers. Its expression is closely associated with ug resistance and poor clinical outcome. In the current study, we compared the effect of Xanthohumol (XN) as one of the bioactive substances derived from hops (Humulus Lupulus L.) with the medicinal plant Aegle marmelos on S100P protein against BC through in-silico analysis.

Methods: In this descriptive-analytical study, ligand preparations for all the 3D structures of bioactive were retrieved from PubChem in sdf file format. Chimera 1.15rc software and Computed Atlas of Surface Topography of Protein (Castp) were used to edit the desired protein and visualize the 3D model. The biologically active 3D structure of targeted protein S100P (PDB ID: 1J55), was extracted from the Protein Data Bank (PDB) as a pdb file. The molecular docking process is carried out in PyRx 8 with AutoDock Vina to determine high-affinity binding sites.

Result: All compounds used in this experiment showed good antitumor activity against BC via binding to the inhibitor site of S100P. Aegle marmelos displayed the work correctly with the lowest binding energy value of -6.7 kcal/mol, RMSD 0.0 as compared to the binding energy value of XN -5.6 kcal/mol, RMSD 0.0.

Conclusion: Our study determined that S100P can be a potential treatment target as well as a prognostic biomarker of BC. Furthermore, in this molecular docking study, the result predicts that with breast cancer cell line (PDB ID: 1J55); Aegle marmelos is more efficient than Xanthotoxol and can be developed to treat cancer.

Keywords: Breast cancer, Xanthotoxol, Aegle marmelos, Molecular docking, S100P protein

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The effects of quercetin on oxidative stress and inflammatory mediators in peripheral blood mononuclear cells

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Introduction: Quercetin (3,3',4',5,7-pentahyoxyflavone) is a dietary flavonoid that has good antioxidant and anti-inflammatory properties. The present study aims to determine these effects in peripheral blood mononuclear cells (PBMCs) evoked by lipopolysaccharides (LPS).

Methods: The mRNA expression and protein secretion of inflammatory mediators were evaluated by enzyme-linked immunosorbent assay (ELISA) and quantitative real-time polymerase chain reaction (PCR), respectively. Western blotting was utilized for assessing p65-NF-κB phosphorylation. Ransod kits were used to evaluate the glutathione peroxidase (GPx) and superoxide dismutase (SOD) activity in the cell lysates.

Results: The findings revealed that quercetin significantly attenuated the expression and secretion of inflammatory mediators and p65-NF-κB phosphorylation in LPS-induced PBMCs. Additionally, quercetin dose-dependently improved the activities of SOD and GPx enzymes and decreased LPS-mediated oxidative stress in PBMCs.

Conclusion: The data show that quercetin plays a vital role in the amelioration of inflammation and oxidative stress caused by LPS in PBMCs.

Keywords: IL-6, NF-κB, Oxidative stress, Quercetin, TNF-α

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The Simulation of CpsA-CpsC-L-Rib-ACAN Peptide fusion anti-Cancer part in the insilico model

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Introduction: Cancer is the second leading cause of death in the world, after cardiovascular disease. Surgery, chemotherapy, radiotherapy, and immunotherapy are the most common treatments for cancer. Each type of cancer treatment has several side effects, such as ug resistance, and for this reason, scientists today are trying to use other methods to treat cancer. One of the new methods of cancer treatment is anti-cancer peptides (ACPs). In addition, they can kill bacteria and fungi and regulate the immune system. Low molecular weight anti-cancer peptides contain 10-60 cationic amino acids, preventing cancer cells from proliferating, causing cancerous blood to form, and may cause ug resistance. With the in silico model, anti-cancer peptides are determined and their anti-cancer properties are determined.

Methods: In this study, the anticancer part (ACAN) of the designed recombinant CpsA-CpsC-L-ACAN fusion peptide was determined and its anticancer properties were evaluated using AntiCP software. In AntiCP software, the amount of anti-cancer property of peptides was determined with the SVM index, and based on different characteristics such as amino acid composition and dipeptide composition. The degree of hyophobicity or hyophilicity of anticancer peptides was also evaluated.

Result: Based on the results obtained from the in silico model and AntiCP software, the ACAN segment of the designed recombinant CpsA-CpsC-L-ACAN fusion peptide had anticancer properties, and also because the SVM score of the anti-cancer sequence was less than 1, The recombinant fusion protein had good anticancer properties. In addition, based on the results of AntiCP software, the anti-cancer sequence of the designed recombinant peptide fusion had both hyophilic and hyophobic parts.

Conclusion: According to the results of AntiCP software, the recombinant fusion peptide CpsA-CpsC-L-ACAN has anti-cancer properties and according to its SVM value of less than 1, it can be used as a recombinant fusion peptide with suitable anti-cancer properties.

Keywords: anti-cancer peptides (ACPs), Cancer, in silico, SVM index

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Associations of SLC6A8 with the pathological stage of hepatocellular carcinoma

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Introduction: Liver hepatocellular carcinoma (LIHC) is one of the most common malignancies that cause death in the world today. The clinicopathological significance and prognostic significance of solute carrier family 6 member 8(SLC6A8) among several carcinomas are disputable heretofore. The diagnostic value of SLC6A8 in LIHC has not been studied completely. Herein, we sought to recognize biomarkers in the prognosis of LIHC related pathological- stage through bioinformatics analysis.

Methods: To identify genes involved in LIHC development, we analyzed the Cancer Genome Atlas (TCGA) and SLC6A8 was selected for further study about clinicopathological characteristics and mRNA expression profiles of patients with LIHC. In addition, differentially expressed genes (DEGs) by the OncoDB online database were identified and then by the TMP method normalized. Finally, functional enrichment analysis was applied. In the current study, the dataset of 287 early-stage (stage-I), and 213 late-stage (stage-II, Stage-III, and stage-IV), were investigated.

Result: The bioinformatics analysis was used to explore classifying LIHC patients in early-stage vs. late-stage and cancerous vs. normal samples using mRNA expression. The TCGA LIHC dataset consists of 50 normal, 371 LIHC samples, and 610 DEGs ($P < 0.05$; $|log FC| > 1$). The common genes between the previous stages were identified, and the results showed that there were twenty-four genes that were both raised in expression and correlated with the late-stage pathology of cancer (p-value:0.0001). Also, the bioinformatics analysis illustrated the relationship between pathological late stages of LIHC and the expression of the SLC6A8 gene. The expression profile of SLC6A8 was included: Cancer sample average: 21.6; Cancer sample median: 5.7; Normal sample average: 1.7; Normal sample median: 1.1; log2 fold change: 2.37.

Conclusion: SLC6A8 promotes the malignant progression of LIHC. Therefore, SLC6A8 is expected to become a molecular target for LIHC treatment.

Keywords: Liver hepatocellular carcinoma, SLC6A8, pathological stage, TCGA

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Resveratrol mitigates lipopolysaccharide-induced behavioral impairments and chronic neuroinflammation in mice

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Introduction: There is evidence that chronic neuroinflammation is involved in the pathogenesis of neurodegenerative disorders, including Alzheimer´s disease (AD), Parkinson´s disease (PD), and Amyotrophic lateral sclerosis (ALS). In this regard, lipopolysaccharide (LPS) has been known as a potent stimulator of neuroinflammation. Resveratrol (RSV) is a polyphenolic compound with strong antioxidant and anti-inflammatory properties, that is abundantly found in red grapes. Based on this evidence, in the present study, we aimed to evaluate the neuroprotective effect of RSV against the detrimental effects of LPS, including behavioral impairments and neuroinflammation in the hippocampus of adult mice

Methods: Adult male BALB/C mice received LPS [0.75 mg/kg/day] intraperitoneally (i.p.) for 1 week and RSV (30 mg/kg/day, gavage) or vehicle for 2 weeks (1 week before the LPS and 1 week co-treated with LPS). After treatment, animals were subjected to behavioral assessments using a Morris water maze (MWM) and Y-maze. Then, qPCR analysis was carried out to measure the expression levels of several pro-inflammatory mediators in the hippocampus of adult mice. Furthermore, immunostaining was performed for the evaluation of astrocyte and microglial density on brain sections.

Results: As expected, systemic LPS injections induced behavioral impairments and neuroinflammation by increasing expression levels of IL-6, TNF-α, NF-κB, and GFAP. Moreover, increased microglia and astrocyte density with degenerated neurons were observed in the hippocampus of LPS-treated mice. In contrast, RSV consumption could alleviate the hippocampal alterations induced by LPS.

Conclusion: These results suggest that RSV pre-treatment significantly reverses the LPS-induced neuroinflammation in the hippocampus of adult mice. These results support the idea that natural compounds can be useful against neurotoxicity.

Keywords: hippocampus, inflammatory markers, natural compounds

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The emerging role of exosomes in the diagnosis and treatment of inflammatory bowel disease

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Introduction: Intestinal mucosal barriers, including chemical and physical barriers, separate the intestinal microbiota from the host's immune system to prevent unwanted immune responses that can lead to intestinal inflammation. In inflammatory bowel disease (IBD), there is mucosal barrier dysfunction with immune dysregulation and dysbiosis. An exosome is a cell-derived vesicle. Exosomes can be released from various cell types or found in many physiological fluids and plants. The discovery of exosomes as regulators of vital functions in physiological and pathological processes has generated much research attention.

Methods: In this systematic review, the desired information was searched from Google Scholar, SID, Pubmed, Scopus, and Science Direct databases with keywords IBD and exosome for the period of 2012-2020. According to Jadad criteria, studies that scored 3 or more were included in the study. Data analysis was done qualitatively.

Results: Finally, 35 trials that met the inclusion criteria were reviewed. Based on the studies, exosome-induced regulation in inflammatory bowel disease (IBD) play an essential role in prevention and treatment due to their potential functions in exosomal pathways.

Conclusion: Designing a new pharmaceutical form using an exosome-like structure can provide new insight into IBD treatment. This systematic review demonstrates the potential importance of exosomes in the diagnosis and treatment of IBD and other infectious diseases.

Keywords: Inflammatory bowel disease, Regulation, Exosomal pathways

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The relationship between the use of anti thyroid ugs during pregnancy and neonatal thyroid function

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Introduction: Hyperthyroidism is caused by an over-active thyroid gland and the prevalence of hyperthyroidism in pregnancy is from 0.1% to 0.4% that may be caused by Graves' disease, toxic adenoma, toxic multinodular goiter, subacute thyroiditis, iodine-induced hyperthyroidism, struma ovarii and these situations typically requires treatment. generally, only ug therapy is used for treating pregnant women. Commonly prescribed ugs for the management of hyperthyroidism in pregnancy include Methimazole (MMI), Carbimazole (CMZ), and Propylthiouracil (PTU). There is some evidence to suggest that the use of ATDs (Anti Thyroid ugs) during pregnancy has an effect on the fetus's thyroid function and induces hypothyroidism in the fetus. whereas other studies don't express the relationship between using anti-thyroid ugs in pregnancy and fetal thyroid function.so, The present study aimed to synthesize data available to clarify the effect of anti-thyroid ugs on fetal thyroid function by comparative of relative articles.

Methods: We systematically searched Pubmed, google scholar, Embase and Scopus, magiran databases. A total of 6 entries were obtained. The acceptable articles were selected by the two authors by checking the titles, abstracts, and full text of the articles.

Result: The neonates of pregnant women treated with antithyroid ugs were evaluated retrospectively in all six of these studies. thyroid hormone levels were measured for their infants. In these studies, congenital defects were shown as a result of a decrease in the level of thyroid hormones in infants, and three of the studies showed a decrease in the level of FT4 thyroid hormones as a result of taking antithyroid ugs.

Conclusion: According to studies, there is a dependence between the doses of antithyroid ugs in mothers and the level of thyroid hormones in infants, and the use of antithyroid ugs increases the risk of birth defects in neonatal caused by thyroid hormone disorders.

Keywords: Hyperthyroidism, Anti Thyroid ugs, pregnancy, neonatal

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A comparison between the loading and release behavior of vancomycin and thymol from the nanotubes reservoir

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Introduction: Given the rise in antibiotic-resistant bacteria, researchers have shown an increased interest in local antibiotic therapy. Titania nanotubes (TNs) are one of the most widely used groups of localized ug delivery systems and have been extensively used for ug-releasing implants (I). Among antibacterial therapeutics, vancomycin and thymol are the most effective antibacterial agents against gram-negative bacteria.

Methods: TNs were fabricated by electrochemical process at voltage of 70 V for 3 hours and temperature of (4°C). Thymol and vancomycin were separately loaded into TNs by immersion method. TNs were divided into four groups which were immersed in the aqueous vancomycin solution (group 1 and 2) with a concentration of 50 mg/mL for a day and 100 mg/mL for 3 days. Groups 3 and 4 were kept in the solution of thymol in ethanol (50 mg/mL) for a day and 100 mg/mL for 3 days. The loading dosage, release profile and mechanism of each ug was investigated by UV-Vis spectroscopy and mathematical modeling.

Results: Loading dosage of vancomycin for groups 1 and 2 was 490 and 3220 µg/cm^2, respectively. The loading dosage of thymol for groups 3 and 4 was 40 and 1600 µg/cm^2 . These results show that in the similar condition, TNs would attract higher amount of vancomycin than thymol. As for their release profile, it was demonstrated that in the first hour, 57% of thymol and 83% of vancomycin were released into the medium. Overall release time extended to 3 hours for TN-Van system and 24 hours for TN-thymol. The first-order model is the proper mathematical kinetic model of ug release for both TN-thymol and TN-Van.

Conclusion: The loading and release of vancomycin were slower than thymol due to the differences between hyophilicity and density of vancomycin and thymol molecules whereas both ugs showed similar release mechanism.

Keywords: Ti substrate, Vancomycin, Thymol, mathematical kinetic modeling, localized delivery systems.

The expression of miR-181b ،CYLD ،CBX-7 ،BCL2 and p53 in osteosarcoma patients and correlation with clinicopathological factors

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Introduction: Osteosarcoma is a prevalent human cancer with a high fatality rate worldwide. Understanding the role of microRNAs (miRNAs/miRs) in the etiology of osteosarcoma has been the focus of recent research. Hence, the current study aimed to measure the expression of miR-181a, cylindromatosis (CYLD), chromo box homolog 7 (CBX7), B-cell lymphoma 2 (Bcl2), and p53 in cancerous tissue and adjacent normal tissues in patients with osteosarcoma and its relationship with clinicopathological factors.

Methods: Using quantitative real-time polymerase chain reaction (qRT-PCR), the expression levels of miR-181a, CYLD, CBX7, BCL2, and p53 were evaluated in the tumor tissues and adjacent normal tissues of 60 patients with breast cancer. Finally, the two statistical tissues of tumor and healthy were compared regarding the link between this gene's levels and clinicopathological variables.

Results: Our findings revealed that the expression levels of miR-181a, BCL2, and p53 in breast tumor tissue were considerably more significant than in normal tissues ($P < 0.05$). CYLD and CBX7, on the other hand, were downregulated in osteosarcoma tumor tissues relative to healthy tissues ($P < 0.05$). Furthermore, miR-181a expression in tumor tissues was substantially linked with patients' age, tumor size, clinical stage, cancer grade, and lymph node metastasis ($P < 0.05$).

Conclusion: Our results from the present study highlighted new insights into understanding the role of miR-181a in the pathogenesis of osteosarcoma. However, further research is needed to elucidate miRNA as therapeutic targets for osteosarcoma.

Keywords: miRNAs, miR-181a, osteosarcoma, tumor tissue.

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Interleukin-2 therapy in type 1 diabetes patients: systematic review of controlled trials

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Introduction: New immunotherapy strategies such as using effective molecules like interleukin-2 on the immune system help to inhibit selectively inflammatory signals that cause dysfunctions of regulatory T lymphocytes in autoimmune diseases. Interleukin-2 plays a central role in the mediate to promote the proliferation of Treg cells to maintain immune tolerance while traditional treatment of type 1 diabetic patients suppresses the immune system and increases the risk of uncontrolled infections. The aim of this systematic review was to determine the role of interleukin-2 therapy in the treatment of patients with type 1 diabetes. Outcomes of interest include adesses the efficacy and side effect profile of IL-2.

Methods: PubMed, Scopus and Cochrane Library databases were searched from 2017 to 2022 for English clinical trials studies evaluating the response to IL-2 for type 1 diabetes. Titles and abstracts were screened for suitability using predetermined inclusion and exclusion criteria.

Results: There is no serious adverse event, main adverse event was a reaction at the injection site that was mild to moderate without any medication aids. T regulatory cells unlike T effector cells are dose dependent responsor. Low-dose IL-2 selectively adjusts FOXP3+ Tregs and increases mean proportion of them which was significantly different from placebo group.

Conclusion: This systematic review suggests that from the results of clinical trials with low dose IL-2 from the transplant immunology and autoimmunity, understanding the effects of IL-2 will help for the improvement and establishment of the most effective therapeutic strategies for patients with a good performance status.

Keywords: Interleukin-2, Type 1 diabetes, Immunotherapy

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Evaluation of the effects of Astaxanthin on biochemical factors of liver health in bile duct ligation-induced cholestasis in male adult rats

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Introduction: Bile duct obstruction and subsequent cholestasis are associated with hepatocellular injury, oxidative stress, inflammation and fibrosis. Numerous studies have confirmed that antioxidant activity of Astaxanthin. Astaxanthin is a non vitamin A pro-carotenoid, and its antioxidant effect which is 10 times higher than that of β-carotene and 100 times stronger than that of vitamin E. the aim of present study was to investigate the effect of long term treatment of Astaxanthin on lipid profile and liver enzymes in cholestatic male rats.

Methods: Forty-two male rats weighing about 250 g were randomly divided into seven groups. Groups one to three underwent bile duct ligation (BDL)surgery. Group1: BDL+ olive oil. Group2: BDL+ Astaxanthin (10 mg/kg), and group3: BDL+ Astaxanthin (20 mg/kg). Group4: sham group underwent laparotomy surgery without the bile duct ligation+ olive oil. Group5: control rats+ olive oil. Group6: control rats+ Astaxanthin (10 mg/kg), and group7:control rats + Astaxanthin (20 mg/kg). At the end of day 35, blood samples were taken from the rats.

Result: Astaxanthin in low dose was clearly effective in improving the levels of liver enzymes including alkaline phosphatase(ALP), Aspartate aminotransferase(AST) and alanine aminotransferase (ALT). It also had a significant effect on triglycerides(TG), high-density lipoprotein(HDL), low-density lipoprotein (LDL), Cholesterol and total Bilirubin blood levels. However high dose of Astaxanthin were not as effective as low dose.

Conclusion: Taking Astaxanthin could prevent changes in serum lipid profile caused by cholestasis. In the future, Astaxanthin can be used as a complementary ug to improve the condition of cholestatic patients.

Keywords: Astaxanthin , cholestasis, bile duct ligation, lipid profile

A-10-1628-1

Identification of Potential Diagnostic and Prognostic Pseudogenes in Gastric Cancer Based on a Pseudogene-miRNA-mRNA Competitive Network

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Introduction: Gastric cancer (GC) is one of the most common cancers in the world. Most patients are diagnosed at advanced stages thus finding new biomarkers to detect cancer in early stages is highly demanded. Various types of RNA molecules can compete and communicate with each other as competing endogenous RNAs (ceRNAs) through their microRNA (miRNA) response elements (MREs) which affect tumorigenesis in various cancers including GC. In the current study, we constructed and analyzed a three-component ceRNA network in GC in order to find potential diagnostic biomarkers for GC.

Methods: Gene expression data of The Cancer Genome Atlas Stomach Adenocarcinoma (TCGA-STAD) dataset including 375 tumors and 32 normal samples were retrieved using TCGABiolinks R package. Differentially expressed mRNAs, pseudogenes and miRNAs between tumor and normal samples with adjusted p-value<0.05 were extracted utilizing DESeq2 R package. RNAInter (RNA Interactome Database) was used to find interactions between miRNAs and pseudogenes with score>0.5. miRDB, miRTarBase and TargetScan were utilized to predict target genes of miRNAs. Cytoscape software (version 3.8.1) was then utilized to construct a three-component ceRNA network including mRNAs, pseudogenes and miRNAs.

Results: 10,145 differentially-expressed mRNAs, 3,576 pseudogenes, and 60 miRNAs were identified in TCGA-STAD tumor vs. normal samples with the defined p-value cut off. A ceRNA network including 277 nodes (263 differentially-expressed mRNAs, 10 pseudogenes and 4 miRNAs) and 284 edges was then constructed with 4 miRNAs, 10 mRNAs and 1 pseudogene with the highest degree centrality.

Conclusion: This study provides an overview of differentially-expressed miRNAs, mRNAs and pseudogenes in gastric cancer that interact with each other as a ceRNA network. Further investigation of the ceRNA hub genes may reveal them as diagnostic and prognostic biomarkers or therapeutic modalities in GC.

Keywords: Gastric cancer, RNA, Pseudogenes, microRNAs, Bioinformatics

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An evaluation of the effectiveness of combined regimens of cisplatin and metformin in the treatment of cancer: a systematic review and meta-analysis

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Introduction: Cancer cell resistance to chemotherapy agents is a challenging issue in treating patients with cancer. Findings suggest that a combination of ugs may have synergistic or additive effects. in the present study, we systematically reviewed the combined regimens of metformin with cisplatin in various treating cancers.

Methods: A comprehensive systematic search was performed in PubMed, Scopus, Embase, Google Scholar up to July 2021 with the following MeSH keyword "metformin", "cisplatin", "combination", "cancer", "neoplasm", and "treatment" using all their equivalents and similar terms. Pooled odds ratio (OR) and 95% confidence intervals of cell viability and tumor volume as primary outcomes were calculated using Der-Simonian and Laird method while random effects meta-analysis was used, taking into account clinical and statistical heterogeneity. Sensitivity analysis as well as publication bias assessment was performed using Stata software.

Results: Overall, 44 studies were retrieved, of which 42 were animal and laboratory experimental studies. Findings of the present meta-analysis showed that combined regimens of metformin plus cisplatin was significantly associated with decreased odds of tumor volume and cell viability for all cancers compared with cisplatin alone (pooled OR: 0.40; 95% CI: 0.27, 0.58) and (pooled OR: 0.49; 95% CI: 0.42, 0.58) respectively. The result was same for cell viability in lung cancer (pooled OR: 0.59; 95% CI: 0.49, 0.70). The tumor size reduction and the response rate were evident in the animal xenografts model. A significant association was observed consistently in a sensitivity analysis. There was no evidence of publication bias.

Conclusion: Findings indicated that combining metformin with cisplatin is a practical therapeutic approach to increase treatment efficacy in the case of cell viability and tumor volume and minimize side effects. A combination of metformin with cisplatin could enhance treatment efficacy through synergistic inhibitory effects on the growth of cancer cells through their different anticancer mechanisms

Keywords: Cisplatin, Metformin, Cancer therapy, Chemotherapy, Cisplatin-resistance, meta-analysis

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Effect of Bisphenol A on the Expression of Histone deacetylase-1 and disease progression in experimental model of breast cancer in BALB/C mice

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Introduction: Numerous factors in modern life increase the likelihood of disease. In recent years, it has been shown that bisphenol A, which is present in plastics in high concentrations, can increase the risk of various diseases. Although several studies have shown the BPA-like function of estradiol hormones in binding to estrogen receptors, the effect of BPA on epigenetic changes in breast cancer is still unknown. Having been treated for breast cancer.The aim of this study was to investigate the effect of BPA on the expression of histone deacetylase-1 (HDAC1) and disease progression in a BALB/c mouse model of breast cancer.

Methods: Five groups of female BALB/c mice were pretreated with BPA two weeks before cancer. Next, 4T1 cells were grown in cell culture and injected into mice in the proliferative phase. The tumor size was measured on the third and tenth days.HDAC1 gene expressions were determined using real-time PCR.

Results: The results showed that the increase in tumor size in mice pretreated with BPA was higher after 10 days compared to the control and estradiol groups. On the other hand, the HDAC1 expressions were significantly increased in the groups that received BPA pretreatment compared to the controls.

Conclusions: The use of BPA can cause epigenetic changes in cells, which may increase the risk of disease progression and developing into malignancy, especially in breast cancer. However, more studies of protein levels and related signaling pathways are needed.

Keywords: BPA, HDAC1, Breaset Cancer, 4T1

A-10-1609-2

Nepeta binaludensis Jamzad attenuates neuronal injury induced by oxygen-glucose-serum deprivation/reperfusion in PC12 cells

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Introduction: Nepeta binaludensis Jamzad is a perennial medicinal plant that exhibits various pharmacological effects. However, the neuroprotective effects of Nepeta binaludensis extracts have not yet been investigated. This study aimed to examine the effects of N. binaludensis hyo-alcoholic extract (NBE) on oxidative stress markers and apoptosis-related proteins in PC12 cells exposed to oxygen-glucose deprivation/reperfusion (OGD/R).

Methods: PC12 cells were pretreated with NBE (at concentration range of 10-200 μg/ml) before exposure to OGD condition for 6 h followed by a 24 h reoxygenation. Cell viability, the production of the reactive oxygen species (ROS), lipid peroxidation (LPO), and the levels of apoptosis-related proteins were evaluated using MTT, fluorimetry, and western blot analysis, respectively.

Results: Survival of the cells preincubated for 6 h with NBE increased to $90.20 \pm 15.62\%$ compared with those subjected to OGD/R alone (51.26 ± 7.77 %, $p < 0.001$). ROS formation was also decreased following incubation with 200 μg/ml of NBE to $125.3 \pm 18.38\%$ compared to OGD/R group ($356.9 \pm 70.48\%$, $p < 0.001$). LPO was also suppressed after incubation with NBE to $155.5 \pm 21.21\%$ compared to the OGD/R group ($260.5 \pm 9.727\%$, $p<0.001$). NBE restored Bax/Bcl-2 ratio (1.3-fold of control), and cleaved caspase-3 (1.58-fold of control, $p < 0.001$). **Conclusion:** These results suggest that NBE may offer neuroprotection properties against OGD/R-induced toxicity through modulation of oxidative stress and apoptotic responses.

Keywords: Nepeta binaludensis Jamzad, Neuroprotection, Oxidative stress, Oxygen-glucose deprivation/reperfusion.

A-10-1603-1

Evaluation of the Effect of Routin On Paraquat Inducdd Liver Toxicity in Rats

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Introduction: and Aim: paraquat poisoning damages liver. the study purposed to examination of paraquat on liver function and superoxide dismutase (SOD)and catalase(CAT) and gene expression NF-kB in rat with paraquat indiuced hepatootoxicity.

Methods:48 wistar male rats divided into 6 groups. The first group was negative control group and the second one was experiment group without treatment, the rats received 50 mg/kg of their weight edible paraquat every day and received distilled water one hour later. Rats in the third group received 50 mg/ kg of their weight paraquat as gvage every day and one hour later received 50 mg/ kg of their weight edible silymarin. In all fourth, fifth and sixth groups, 50 mg/ kg of rats' weight (soluble in distilled water) was gavage and then the fourth group was routin gavage for 14 days with 25 mg, the fifth group was routin gavage for 14 days with 50 mg and the sixth group was routin gavage for 14 days with 100 mg. 14 days later of experiment liver SOD and CAT activites and gene expression NF-kB investigate.

Results: The activity of SOD and CAT significantly decreased (p <0.05) in paraquat group than in control group. The results showed that routin with antioxidant effect prevents the reduction of SOD and CAT. Routin also decreased gene expression NF-kB in liver tissue. Unlike the paraquat-administrated rats, which showed a remarkable increase in the expression levels of pro-inflammatory cytokines, including NF-κB as compared to the control rats, those rats which were exposed to increasing concentrations of rutin (25, 50, and 100 mg/kg) after exposing to paraquat showed to have lower expression of cytokines.

Conclusion: routin may prevent liver damages resulted from paraquat due to antioxidant effects.

Keywords: Routin, Hepatotoxicity, Paraquat, Silymarin

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Evaluation of the effects of Astaxanthin on Activity of liver antioxidant enzymes in bile duct ligation-induced cholestasis in male adult rats

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Introduction: Bile duct obstruction and subsequent cholestasis are associated with hepatocellular injury, oxidative stress. Numerous studies have confirmed that antioxidants can protect the liver in cases of inflammation and injury. Astaxanthin is a non vitamin A pro-carotenoid, and its antioxidant effect which is 10 times higher than that of β-carotene and 100 times stronger than that of vitamin E. the aim of present study was to investigate the effect of long term treatment of Astaxanthin on antioxidant enzymes activity in cholestatic male rats.

Methods: Forty-two male rats weighing about 250 g were randomly divided into seven groups. Groups one to three underwent bile duct ligation (BDL) surgery.Group1: BDL+ olive oil. Group 2: BDL+ Astaxanthin (10 mg/kg), and group3: BDL+ Astaxanthin (20 mg/kg). Group4: sham group underwent laparotomy surgery without the bile duct ligation+ olive oil. Group5: control rats+ olive oil. Group6: control rats+ Astaxanthin (10 mg/kg), and group7: control rats+ Astaxanthin (20 mg/kg). At the end of day 35, Animals were euthanized with a mixture of ketamine (90 mg/kg) and xylazine(10 mg/kg). Then liver tissue was removed from their bodies and tissue homogen was prepared to measure the activity of antioxidant enzymes: catalase(CAT), glutathione(GSH) and superoxide dismutase(SOD).

Result: Induction of duct obstruction severely reduced the antioxidant activity of the liver. Astaxanthin in low dose was clearly effective in improving the levels of antioxidant enzymes including CAT, GSH and SOD. Due to the high level of these enzymes has been identified. However high dose of Astaxanthin were not as effective as low dose.

Conclusion: It seems that Astaxanthine can improve the function of liver by improving the antioxidant level of the liver in cholestasis conditions. It can be suggested as an antioxidant combination in complementary therapies.

Keywords: Astaxanthin, cholestasis, bile duct ligation, antioxidant enzymes

A-10-1215-2

Relationship between Life Style and Premenstrual Synome

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Introduction: All over the world around 75% of girls are experiencing problems associated with menstruation. These disorders may lead to problems in daily activities such as academic excellence, achievements in sports, and loss of self-confidence. The major abnormalities are dysmenorrhea, premenstrual synome (PMS), and menstrual irregularities. Premenstrual synome is a cyclical late luteal phase disorder of the menstrual cycle whereby the daily functioning of women is affected by emotional and physical symptoms substantially interfering with her quality of life. **Methods:** In the current study, keywords including Premenstrual Synome, Life Style, and Menstrual Disorders were searched in the list of Mesh and other credible websites including PubMed, Science Direct and Google Scholar and the data was organized.

Results: Many studies have reported an association of smoking with increased premenstrual symptoms and menstrual irregularity. Other menstrual problems and miscarriage with smoking for 5 or more years was associated with an increased prevalence of such symptoms. The documents demonstrated in Pakistanian, Korean, Iranian, and US adult females, in which high body mass index, body fat and visceral fat were risk factors for reporting the prevalence and severity of premenstrual synome. Other references showed a positive and significant relationship of food intake such as fried foods, sweet ink, fast food, and fruit, not having sports habits, with premenstrual synome.

Conclusion: Like many other synomes, PMS is the output of the interaction between various genetic and lifestyle behaviors with dietary factors considered among the most influential. In short, studies suggested an approach to control individual lifestyles such as body mass index, ratio of body fat, smoking, inking, physical activities, stress, dietary uptake, and sleep to improve menstrual health for women.

Keywords: Premenstrual Synome, Life Style, Menstrual Disorders

A-10-1651-1

Evaluation of cytotoxicity effects and induction of rubiadine-induced apoptosis on HT29 colon cancer cell line

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Introduction: Colorectal cancer (CRC) is malignant cancer that affects both men and women and accounts for the third most common cancer in the world. Rubiadin is a natural anthraquinone compound isolated from Morinda officinalis root and is an herbal ug used for the treatment of inflammatory diseases such as appendicitis, arthritis, bronchitis. It is also used for various kinds of cancers including liver, lung, colon, and thymus, with more mild and fewer side effects. This study was aimed to investigate the cytotoxic and apoptotic effect of rubiadin and its impact on ROS and cell cycle arrest in CRC cell line HT29.

Methods: Rubiadin was utilized in 0.01, 0.05, 1.56, 3.125, 6.25, 12.5, and 50 µl/ml, and cytotoxicity was measured after 48 hours by MTT test. The HT29 cultured cells were treated with 10, 18, and 25 µg/ml of rubiadin. Then, ROS, cell cycle arrest, and apoptosis were evaluated by flow cytometry.

Results: The analysis of the cell viability of the HT29 cell line showed the IC50 value of 18.05 µl/ml in 48 hours. Flow cytometry assay revealed a significant increase in ROS of 41.1 ± 9.05, 58 ± 2.9, and 82 ± 1.56 in 10, 18, and 25 µl/ml concentrations, respectively compared to the control group (0.26 ± 0.4). A dose-dependent manner was detected in cell cycle arrest at G1 and G2 phases after treatment with rubiadin in 25 µl/ml concentration which was statistically significant. The highest impact of rubiadin on apoptosis was observed at 25 µg/ml at late apoptosis (61.533 ± 1.242) which was significantly higher than the control group.

Conclusion: The results of this study indicated rubiadin as an anticancer compound that has a significant effect on cytotoxicity, ROS, cell cycle arrest, and apoptosis.

Keywords: Cancer, CRC, Rubiadin, cytotoxicity, ROS, apoptosis, MTT

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Sex Hormones and Cardiovascular Disease in Postmenopausal Women

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Introduction: Cardiovascular disease (CVD), which includes coronary heart disease (CHD) and ischemic stroke, affects men and women differently. In women, the risk of cardiovascular disease is much lower than in men until 50 years of age, but it rises amatically after menopause. Hormonal changes after menopause such as low plasma estrogen level and elevated luteinizing hormone (LH) and follicle stimulating hormone (FSH) level have significant effect on plasma lipid and lipoprotein metabolism resulting in ultimate cardiac related disorders.

Methods: In the current study, keywords including Postmenopausal, Coronary Heart Disease, Cardiovascular Disease, and Sex Hormones were searched in the list of Mesh and other credible websites including PubMed, Science Direct and Google Scholar and the data was organized.

Results: Articles reported a 2.6-fold higher incidence of cardiovascular events in age-matched postmenopausal women when compared with premenopausal women. Also, menopause is associated with greater percentage of both epicardial and pericardial adipose tissue, two emerging risk factors for ischemic heart disease. Some documents demonstrated 17-beta-estradiol reduces the rate of apoB-100 synthesis, and reducing the very low-density lipoprotein (VLDL) concentration which is risk factor for atherosclerosis. Among racially/ethnically diverse postmenopausal women followed for >12 years, references show that higher testosterone/estradiol ratio was associated with an elevated risk for incident cardiovascular disease, coronary heart disease, and heart failure events. Higher total testosterone was associated with increased risk of cardiovascular and coronary heart disease, and higher estradiol levels were associated with a lower risk of coronary heart disease.

Conclusion: Identifying potential risk factors for cardiovascular disease development in women at midlife will enhance our understanding of the reasons that women after menopause are subjected to a higher risk of coronary heart disease.

Keywords: Postmenopausal, Coronary Heart Disease, Cardiovascular Disease, Sex Hormones

A-10-1914-1

Epigenetic changes induced by curcumin on miR-193a and miR-663 expression in human cell line U937

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Introduction: In addition to genetic factors, epigenetic agents also contribute to the formation of tumors. DNA methylation is the most recognized epigenetic mechanism performed by the DNA Methyltransferse (DNMT) family of enzymes. Curcumin, as the main polyphenolic compound of turmeric, has an inhibitory effect on DNMT. Due to the similarity of curcumin to RG108, a kind of DNMT1 inhibitor, the effects of curcumin and RG108 on the expression and methylation status of mir-663 and mir-193a in U937 cell line were studied.

Method: First, the MTT test was used to calculate non-toxic doses of curcumin and RG108 on the leukemic cell line U937, which were 13.63 and 48 µM, respectively. Using RT-PCR and Methylation Specific PCR techniques, the effects of curcumin and RG108 treatments on mir-663 and mir-193a expression and methylation statuses at 12, 24, 48 and 72 hours were compared with the control group, which was not treated with any drugs.

Results: Both RG108 and curcumin increased the expression of mir-663 and mir-193a in the U937 cell line after 24 hours of treatment ($P < 0.05$), but curcumin had a weaker effect compared to RG108. The qualitative analysis of MSP showed that curcumin and RG108 decreased the methylation status of the promoter of mir-663 and mir-193a in this cell line time-dependently ($p < 0.05$) after 72 hours of treatment. In this case, it was also weaker than RG108.

Conclusion: Curcumin can be used as a natural formulation to reduce the methylation status and increase the expression of genes that have been downregulated by hypermethylation of their promotors in cancers

Keywords: Curcumin, epigenetics, methylation, RG108, mir-663, mir-193a

A-10-1787-1

The impact of intravenous administration of Dendemire G4 on cognitive and anxiety assessment

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Introduction: In many biological applications, such as ug, DNA, RNA, and protein delivery, denimers are considered suitable synthesized polymers for ug delivery systems due to their Simple fabrication, nanometer size, non-immunogenicity, water-solubility, and biocompatibility. There are some studies that demonstrate Denimer acts in the nervous system by reducing either neuroinflammation or protein aggregation. This research intended to study the effect of Denimer G4 on anxiety and memory parameters.

Methods: The male Wistar rats weighing 200-220 gr were randomly divided into three groups (n=6): Control, Dendemire G4 550, and Dendemire G4 8000. An intravenous (IV) administration of denimer G4 550 and G4 8000 is performed on the tail of animals. Then, behavioral tests, including NORT; Novel Object Recognition Task, and EPM; Elevated Plus Maze were conducted in order to assess cognitive function.

Results: the results showed recognition memory parameters in the NOR test significantly improved in the G4 group than control (p<0.0001). Denimer groups showed decreased anxiety compared to the control (p<0.01) in the EPM test.

Conclusion: The outcome of this project proposes characteristics of denimers that are valuable for their potential use in neuroscience research and could be an appropriate method for loading the ug to form a safe and effective delivery system to the brain.

Keywords: Denimer G4, Nanoparticles, Anxiety, Recognition memory

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Production of Chitosan/Graphene Quantum Dot Hybrid Nanohyogels with ug Delivery Purposes

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Introduction: Nanohyogels are three dimensional, cross-linked water soluble polymer networks that swell in an aqueous environment. The factor that makes nanohyogels very important is their advantages including biocompatibility, biodegradability, non-toxicity and high strength, pH and temperature sensitivity and ionic strength. Also, the physico-chemical similarity of nanohyogels with the native extracellular membranes made them used in ug delivery systems. Chitosan is used as the first choice polymer in the manufacture of nanohyogels due to its outstanding properties such as biodegradability, antimicrobial capacity and mucoadhesivity. Graphene quantum dots are two dimensional semiconductor that are used in the field of ug delivery. some of the features of GQDs are stable photo luminescence, high biocompatibility, small size, pH and temperature sensitivity. Curcumin is a polyphenolic hyophobic substance derived within the rhizome of Curcuma Longa. Curcumin show to be a potent antioxidant, anti-metastatic in cell culture.

Methods: In this study, firstly chitosan (CS) and Chitosan-Graphene quantum dot (CS-GQD) nanohyogels were synthesized by ionic gelation method using Tpp as a cross-linker. Then, curcumin was trapped in nanohyogels as anti-cancer zeicompound. The spectrophotometric, DLS and FTIR analysis were used to confirm the production of nanohyogels, size estimation and entrapment of curcumin.

Results: The results show that the entrapment of curcumin in CS nanohyogels with 93.55 %, is more than the amount of curcumin entrapment in the CS/GQD with 90.71%. Also DLS and FTIR analysis confirmed the formation of CS/GQD nanohyogels as hybrid nanohyogels.

Conclusion: Finally, the release of curcumin from nanohyogels was examined at Physiological conditions (pH = 7.4 and Tem = 37 ° C). The results showed that the release of curcumin in the first hours in CS/GQD nanohyogels was more than CS nanohyogels, which is probably due to the effect of pH on the surface charges of graphene sheetsand the weakening of curcumin connections with the supportof hybrid nanohyogels.

Keywords: Nanohyogel, Chitosan, Graphene Quantum Dot, Curcumin, ug Delivery

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Addition of EEAEAEAEPR for enhanced expression and SUMO tag removal of proinsulin

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Introduction: Diabetes is a chronic metabolic disease that is caused by either lacking insulin hormone secretion from the pancreas cells or inability of body cells in receiving it. Due to the benefits of Escherichia coli and the importance of insulin, this project was carried out to obtain an increase in soluble expression of insulin and efficient removal of SUMO tag by adding EEAEAEAEPR to the construct.

Methods: The construct was first designed (SUMO + EEAEAEAEPR + proinsulin), optimized and then synthesized. The synthesized gene was cloned into pET26a within Nde1 and XhoI restriction sites. Subsequently, the vector was transformed into E. coli Bl21 and different expression parameters (IPTG, temperature, medium) were examined. Then bacterial pellet was obtained and lysed in 50 mM Tris buffer at pH = 7.5 containing 300 mM NaCl. SUMO-proinsulin was purified by Nickel-Sepharose chromatography and imidazole was removed by dialysis. Finally, the SUMO tag was removed by sumo protease at various conditions.

Results: The optimum soluble expression was induced with 1 mM IPTG at 28 °C and 180 rpm for 8h. The designed construct led to a soluble expression up to 20% of total protein. The expressed SUMO-proinsulin was purified using Nickel-Sepharose and eluted in 250 mM imidazole. The SUMO-proinsulin was then dialyzed against 40 mM Tris-HCl containing 300 mM NaCl at pH = 7.5. Finally, The optimum SUMO tag removal by SUMO protease was obtained in 40 mM Tris-HCl containing 300 mM NaCl at pH = 7.5 buffer, 28°C for 3h. In comparison with the construct without the EEAEAEAEPR, an increase in the tag removal was observed.

Conclusion: In this study, the recombinant proinsulin was expressed in soluble form. In addition, the removal of SUMO tag was much more efficient. This strategy can reduce steps and costs in the insulin production process.

Keywords: SUMO-proinsulin, proinsulin, Diabetes

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Effect of Apigenin on Hedgehog signaling pathway in colorectal cancer cells: Gli1, Patched1 and Hhip gene expression

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Introduction: Apigenin is a natural flavonoid that has low cytotoxicity effect on normal cells but has been shown to have several antitumor effects on cancer cells, such as induction of ROS production, apoptosis, necroptosis, cellular autophagy and suppression of cell cycle, migration, cell invasion, stimulation of immune response and inhibition of Self-renewal characteristics of cancer stem cells. Hedgehog signaling pathway is involved in cell proliferation, differentiation, angiogenesis, apoptosis and survival in colorectal cancer cells. Therefore, in this study, we investigated the effect of apigenin on the Hedgehog signaling pathway in colorectal cancer cells. **Methods:** Apigenin cytotoxicity was assessed by MTT assay and IC50 was obtained using prism. Then Cancer cells (HT-29 and SW480) were treated with two selected concentrations of apigenin (6.25 and 25 µM). Primers were designed and synthesized for Gli1, Hhip and Patched1 genes. Subsequently, RNA extraction and cDNA synthesis were done and the expression of genes were measured using real time PCR. ROS was evaluated in the presence and absence of apigenin. Flow cytometry was used to study the effect of apigenin on cell cycle arrest and cell surface markers. Scratch assay was used to measure cell migration. Annexin V/PI was used to check apoptosis. **Results:** Cells were treated with apigenin for 48 h. Based on MTT assay, IC50 value was calculated to be 21 µM. Our study showed that apigenin can downregulate Hedgehog signaling pathway in both colorectal cancer cells by affecting Gli1, Hhip and Patched1 gene expressions. Apigenin induced apoptosis, increased ROS production and inhibited migration in colorectal cancer cell lines. In addition, it caused cell cycle arrest and affected cell surface markers. **Conclusion:** Considering that apigenin can affect the Hedgehog signaling pathway involved in colorectal cancer, it can be used as a therapeutic strategy to alleviate colorectal cancer severity.

Keywords: Colorectal cancer, Apigenin, Hedgehog

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A-10-1606-1

Docking Prediction of Memantine Binding in the Domain Bound to the Spike Protein Receptor in SARS-CoV-2

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Page | 209

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Introduction: The SARS-CoV-2 virus (COVID-19), which causes an acute respiratory synome, has been able to multiply and stabilize itself worldwide with its extensive mutations. The virus binds to the human ACE2 receptor via the RBD spike protein. Memantine is one of the Adamantane family members, and in addition to its therapeutic roles against neurological disorders, it also has antiviral properties. This study aimed to predict the pharmacological effect of Memantine in preventing or reducing the severity of COVID-19.

Methods: In this study, the binding energy and interaction of Memantine with spike SARS-CoV-2 protein were investigated by the molecular docking method. In this regard, with the help of AutoDock Vina software, the binding energy between the ligand atoms and the receptor was investigated.

Results: Molecular docking results showed that Memantine could interact and bind to the SARS-CoV-2 spike RBD (-6.3 kcal.mol-1) amino acids Glu471, Ser469, and Lys458. So it can prevent SARS-CoV-2 spike protein interaction and binding to ACE2 as its receptor. The results obtained in this study indicate the potential usage of Memantine in preventing COVID-19.

Conclusion: The molecular docking results that examine the interaction of the ug Memantine and the spike receptor of the SARS-CoV-2 virus release the desired binding energy of -6.3 kcal per mole. It confirms the antiviral effect of Memantine against the SARS-CoV-2 virus. Considering the observed preventive potential of Memantine against covid-19, the use of Adamantane derivatives is supposed to be effective in preventing this disease. The results of this study can be applied as a national protocol to people at risk of COVID-19 and to help the medical staff.

Keywords: SARS-CoV-2, COVID-19, ACE2, RBD, Memantine, AutoDock Vina.

A-10-1690-1

Antiviral effect of natural biotherapeutics: with a glance on Propolis against COVID 19

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Introduction: The Coronavirus Disease 2019 (COVID-19) global pandemic caused by coronavirus2 (SARS-CoV-2) has been ongoing in the world since November 2019. A number of medications and vaccinations were studied to treat COVID-19, which could have negative consequences on humans. Propolis is a resinous substance produced by honeybees from plant exudates, and as a natural product, it can be an effective alternative to modern medications. It contains a variety of bioactive substrates, including polyphenolic acids ،flavonoids and vitamins. Recent laboratory investigations have reported a wide range of potential therapeutic bioactivities such as anticancer, antioxidant, antimicrobial (including antiviral), anti-inflammatory, and immunomodulatory properties. The present systematic review aimed to investigate antiviral, anti-inflammatory, and immunoregulatory mechanisms of Propolis in COVID-19 prevention as complementary natural biotherapeutics.

Methods: We navigated the literature search using the terms of "COVID-19" and "propolis" in the databases (PubMed, Scopus, EMBASE, Science Direct, Cochrane Library, Cinahl, Medline, and COVID-19 Primer) until July 1, 2022. Investigations that used clinical trials to assess the effectiveness of propolis against SARS-CoV-2 were included.

Results: The analysis included 5 studies involving 226 patients with laboratory-confirmed COVID-19. The majority of trials demonstrated that the intervention group had shorter hospital stays and a reduction of Covid-19 clinical symptoms than the control groups. Additionally, it was discovered that flavonoid components have a positive effect on the protein kinase-1 (PAK-1), which results in the regression of pulmonary fibrosis associated with respiratory failure. In addition, these components prevent the increase of pro-inflammatory cytokines such as TNF-, IL-6, and IL-2, known as a cytokine storm.

Conclusion: These clinical studies confirmed the effectiveness of propolis against COVID-19 as a natural antiviral agent. Furthermore, the anti-inflammatory and immunomodulatory properties of propolis have been highlighted. However, additional investigations and future clinical trials with larger sample sizes are required.

Keywords: SARS-CoV-2, Propolis, Coronavirus disease 2019, Systematic review

A-10-1336-1

Intraperitoneal administration of Benzo (a) pyrene on liver FGF21 expression status in C57bl / 6 mice

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Introduction: Benzo (a) pyrene (BaP) is a polycyclic aryl hyocarbon and known as a potent agonist for the aryl hyocarbon receptor (AHR). Studies indicated that exposure to high fat diet and environmental toxicants such as BaP has been implicated as one of the risk factors for atherosclerosis disease. Recently studies showed that activation of AHR changes hepatic FGF21 expression in the liver. FGF21 known as anti-atherogenic adipokine. In the current study, we investigated the chronic effect of BaP injection on hepatic FGF21 expression in mice liver with or without high-fat/high-cholesterol diet (HFHCD).

Methods: Twenty male 6 weeks C57Bl/6J mice were randomly divided into 4 groups: 5mg/kg/week BaP with HFHCD, 5mg/kg/week BaP without HFHCD, HFHCD without BaP and control groups with normal diet received just corn oil for 16 consecutive weeks. Blood samples were collected and concentrations of cholesterol and LDL were measured using an enzymatic assay kit. FGF21 expression was assessed by q-RT-PCR. Atherosclerotic lesion in mice investigated with Oil Red O staining.

Results: BaP caused a significant increase in the expression of the FGF21 in liver. It seems HFHCD and BaP co-exposure lead to further increase of FGF21 expression. Adding of HFHCD to BaP also caused a significant increase in blood cholesterol and LDL levels and exacerbate the development of atherosclerosis lesion. A positive correlation between FGF21 expression with cholesterols and LDL levels were found. Besides exacerbation of atherosclerotic plaque accompanied by a significant expression of FGF21.

Conclusion: According to the results it seems expression of liver FGF21 increased for protection of the heart from atherosclerosis that induced by HFHCD and BaP exposure.

Keywords: FGF21, BaP, HFHCD, Atherosclerosis, Liver

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The effect of deca-peptide in the expression and proteolytic cleavage of proglarine

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Page | 212

Introduction: Diabetes is the fifth leading cause of death in most developed countries. Insulin is one of the most important and vital ugs. Glargine insulin is one of the long-acting insulin analogues. Glargine is similar in structure to regular insulin, except for the replacement of asparagine to glycine in A-chain and the addition of two positively charged arginine residues at the C-terminus of B-chain. the majority of recombinant insulin therapeutics are produced from E. coli inclusion bodies. The aim of this project was to improve the soluble expression and cleavage process.

Methods: To increase the production of soluble proglargine and its conversion to glargine a new construct containing a sumo tag and a deca-peptide in the C-chain was designed. The gene construct was then optimized and synthesized. The synthesized gene was cloned into the pET26 expression vector and then transformed into E. coli BL21. Different conditions for expression and cleavage were examined and confirmed by SDS-PAGE. The expressed proglargine was then purified by nickel Sepharose and finally was digested.

Results: The optimum soluble condition was obtained with 1 mM IPTG at $30°$C and 220 rpm for 6 h (0.3g/l culture). The added SUMO tag led to a soluble expression of the protein. The expressed and purified proglargine finally converted to glargine by using SUMO and trypsin proteases. In comparison with the construct without the decapeptide, an increased in the protease cleavage was observed. The best condition for SUMO protease digestion was in $37°$C for 12h and for trypsin was obtained in $25°$C for 6h.

Conclusion: The recombinant glargine was produced with fewer production process and thus lower cost. It is hoped that it will be available for medicine in the future.

Keywords: Diabete, Glargine, deca-peptide

A-10-1338-1

Benzo[a]pyrene (BaP) increase Fibroblast Growth Factor-21 (FGF21) gene expression in HepG2 cell line

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Page | 213

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Introduction: BaP, a common environmental pollutant, is a potent agonist for the aryl hyocarbon receptor (AHR). Recent studies indicate that activation of AHR changes hepatic fibroblast growth factor 21 (FGF21) expression in the liver. The FGF21 is a multifunctional protein that regulates lipid and glucose metabolism, and it is mainly expressed in the liver. The present study was performed to determine whether BaP can induce FGF21 expression in HepG2 cell line through AHR signaling.

Methods: HepG2 cell line was grown in a high glucose 1:1 DMEM: F12 medium supplemented with 10% fetal bovine serum, 100 units/mL penicillin, and 0.1 mg/ml streptomycin at 37° C and 5% CO2. The BaP cytotoxicity on Hep-G2 cells was determined using MTT assay. These cells were exposed to two non-toxic concentrations of BaP (2 and 16 µM) either in the absence or presence 6,2′,4′-trimethoxyflavone (TMF), a well-known AHR antagonist. After 24 hours, cells were harvested and qRT-PCR was used to detect FGF21 and Cyp1A1 (an AHR non-specific stimulation biomarker) genes expression.

Results: The current study showed that BaP treatment at non-toxic doses could increase the expression of FGF21 and Cyp1A1 in Hep-G2 cells. Treatment of these cells with the AHR antagonists 6, 2', 4'-trimethoxyflavone reduces the BaP induced expression of FGF21 and Cyp1A1.

Conclusion: According to our findings, BaP might induce FGF21 expression in HepG2 cell line via AHR, and FGF21 could be a target gene of the AHR-signaling pathway in Hep-G2 cells. These finding might partly clarify the mechanism behind BaP induced hyperlipidemia and glucose metabolism deterioration.

Keywords: FGF21 , HepG2 cell line, Aryl hyocarbon receptor, 6, 2', 4'-trimethoxyflavone

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Cloning, Expression and Purification of an Analgesic Peptide from the Iranian Scorpian, Hemiscorpius lepturus and Evaluation of its Structure and Activity

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Page | 214

Introduction: Pain is an unpleasant sensation along with an actual or potential tissue damage. Current pain therapeutics exhibit limitations in efficacy, unwanted side effects and the problem of ug abuse. Due to this point their use has been limited and researchers are looking for other compounds with less side effects. One of these compounds can be peptides in venomous animals that have very high selectivity and specificity for their target due to million years of evolutionary selection. Most of the analgesic peptides are disulfide bond rich which can cause specific conformation.

Methods and Results: Hemiscorpius lepturus is a venomous scorpion in Iran with painless sting. Leptucin, analgesic peptide, sequence has been previously identified based on the data from the CDNA library of H.lepturus venom gland generated by Illumina RNA sequencing. The peptide was synthesized and its characteristics was investigated. In this work, we designed primers for SUMO tag sequence and leptucin gene, amplified them with PCR and ligated them into PET28a vector. Then it was transformed in E. coli SHuffle strain. The fusion protein containing leptucin expressed at 24 ℃, IPTG 0.5 mM, TB culture medium. Due to its His Tag, it was purified with Ni-NTA-agarose and the tag was removed by TEV protease

Conclusion: Results indicated that SUMO tag has an efficient effect on peptide expression. Furthermore disulfide bonds formation and peptide folding will be studied by spectroscopic techniques. Also, analgesic activity of this peptide will be studied on mice.

Keywords: Analgesic peptide, Hemiscorpius lepturus, Leptucin, SUMO tag, SHuffle strain, TEV protease

A-10-1696-1

Propolis as a natural anti-inflammatory product for improving diabetic wounds

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Page | 215

Introduction: A diabetic foot ulcer is one of the most common chronic complications of diabetes. Recently, the use of natural products such as Propolis has been suggested for the treatment of diabetic foot ulcers due to its anti-inflammatory and antimicrobial properties. The positive effects of Propolis to improve diabetic wounds have been reported in several clinical and experimental studies. The aim of this systematic review is to evaluate experimental studies evaluating the anti-inflammatory effect of Propolis in diabetic wounds.

Methods: A comprehensive systematic search of articles was conducted in PubMed, Scopus, scholar, and ProQuest with the entry terms of "Propolis anti-inflammatory", "Propolis diabetic foot ulcers" and "diabetic foot ulcers" from 2012 to 2022. This search yielded 30 results, 5 of which were used in this systematic study.

Results: According to the studies, diabetic rats were induced with streptozocin and then treated with Propolis as well as diabetic individuals. The diabetic groups were exposed to Propolis for 4 to 8 weeks (5-800mg, topical application) and the results were compared with the control groups. According to the results, it was found that Propolis can reduce the expression level of pro-inflammatory cytokines such as TNF-α, IL-1β, IL-4, and IL-6 and increase the expression of IL-10 as an anti-inflammatory cytokine.

Conclusion: These findings confirmed the positive effect of Propolis on inflammatory conditions, especially in diabetic wounds without any major side effects, which could be suggested its promising potential as an anti-inflammatory natural agent for the development of new ugs. But there is still demand for more studies at the molecular level to confirm its positive effect on wound healing.

Keywords: Propolis, diabetic wounds, anti-inflammatory, Propolis anti-inflammatory, Propolis diabetic wounds

A-10-1703-1

Digoxin enhanced antitumor property of cisplatin against bladder cancer cell lines

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Introduction: Cisplatin based chemotherapy is the main treatment for advanced bladder cancer (BC). Several chemotherapy regimens have been developed for curing BC. However, chemotherapy resistance are still major problems in this cancer. Developing new protocols for overcoming these problems is required. The aim of the present study was to investigate the ability of digoxin to improve the cytotoxic effects of cisplatin. In addition, the potential molecular mechanisms of digoxin cytotoxicity were investigated.

Method: To assess the effect of digoxin on cisplatin cytotoxicity, 5637 and EJ138 bladder cancer cells were co-treated with the low concentration (IC30 value) of digoxin and different concentrations of cisplatin (0-5µM). Then MTT assay was used to evaluate the combination ug cytotoxicity. The cytotoxicity of standard ug combination i.e., gemcitabine+cisplatin was also determined. To assess the mechanism of action of digoxin, cells were treated with the IC30 value of digoxin for 72 h and Real-time PCR was used to evaluate mRNA expression levels of HIF-1α, topoisomerase I and bax genes.

Results: The IC30 values of digoxin for 5637 and EJ138 cells were 0.04 and 0.03 µM and the IC30 values of gemcitabine for 5637 and EJ138 cells were 0.007 and 0.004 µM, respectively. Combination of IC30 values of digoxin with cisplatin could significantly reduce the IC50 of cisplatin, compared to when cisplatin is used as a single ug. The same result was obtained when cisplatin was co-treated with IC30 of gemcitabine. The IC50 value of cisplatin was not statistically different between cisplatin+ gemcitabine and cisplatin+digoxin treatment. Digoxin significantly reduced the mRNA expression of topoisomerase I with no effect on HIF-1α and bax expression.

Conclusion: Our findings reveal that digoxin significantly augment the antitumor activity of cisplatin in human BC by downregulation of topoisomerase I expression. Therefore, digoxin may be considered for the treatment of cisplatin-resistant BC.

Keywords: Bladder cancer, cisplatin, digoxin, chemotherapy

A-10-1693-1

Some biochemical effects of sodium nitrite on the blood of middle aged people under in vitro conditions

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Introduction: Nitrite is present in water, plants and processed meats and studying its effects is important because of the possibility of producing reactive nitrogen compounds (RNS) that can increase oxidative stress.

Methods: For this purpose, in this study, erythrocytes and plasma of blood samples taken from 30 people with an average age of 55.5 years were incubated in phosphate buffer with concentrations of 10, 25 and 50 micromolar sodium nitrite for 60 and 240 minutes. To evaluate the erythrocytes, the absorption spectrum of hemoglobin was investigated at wavelengths of 275, 340, 420, 560, 577 and 630 nm. To investigate the effects of nitrite on plasma, the carbonyl groups of plasma proteins and the antioxidant power of plasma were measured.

Results: In examining the absorption spectrum of hemoglobin of erythrocytes incubated in a concentration of 50 micromolar sodium nitrite for 240 minutes, at 560 and 630 nm, a significant difference was observed, which can indicate an increase in the conversion of oxyhemoglobin to methemoglobin and an increase in the production of hemichrome. However, no significant change was observed in other conditions. In examining the effect of sodium nitrite on the antioxidant power of plasma, only at the above concentration and time, it showed a significant effect on this index, while it did not have a significant effect on the amount of carbonyl.

Conclusion: Finally, this study showed that sodium nitrite under our in vitro conditions has a concentration and time dependent effect on erythrocytes and plasma antioxidant status, but determining other effects and the response of the human body to these changes requires more studies.

Keywords: Erythrocytes, Hemoglobins, Middle aged, Oxidative stress, Sodium Nitrite

A-10-1044-2

Investigating calcium-induced structural changes the photoprotein aequorin by excitation-emission and time-resolved fluorescence spectroscopy

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Introduction: Photoproteins contain a chromophore, which is surrounded by four EF-hand loops that provide a hyophobic cavity for the coelenterazine. Binding of calcium to the EF-hands induces conformational changes resulting in oxidative decarboxylation of coelenterazine. By returning the excited coelenteramide to its ground state, a blue light emits. Thus, it is important to obtain more information about structural changes and protein flexibility in the presence of calcium. Here, a study performed on aequorin to understand the structural transitions resulting from calcium binding into its EF-hand motifs.

Methods and Results: We attempted to consider the effect of different calcium concentration on the secondary and tertiary structure of aequorin. Circular dichroism, three-dimensional (3D) fluorescence, and time-resolved-fluorescence (TRF) were applied to investigate the conformational changes resulting from calcium binding. As calcium increases, the Far-UV CD shows an increase in positive ellipticity at 208 and 222 nm, which implicates the loss of the helical content of the protein. Based on the Stern-Volmer constant derived from the slope of plots in different concentrations of calcium ion, the permeability of the protein structure to acrylamide was increased at higher concentrations of calcium and much more quenched. Based on the TRF results, the half-life of fluorescence decreases with calcium increases which can be related to the interaction of calcium with EF-hand loops and hyophobic groups accessibility. In agreement with other results, 3D fluorescence studies also indicate that the fluorescence intensity decreases with calcium increases which may bring some tryptophan residues to a more hyophilic environment and or expose them to the solvent.

Conclusion: The experimental results obtained from the aforementioned spectroscopic studies indicate aequorin structure undergoes conformational changes induced by calcium binding, which was necessary to initiate the oxidative decarboxylation reaction of coelenterazine.

Keywords: bioluminescence, photoprotein, circular dichroism, time-resolved-fluorescence, 3D fluorescence.

A-10-1786-1

Study of the Effect of Regorafenib on APC and BCL-2 Proteins Using Molecular Docking in Colorectal Cancer

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Introduction: Regorafenib is used in the therapy of refractory metastatic colorectal cancer. Adenomatous polyposis coli (APC) is a tumor suppressor protein and APC mutations are mainly prevalent in colorectal cancer. BCL-2 (B-cell lymphoma 2) is an oncoprotein involved in the growth of cancer by impeding apoptosis. In silico study, the identified Regorafenib structure was subjected to molecular docking studies to find the effects of target proteins on colorectal cancer.
Methods: For ligand selection, Regorafenib the 3D structure received from the PubChem database and download the SDF file. Used as receptors, the selection of target proteins of APC and BCL-2 were taken from the Uniprot database. The 3D structure of APC protein was obtained from the PDB database chosen 5IZ8. Also, The 3D structure of BCL-2 was chosen 2XA0. Target proteins were edited using Chimera 1.15 software. APC and BCL-2 proteins each had four chains, and for a better match, we used only the A and B chains, and the rest of the chains, water molecules, and ions were removed from the protein.
Results: Using PyRx software, molecular docking was initiated in which the grid box was used to select the appropriate binding site of Regorafenib for each chain. The results after molecular docking were the best binding affinity for both chains of APC was (-8.2 kcal/mol) also for the A chain of BCL-2 was (-7.9 kcal/mol) and for the B chain was (-8.3 kcal/mol) and these results show that the B chain of BCL 2 is a better choice and the affinity of other Target proteins is also very close to the ug.
Conclusion: conformation Regorafenib with negative binding affinity has the potential to treat colorectal cancer due to its suitable affinity binding for the appropriate target proteins APC and BCL-2 protein to induce apoptosis and prevent cancer cell growth.

Keywords: Regorafenib, APC, BCL-2, Molecular docking, Colorectal Cancer

A-10-1725-1

Green Synthesis of Cu, N-doped Carbon Dots from Saffron and Their Cytotoxic Effects on Human Colorectal Cancer Cell

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Introduction: Green synthesis from the natural sources through one-step simple hyothermal method have been identified as a desirable method for carbon dots (CDs) preparation. Copper (Cu) as a metal dopant is used to increase the CDs applications in different fields. In this study, we synthesize for the first time the Cu, N doped carbon dots (Cu, N-CDs) and evaluated the effects of Cu, N-CDs on viability of the HCT-116 colorectal cancer (CRC) cells.

Methods: The Cu, N-CDs synthesized from Saffron as nitrogen source and Cu (II) acetate as Cu sources. Techniques such as fourier transforms infrared (FT-IR), transmission electron microscopy (TEM), ultraviolet-visible (UV-Vis) absorption spectroscopy, energy-dispersive X-ray (EDS), and fluorescence spectroscopy methods were used to characterize Cu, N-CDs nanoparticles. MTT assay, uptake assay, reactive oxygen species (ROS) production test, and Oil Red O staining were performed for anti-cancer investigations.

Results: The Cu, N-CDs were successfully synthesized and then characterized for their size, the structure, surface functional groups, and the optical properties. Data showed that Cu, N-CDs decreased the cell viability dose-dependently ($p < 0.05$). The 50% inhibitory concentration (IC50) value for Cu, N-CDs were 0.40 mg/mL and 0.28 mg/mL for 24 h and 48 h treatment, respectively. HCT-116 cells successfully uptaked Cu, N-CDs. We found high levels of Oil Red O positive cells and an increased level of intracellular ROS in treated HCT-116 cells compared to normal cells.

Conclusion: Our findings indicated that Cu, N-CDs decreased the viability of HCT-116 cells through ROS /lipotoxicity axis, proposing new nanoparticle for CRC treatment.

Keywords: Saffron, Cu, N-doped CDs, Colorectal Cancer, ROS, Lipotoxicity

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Therapeutic potential of Algae in manaegment of skin diseases: anti-inflammatory roles of bioactive components

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Introduction: Inflammatory skin diseases are the most frequent types of dermatologic disorders. Almost current treatment plan fails in control of those disease symptoms and usually lead to major systemic complications. Here, we aimed to review the studies focused on the implication of different genus of Algae in treatment of inflamamtory skin diseases. Materials and

Methods: We explored the search engines and websites including Google Scholar, PubMed, PubMed Central, Scopus and Bing using key words including inflammatory skin disease, microalgae, macroalgae and bioactive components, bioactive compounds and treatment.

Results: Among microalgae, Spirulina plantesis was the most successfull genus in treatment of symptoms of inflammatory dermatologic disese, in particular, acneic disease and psoriasis owing to its rich γ-linolenic acids. Among macroalgae, Codium tomentosum, Palmaria palmata, Gracilaria gracilis, Porphyra dioica, and Fucus vesiculosus demonstrated promising results in management of melanoma and atopic dermatitis due to their antioxidant lipids, as well.

Conclusion: In spite of amazing therapeutic effects of different genus of algae in control of inflammatory diseases progression, reporting some critical side effects regarding to the heavy mental and toxin components make using of algae limited in current protocols of treatment. Further studies are required to determine strategies in purification of bioactive components to reduce side effects.

Keywords: Skin inflammation, microalgae, macroalgae, Bioactive compound

BUN/Albumin ratio as a biomarker for covid-19 patients

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Page | 222

Introduction: The novel coronavirus disease 2019 (COVID-19) emerged as the source of a global pandemic in late 2019 and early 2020. There are ongoing efforts to better understand the pathophysiology and clinical outcomes of the disease, including the identification of biomarkers for diagnosis, disease monitoring and prognosis. As such, we investigated whether the blood urea nitrogen (BUN), Albumin and BUN/albumin ratio (BAR) in positive PCR patients who were not hospitalized. There have been studies that aimed to predict mortality using the BUN/albumin ratio (BAR) in geriatric and pneumonia patients. Our objective was to investigate the associations between serum albumin concentrations and BUN and BAR with disease severity and adverse outcomes in COVID-19 patients.

Methods: A total of 30 COVID-19 patients all PCR positive who have been tested in the laboratory of Milad hospital of Urmia city included in the study. The BUN level, albumin level, age, gender of the patients was recorded. Statistical comparison was conducted between the patients and 30 healthy individuals as control groups.

Result: of the 30 patients included in the study, 13 (43.3%) were male, and 17(56.7%) were women. Also the control group included 19 men (63.3%) and 11 women (46.7%). The serum BUN level remained significantly higher in the patients with positive covid19 PCR test result (21.33 vs 15.54, respectively; $p < 0.001$)). By contrast albumin level was significantly higher in control group as compared with covid19 patients (4.66 vs 4.32, respectively; $p < 0.001$). The BUN/Albumin ratio (BAR) value was significantly higher in the patients with positive covid19 PCR test result (4.99 vs 3.37, respectively; $p < 0.001$).

Conclusion: The BUN, albumin, and BAR levels were found to be reliable predictors for early diagnosis in COVID-19 patients.

Keywords: Blood Urea Nitrogen, COVID-19, Serum Albumin

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FosB overexpression as a potential contributor to colorectal cancer: a study based on gene expression omnibus (GEO) and bioinformatics analysis.

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Introduction: Colorectal cancer (CRC) is known as the third most common malignancy and the second deadliest cancer in the world. CRC, also known as bowel cancer, colon cancer, or rectal cancer, is the development of cancer from the colon or rectum. Most colorectal cancers are due to old age and lifestyle factors, with only a small number of cases due to underlying genetic disorders. This study aims to discover the regulatory network formed by lncRNA, miRNA, and related mRNA.

Methods: The significance of gene expression in CRC was analyzed by analyzing raw data (GSE4107) from the Gene Expression Omnibus (GEO) database and then by GEO2R to find differentially expressed genes (DEGs) as well as from miRWalk, KEGG PATHWAY database, lncBase v.3 was used.

Results: Finally, the FOSB gene was selected with logFC=9.96. FosB transcription factor regulates COX-2 expression in colorectal cancer cells, Cyclooxygenase (COX)-2 expression level is associated with colorectal cancer (CRC). By using KEGG PATHWAY Database, the IL-17 signaling pathway was selected for the FosB gene, Interleukin 17 (IL-17), a pleiotropic proinflammatory cytokine, can promote cancer-induced inflammation; IL-17 is generally regarded as a promoter in CRC progression. Then, miRWalk was used to find significant miRNA interactions with FosB mRNA in the 3'UTR region, and miRNAs hsa-let-7c-5p, hsa-let-7a-2-3p, hsa-let-7c-5p were selected. Analysis of putative interactions revealed hsa-let-7c-5p as an important interactor for FosB mRNA. The selected miRNA was searched in lncBase v.3 to find strong interactions with lncRNAs and finally, lncRNA A1BG-AS1 was found which had the strongest interactions.

Conclusion: According to these findings, it can be concluded that the overexpression of FosB gene and the effect on IL-17 signaling pathway, as well as the creation of a possible ceRNA regulatory network between hsa-let-7c-5p and A1BG-AS1 and their regulatory effect on mRNA, can cause colorectal cancer.

Keywords: Colorectal cancer (CRC),FosB, hsa-let-7c-5p,IL-17 signaling pathway

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Fabrication of Magnetic chitosan Nano hyogels for Targeted Delivery of Curcumin

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Page | 224

Introduction: Nanohyogels are polymers that are specifically used for ug treatment. The most common materials in ug delivery in the form of Nanohyogel are polymers such as chitosan. There is special attention to the design of a ug delivery system based on magnetic nanoparticles. Among the various magnetic materials, Fe3O4 offers many potential applications in cancer diagnosis and treatment due to its stable quality, high magnetic responses, and biocompatibility. Curcumin (Cur) is a polyphenol derived from Curcuma longa, commonly called turmeric, which has anti-cancer and tumor-suppressing properties.

Methods: In this study, chitosan/cur (CS) Nanohyogel was made by ion-gel method. Then Fe3O4 nanoparticles were loaded on the Nanohyogel produced by co-precipitation method. Then, spectrophotometry, DLS and FTIR analysis are used to confirm the nano-hyogel and check its structural features and curcumin entrapment.

Result: FTIR results showed the presence of Nanoparticles in the chitosan substrate, and finally the release of curcumin from magnetic Nanohyogels was investigated at physiological pH and temperature (pH = 7.4 and T = 37).

Conclusion: The results showed that the release rate of curcumin in magnetic chitosan Nanohyogels is lower than non-magnetic Nanohyogels, which could be due to iron nanoparticles. Based on this study, the prepared nano hyogel is suitable for ug delivery purposes.

Keywords: Nanohyogel, Chitosan, Fe3o4, curcumin, ug delivery

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Fabrication of nanoparticles containing papain effective in wound healing

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Introduction: Chitosan (CS) has been used for many years as a ug carrier in ug delivery systems, in tissue engineering as a scaffold, in agriculture, food industry, cosmetics, etc. due to its high biocompatibility, tissue repairing, anti-inflammatory, and antibacterial properties. Papain (Pa) enzyme can activate cell signaling pathways and use as debridement, which has made it applicable in the cosmetics and wound healing.

Methods: In this study, CS/Pa nanoparticles were synthesized using ion-gel method and then their physical, chemical and biological properties were investigated.

Results: FTIR results showed that the nanoparticles containing CS/Pa were prepared. By analyzing degradation, test and swelling test the results showed that CS/Pa nanoparticles have higher water absorption property and less degradation compared to chitosan nanoparticles. The results of the porosity test indicated that the manufactured nanoparticles have good porosity. Papain release from nanoparticles was investigated, and the results showed that most release occur at 37 ° C and almost acidic environment (pH 6.4). Enzymatic activity assays showed that papain in the nanoparticles is active. MTT cell test showed that nanoparticles have good compatibility and this compatibility increases with the presence of papain.

Conclusion: According to the results, CS/Pa nanoparticles can be a good option to use for wound essing.

Keywords: Wound Healing, Chitosan Nanoparticle, Papain, Debridement

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Large amounts of cytochrome c might be required for apoptosome formation, blind dock suggests

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Introduction: Binding of apoptotic protease-activating factor 1 (Apaf-1) to cytochrome c and dATP leads to its oligomerization into a heptameric complex known as the apoptosome which eventually causes cell death. In order to study the possible interactions of Apaf-1 and cytochrome c, upon possible cytochrome c leakage from mitochonia, blind dock approach was used.

Methods: ClusPro 2.0 server was applied. Chain A of 3JBT PDB file (Apaf-1) and chain B 3JBT PDB file (cytochrome c) were uploaded as receptor and ligand respectively. In each run 70,000 rotations of ligand around the fixed receptor were considered based on Fast Fourier Transform on a grid using PIPER program which means sampling billions of conformations. Then, 1000 lowest energy structures were clustered based on 9Å IRMSD radius to find highly populated clusters of low energy conformation. Finally, selected structures were refined using Charmm potential minimization to remove steric clashes.

Results: It results 24 highly populated clusters. The first cluster consisted of 127 members and the last cluster contained 11 members. Among all the clusters, only the 16th cluster, which contained 16 members, revealed a graphical model almost similar to the atomic structure of the apoptosome. In other words, in 984 other structures, cytochrome c did not bind to a correct position of Apaf-1. The weighted score of the 16th model was -543.2. Furthermore, a close up view of the interface between Apaf-1 and cytochrome c of this model, revealed that it could not make proper interactions.

Conclusion: To aw a conclusion, a large excess of cytochrome c might be required to effect proper binding to the Apaf-1 to form apoptosome if we assume each of 1000 structures as a cytochrome c with only 70 rotations around the Apaf-1. Given the high dense condition inside the cells, this assumption might be true.

Keywords: Apaf-1, Cytochrome c, Blind dock

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Evaluation of Berberine alkaloid supplement on Schizophrenia patients during treatment with Risperidone

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Introduction: After the first episode of schizophrenia, risperidone is used for the treatment. However, risperidone has not been able to fulfill the treatment purposes so far, therefore we have considered a neuroprotective ug-like berberine alkaloid(antioxidant)as add on-therapy with risperidone to investigate the effect of the combined ug (risperidone and berberine supplement) on the treatment of schizophrenia with reference to neurotransmitters parameters such as dopamine, y-aminobutyric acid, glutamate, and hormones, like prolactin, insulin, and superoxide dismutase enzyme.

Methods: 46 first-episode, s schizophrenia patients were divided into two groups. First group (control n=21) received risperidone (2mg/twice daily) plus placebo and second group (intervention n=25) received risperidone (2mg/twice daily) plus berberine supplementation(500mg/day) for 45days.The patient's state of health was monitored during this period.

Results: Dopamine was decreased significantly in the control and intervention groups. However, the decreased level of dopamine in the intervention group was more intense. Superoxide dismutase was decreased significantly in the control group in contrast to its increase in the intervention group. Prolactin and y-amino butyric acid were increased significantly in both groups, but their increased levels were higher in the intervention group. Although there were no significant changes in glutamate in any of the groups, insulin was increased significantly after treatment with risperidone but not with the combined ugs.

Conclusion: A significant positive correlation was observed between dopamine, prolactin, insulin, y-aminobutyric acid, and superoxide dismutase enzymes at pre-and post-treatment with a combination of risperidone and berberine. Moreover, the combination treatment has a recovery effect on the superoxide dismutase levels. Berberine exerts its effect via reducing tyrosine hyoxylase activity in the brain which leads to reduced dopamine synthesis, subsequently increases prolactin levels, and reduces insulin resistance and oxidative stress caused by risperidone. Ultimately, we suggest that the use of berberine along with risperidone will improve the efficacy of risperidone during the treatment of schizophrenia.

Keywords: berberine, endocrine, neurotransmitter, schizophrenia

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Design, cloning, expression, and purification of a fusion peptide derived from human endostatin

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Introduction: Endostatin is an associated endogenous antiangiogenic fragment of the C-terminus of collagen XVIII. It has produced after proteolytic cleavage of the parental molecule within the circulation. Notably, its antiangiogenic and antitumor activities are mimicked by its peptide fragments, particularly those from the N-terminal segment. Endostar is recombinant human endostatin with nine additional amino acid residues at the N-terminus.

Methods and Results: To increase the structural stability and circulation half-life, we designed a novel peptide molecule containing MGGSHHHHH at the N-terminus and some stabilizing mutations. We exploited a SUMO-endostatin peptide fusion platform to improve solubility, extracellular secretion, and increased production potency. The SUMO-tagged fusion peptide containing Tobacco Etch Virus (TEV) protease cleavage site was cloned simultaneously in a pET-28 a (+) vector and replicated in E. coli DH5α. After plasmid extraction and confirming the sequence, the soluble fusion peptide was expressed in E. coli BL21 (DE3) and purified by Ni-NTA affinity chromatography. The optimum expression condition becomes observed at 0.5 mM of IPTG, 25°C at 24 hours, LB culture medium. Fusion peptide purification became confirmed by a single band in the SDS-PAGE.

Conclusion: This novel peptide would be expected to inhibit angiogenesis and tumor growth in solid tumors. Consequently, the activity of the identified peptide after purification is measured by the antiproliferative activity against the endothelial cells. Keywords: Peptide Design, Endostatin, Purification, SUMO tag

Keywords: Keywords: Peptide Design ،Endostatin ،Purification ،SUMO tag

The status of Nail lead, selenium, cadmium, copper, chromium, and strontium levels in type 2 diabetic patients: Results from the AHAP cohort

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Introduction: trace elements as components of biological activity play an important role in the metabolism of carbohyates. In the current study, we aimed to investigate changes in nail levels of lead, selenium, cadmium, copper, chromium, and strontium and their correlation with the incidence of diabetes.

Methods: 124 participants among the newly diagnosed type 2 diabetes mellitus (T2DM) and 73 healthy individuals were selected from the cohort base study Amirkola Health and Ageing Project (AHAP). Nail levels of selected trace elements (Se, Cr, Cu, Cd, Pb, and Sr) were quantified using an atomic absorption spectrophotometer (AAS).

Results: The nail levels of Pb and Cd were significantly higher in the T2DM patients compared to the healthy ones. Besides, the nail's Se, Cr, and Cu levels were reduced in T2DM patients relative to the normal subjects.

Conclusion: Se, Cr, Cu, Pb, and Cd play a critical role in the pathophysiology of T2DM. It seems that low nail levels of Se, Cr, and Cu and high levels of Pb and Cd are remarkably associated with T2DM. Probable causes should be assessed in other factors such as urine, blood, hair, and intervention factors in absorption and utilization and individual conditions.

Keywords: Diabetes, Trace element, Selenium, Cadmium, Copper, Chromium

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Identification of Potential Key Genes and Potential Pathways in Breast Cancer by Bioinformatic Analysis

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Introduction: Breast cancer is a severe malignant disease with a high occurrence and a susceptibility to recurrence. The purpose of this study was to investigate the hub genes and potential molecular pathways in breast cancer.

Methods: From the Gene Expression Omnibus database (GEO), the gene expression profiles from accession series GSE109169 were downloaded. Subsequently, differentially expressed genes (DEGs) with an adjusted P-value<0.001 and fold change ≥1.5 or ≤-1.5 were revealed. The protein-protein interaction (PPI) network of the DEGs was identified using the Search Tool for the Retrieval of Interacting Genes/Proteins (STRING). Following this, Cytoscape was used to visualize the PPI network and further analyzed by Gepia. Finally, DEGs were analyzed using the KEGG pathway database.

Results: 1190 up-regulated DEGs and 974 down-regulated DEGs in total were discovered. The main enriched pathways for the up-regulated and down-regulated genes were the pathways in cancer and the PI3K-Akt signaling pathway, cell cycle, and progesterone-mediated oocyte maturation, respectively. Furthermore, five hub genes, including CDK1, CCNB1, CCNA2, TOP2A, and BRCA1, identified in up-regulated DEGs and five hub genes, including EGFR, IL6, JUN, FGF2, and PPARG, were identified and validated in down-regulated DEGs for further research due to their high degree of connectivity.

Conclusion: In conclusion, these results indicated potential pathways accountable for breast cancer progression, and the introduced hub genes could be used as new biomarkers for prognosis and prospective new targets for breast cancer therapeutic synthesis.

Keywords: breast cancer, pathway enrichment analysis, bioinformatics, hub gene

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The effect of truncate C-peptide on the folding of proglargine

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Introduction: Insulin glargine is one of a human insulin analogues prepared by recombinant DNA technology. Proglargine is made up of 86 residues in human, and formed by three distinct chains. The A chain, B chain, and the C peptide. According to the importance of the C-peptide and its role in folding, in this study, the effect of C-peptide length on the expression and correct folding of proglargine was investigated.

Methods: The new construct was designed containing truncated C peptide. The gene construct was optimized, synthesized, cloned into pET26b expression vector and transformed into E. coli BL21 (DE3). Different expression conditions such as incubation time (6, 12, 20 and 30 h), IPTG concentration (0.2, 0.5 and 1 mM), temperatures (18, 25, 30 and 37°C) was evaluated. The expressed protein in the form of inclusion body was unfolded and purified by Ni-NTA column. The purified protein was then refolded in various buffers to obtain optimum refolding condition. Finally the SUMO tag was separated by SUMO protease.

Results: The protein was expressed in insoluble form in all examined conditions. The highest yield was achieved in 1mM IPTG, 180 rpm, at 30°C for 6 h. The inclusion bodies were unfolded in 8M urea containing 100 mM DTT. The refolding was done using 0.6 mg/ml protein in10 mM glycine (pH 10.6) containing 0.6M urea, 0.3 mM DDT at 4°C for 24 h. Subsequently, SUMO tag was removed in 50 mM Tris-HCl (pH 7.5) containing 2 mM CaCl2 at 37°C for 18 hours. **Conclusion:** Our results revealed that truncated C-peptide could increase the expression of proglargine as insoluble form. The SUMO tag was removed efficiently in the truncated C-peptide construct. We hope that this construct could be used for further processing of   proglargine and finally improve glargine production.

Keywords: proglargine , glargine , C-peptide

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Synthesis of gold nanoparticles based on artemisia absinthium l plant extract and cytotoxicity evaluation and apoptosis induction in breast cancer cell line

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Introduction: Green synthesis is known as a simple, low-cost, non-toxic, environmentally friendly method with high purity and widespread use. In this study, the green synthesis of gold nanoparticles based on Artemisia absinthium l extract with anti-cancer properties for the treatment of breast cancer has been carried out.

Methods: In the present study, the green synthesis of gold nanoparticles was carried out using Artemisia absinthium l extract. In the next step, the synthesized gold nanoparticles were characterized by using spectroscopic devices (FTIR), (EDX), (map analysis) and (FE-SEM). Then, the cytotoxicity of the synthesized gold nanoparticles was investigated by MTT test and also the induction of apoptosis with Annexin V kit on MCF7 breast cancer cell line was Checked out.

Results: The results of the confirmatory tests were indicative of the synthesis of gold nanoparticles from Artemisia absinthium l plant extract. A significant decrease in the viability of the treatment with gold nanoparticles compared to the Artemisia absinthium l plant extract (AA) was observed on the MCF-7 cell line depending on the concentration. IC50 of Artemisia absinthium l extract and gold nanoparticles were reported as 161.5 and 92.76, respectively. The increase of total apoptosis in IC50 concentration of gold nanoparticles compared to Artemisia absinthium l extract is respectively 36.3 and 26.3. Also, apoptosis was reported more in the mentioned cell line at a concentration of 125 µg/ml of gold nanoparticles compared to a concentration of 250 µg/ml of Artemisia absinthium l plant extract.

Conclusion: In the present study, it was observed that gold nanoparticles synthesized by green synthesis method based on Artemisia absinthium l plant extract increased cell death and induced apoptosis more than Artemisia absinthium l extract in breast cancer cell line (MCF7).

Keywords: gold nanoparticles, Artemisia absinthium l , breast cancer , green synthesis , apoptosis , MTT test

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Role of miR-552-3p and miR-337-3p in PCSK9 expression and non-alcoholic fatty liver disease (NAFLD)

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Page | 233

Introduction: Non-alcoholic fatty liver disease (NAFLD) is one of the most common chronic liver diseases, one of the symptoms of metabolic syndrome and develops with obesity, diabetes mellitus type II, and hyperlipidemia. One of the proteins involved in NAFLD is PCSK9, which causes a decrease in LDLR on the surface of hepatocytes and an increase in serum LDL-c level. Different factors such as miRNAs can affect the expression and activity of PCSK9. Among these miRNAs, miR-337-3p and miR-552-3p have been shown in various studies to suppress PCSK9, increase LDLR and decrease serum LDL-c.

Methods: A comprehensive search was performed for all relevant data. The keywords PCSK-9, miR-337-3p, and miR-552-3p were used to search for articles in Google scholar, PubMed, and NCBI databases. The searched time frame was from January 2022 to April 2022. Four articles were reviewed that were directly related to the effect of miR-337-3p and miR-552-3p on the expression of PCSK 9, which were published in 2021.

Results: It has been reported that the expression of miR-337-3p significantly increased in people with NAFLD and had a negative correlation with the serum level of LDL-c. Moreover, miR-337-3p inhibits the translation and transcription of PCSK9 by its impact on the 3´UTR mRNA PCSK9 and the PCSK9 promoter. Furthermore, miR-552-3p binds to 3´UTR mRNA PCSK9, inhibits PCSK9 translation, and suppresses transcription by binding to the PCSK9 promoter. As a result, inhibiting PCSK9 increases LDLR expression in hepatocytes and decreases serum LDL-C.

Conclusion: Our study shows that the function of miR-337-3p and miR-552-3p in regulating PCSK9 expression and LDL-c absorption propose them as two potential therapeutic targets for the treatment of hypercholesterolemia and non-alcoholic fatty liver disease.

Keywords: miR-337-3p ،miR-552-3p ،PCSK9 ،NAFLD

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Investigating spike protein N-terminal domain mutations in antibody evasion by molecular dynamics simulation and designing a multi-epitope-based peptide vaccine against Omicron variant (BA.1) proteins

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Introduction: Since the outbreak of SARS-CoV-2 in 2019, many people in the world have been infected with this virus. One of the variants of concern that contain a number of mutations, especially in the spike protein, is Omicron.

Methods: Since studies show that the N-terminal domain (NTD) near the RBD has been less studied, here it has been tried to investigate the effect of mutations in this domain on antibody (4A8) escape by molecular dynamics simulation. Also, antigenic epitopes were examined in order to design a multi-epitope vaccine against Omicron, and the best epitopes were selected in terms of immunogenicity, antigenicity, toxicity, allergenicity, and the potential to create cellular and humoral immunity with high population coverage. The vaccine designed cloned into the pET28a (+) vector. And the molecular docking between the multi-epitope vaccine and the immunological receptor was performed.

Results: The results of molecular dynamics simulation indicate the escape of the N-terminal domain (NTD) of the Omicron variant spike protein from the antibody. Also, the designed vaccine showed a strong binding affinity to the immunological receptor. According to the studies, the selected epitopes had the ability to induce some cytokines, including IFN-γ, which are necessary to inhibit virus replication.

Conclusion: According to the results of this study, the proposed multi-epitope vaccine can have an acceptable prevention against the Omicron variant.

Keywords: Omicron (B.1.1.529), Molecular dynamics simulations, N-terminal domain, Epitopic vaccine

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Turmeric and White Tea Silver Nanoparticles Induce Oxidative Stress and Inflammation in MCF-7 Cancer Cells

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Page | 235

Introduction: Green synthesis of silver nanoparticles (AgNp) using plant extracts is a relatively new field in nanotechnology. In the present study, the possible anti-cancer effects of silver green nanoparticles of white tea, and its combination with turmeric were evaluated by the induction of oxidative stress and inflammation in MCF-7 cells.

Methods: MCF-7 cells were cultured with the prepared ugs of AgNp, 3% turmeric extract and a combination of that with 3% white tea extract in concentrations of 0, 25, 50, 75 and 100 µg/ml for 24 Hr. Afterward the amount of produced NO by the cells was measured through GRIESS technique. Thereafter, an ELISA test was performed on the cell supernatant to estimate the quantity of the proinflammatory IL-6 induction.

Results: Upon 24Hr of treatment in group A (AgNp) with 0, 25, 50, 75 and 100µM of the total 2mM concentration of silver nanoparticles the produced levels of NO in the cell culture were 26.03±12.4, 36±7.31, 30±4.17, 23.9±1.03 and 41.17±8.49µM, respectively. In group B (AgNp + white tea) the findings were 23.11±10.13, 27.51±5.44, 26.3±3.41, 32.31±4.20, 43.95±11.42µM respectively. In group C (AgNp + white tea + turmeric) correspondingly 23.11±12.4, 28.98 ± 0.65, 31.76 ± 1.69, 41.26 ± 6 and 66.29 ± 28.34µM of NO were obtained. Also, the average concentration of IL-6 in cells treated by 100µM of groups A, B and C were 4.4 ± 0.36, 4.2 ± 0.26 and 8.4 ± 0.34, respectively.

Conclusion: The results showed that the amount of NO secretion was more induced by the highest concentration of combined extract of 3% white tea and 3% turmeric AgNp. Also, the level of IL-6 secretion was augmented by the same combination of treatment. The high synergistic potential of these green silver nanoparticles can be considered as a promising strategy in the treatment of cancer.

Keywords: Silver nanoparticle, Oxidative stress, Cancer cell, GRIESS technique, ELISA

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Aptamer-G-quauplex design and binding to ochratoxin A along with its binding optimization in colorimetric mode

Introduction: Ochratoxin A (OTA), produced by some Penicillium species, is of interest due to its presence in ied fruit and spices. OTA causes serious risks such as teratogenicity, carcinogenicity, hepatotoxicity, immunotoxicity and nephrotoxicity. Rapid and accurate diagnosis of OTA is necessary to prevent its complications. Several methods have been reported for OTA analysis, such as high-performance liquid chromatography, fluorometric methods, and mass spectrometry, as well as immunoassays based on antigen-antibody interactions. However, each of the mentioned methods has awbacks, including expensive and time-consuming equipment. It is also difficult to prepare antibodies against mycotoxins due to the low antigenicity of OTA. In this study, the design and bioinformatics investigation of a new aptasensor was performed by connecting the OTA-binding aptamer to G-quaruplex.

Methods: In order to produce a specific aptasensor some parameters that can the performance of the aptasensor were investigated. First the sequence (5'-GGGACATAGTGGGGAAAGAGGGGAAGAGTGGG-3') was selected as a G-quauplex with a high G-Score, then some parameters such as ion concentration, Tm, the secondary structure and intramolecular interaction of the G-quauplex and the aptamer (5'-GATCGGGTGTGGGTGGCGTAAAGGGAGCATCGGACA-3') were investigated using bioinformatic methods. The sequence (TTATTA) was then designed as a random hexamer between G-quauplex and aptamer, and an aptasensor for OTA detection was obtained.

Results: Our results clearly demonstrated that there is not any interference between G-quauplex and related aptamer. Moreover, the G-quauplex region with a G-Score of 71 has the ability to form a stable artificial enzyme. Therefore, designed aptasensor (5'-GGGACATAGTGGGGAAAGAGGGGAAGAGTGGGTTATTAGATCGGGTGTGGGTGGCGTAAAGGGAGCATCGGACA-3') can probably bind to OTA specifically and probably signal can be monitored colorimetrically using peroxidase-like activity.

Conclusions: Our study led to the prediction and design of a new aptasensor suitable for OTA detection. This study may be used to develop a rapid screening method for OTA detection in the future and appears to have significant potential for commercialization.

Keywords: Keywords: Ochratoxin A (OTA), Aptamer, G-quauplex, Aptasensor

Evaluation of Caspase-3 Serum Levels in Patients with Hypothyroidism and Hyperthyroidism and the Study of these Serums on the Growth and Survival of MCF-7 Cells

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Page | 237

Introduction: Thyroid dysfunction, including hypothyroidism and hyperthyroidism is one of the most common and important endocrine disorders that disrupts cell growth and homeostasis in various organs of the body. These imbalances might affect the apoptotic pathways of normal cells, triggering the induction of new diseases. Hyperthyroidism appears to increase the risk of multiple solid malignancies with a decrease in caspase-3, while hypothyroidism might delay the onset or reduce the severity of the cancer by stimulating caspase-3 activity. The aim of this study was to measure the levels of caspase-3 in the serum of people with hypothyroidism and hyperthyroidism and to evaluate the effect of their sera on the growth and survival of MCF-7 cancer cells.

Methods: Three groups of normal, hypothyroid and hyperthyroid samples were collected. Three sera from each group were selected for the caspase-3 activity measurement by ELISA test. Afterwards, based on this level and the hormonal and biochemical factors, particular serums were added to the MCF-7 cell culture medium. After 24 and 48 hours of treatment, the cell viability was evaluated by MTT assay.

Results: Upon treatment by the selected sera of both disorders, the production of caspase-3 in MCF-7 cells, were generally higher than the normal group. Induction of apoptosis in MCF-7 cancer cells after the treatment time was directly associated to the sera caspase-3 concentrations.

Conclusion: Decreased cell growth in both of these conditions might be directly related to increased caspase-3 activity in the serum of their cell culture media. Given that the caspase-3 concentration in hypothyroid and hyperthyroid serums is not necessarily a direct factor in inducing apoptosis in cells, to better understand the mechanism of action of this event, assessing the effect of other thyroid derived hormonal and biochemical factors in the cell microenvironment is required.

Keywords: Hypothyroidism, Hyperthyroidism, Caspase-3, Apoptosis

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MEDICAL SCIENCES

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The Role of miR-23a in the expression of MYL9 Gene in the uterine cancer patient

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Page | 238

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Introduction: One of the most common cancers in the female reproductive system is cervical cancer. It occurs due to the abnormal growth of cervical cells (the lower part of the uterus that connects to the vagina). The purpose of this study is to find the genes that play a role in the expression of uterine cancer.

Methods: The GSE 36389 profile was obtained from the (GEO) database and was analyzed. Then we select gene symbols with (p-value<0.05, log2fold change (FC)>1) the genes are on the DAVID site, then we select the (Kegg-pathway) section. Among the genes found, the (MYL9) gene site is one of the most important genes in the signaling pathway of uterine cancer. In the next step, on the Mir walk site, the gene symbols gene selected that were previously used on the DAVID site, then we selected hsa-miR-23a-5p. On the DIANATool site, we select the miRNA-lncRNA section and execute the search for the desired miR.The next step is to examin the relationship between the lnc genes, use the lncRRISEARCH site.

Results: The MYL9 (logFC: 1.988, adj.P. Val: 0.005387) could regulate the uterine cancer progression as a high expressed mRNA in the patients. MiR-23a-5p (score: 1, energy: 0.95, 3utr) and lncRNAGas5 (interaction energy: -26.32 kcal/mol) regulates the expression level of MYL9 in the regulation of actin cytoskeleton and cGMP-PKG signaling pathways.

Conclusion: miR-23a-5p and lncRNA Gas5 regulate the expression level MYL9 in regulating the actin cytoskeleton and cGMP-PKG signaling pathways in uterine cancer patients. High expression of MYL9 protein increases uterine cancer's development risk, and miR-23a-5p and lncRNA GAS5 can control this dysregulation

Keywords: cervical cance, lncRNA, GEO, microRNA

Identification of Potential Key Genes and Pathways by Using Bioinformatic Analysis in prostate cancer

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Introduction: The second most common cancer diagnosis for males and the fifth most common cause of death globally is prostate cancer (PCa). Early stages of prostate cancer frequently have no symptoms and progress slowly. Here, we used bioinformatics analysis to identify potential key genes and pathways for prostate cancer.

Methods: In this study, the GSE6910 dataset was obtained from the Gene Expression Omnibus database (GEO) and was normalized using the Transcriptome Analysis Console (TAC). Genes with an adjusted p-value (F) of 0.05 and $-1.5 \leq |[\log FC]| \leq 1.5$ were identified as differentially expressed genes (DEGs) between 6 normal prostate and 6 prostate cancer samples. Protein-protein interaction (PPI) and visualization were created using STRING, Cytoscape, and Gephi, respectively. We investigated them using KEGG pathway enrichment analysis to see whether biological processes and molecular activities could be associated with the DEGs that overlapped.

Result: According to the findings, 2209 DEGs (1026 up-regulated and 1183 down-regulated) were discovered. Mal, T Cell Differentiation Protein 2 (MAL2), Desmoplakin (DSP), ATP Binding Cassette Subfamily B Member 1 (ABCB1), Kinase Insert Domain Receptor (K), and Cadherin 1 (CDH1) are five overexpressed genes enriched in the KEGG pathway of PI3K-Akt signaling pathway. Fibroblast Growth Factor 2 (FGF2), Peroxisome Proliferator-Activated Receptor Gamma (PPARG), Cell Division Cycle 42 (CDC42), Brain-Derived Neurotrophic Factor (BDNF), and Histone Deacetylase 1 (HDAC1) are five low-expressed genes enriched in the KEGG pathway of pathways in cancer. The following GO terms (most significant) were highly increased in DEGs in PCa within the biological process category: " regulation of bone remodeling (GO:0046850), " regulation of endothelial tube morphogenesis (GO:1901509), and " cellular response to vitamin (GO:0071295).

Conclusion: We identified new potential key genes in prostate cancer that might serve as robust pathways and offer valuable information for future molecularly targeted treatments when executed effectively.

Keywords: Prostate Cancer, Bioinformatics, Pathway, Differentially Expressed Genes

Comparison of proteolytic and hemolytic activities of the venoms from four Iranian vipers

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Introduction: Based on recommendations from the WHO, anti-venom therapy is typically used to treat snake envenomations. Viperidae snake venoms contain a variety of proteins that prevent coagulation cascades from working properly. Additionally, various toxic proteases and phospholipases are included in the venom of vipers, which is how toxicity and lethality develop after envenomation. Characterization of the venoms of medically important snakes should be of high value to improve the clinical management of envenomation and to seek after potential candidate pharmaceutical ugs. Because Iranian vipers have not been investigated so far, we characterized the venoms of four medically significant Iranian vipers, i.e., Macrovipera lebetina, Vipera albicornuta, Echis carinatus, and Pseudocerastes persicus.

Methods: The snake specimens were collected from different locations in Iran. Proteolytic and hemolytic activities were determined for each type of extracted venoms. Using the Mandelbaum, F.R. et al. approach. For the hemolytic activity test, a minor modification to the Memar et al. approach was applied.

Results: We found that proteins from these viper venoms ranged from 5 to 180 kDa in molecular mass. The greatest proteolytic and hemolytic activity of crude venom were attributed to Vipera lebetina and Pseudocerastes persicus respectively. The highest and lowest activity in proteolysis were found in the venoms of V. albicornuta and P. persicus, respectively. The venoms' proteolytic activity generally did not exhibit any significant differences. All vipers, with the exception of P. persicus (250 g venom), reached their maximum hemolytic activity at 500 g of venom.

Conclusion: Our study might be useful in the management of (local) snake envenomation and in the development of novel candidate chemotherapeutic agents. This work would also help to set up new rational strategies for an 'optimized' anti-venom production.

Keywords: Keywords: Iranian vipers, animal venom, V. lebetina, V. albicornuta, E. carinatus, P. persicus, Proteolysis, Hemolysis, Toxicity, characterization

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Comparative effect of hesperetin and melphalan on p53 protein by molecular docking method

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Introduction: Breast cancer is one of the most common cancers among women. One of the causes of this cancer is the lack of expression of p53 protein, the lack or lack of expression of this protein causes cancer, one of the drugs that can induce this protein (1) It is a drug of melphalan and hesperetin. In this study, we compare the effect of this drug on p53 protein by molecular docking (2)

Methods: In this descriptive-analytical study, we used the uniprot site to obtain the structure of p53 protein and obtained a three-dimensional structure through this site. The protein with a higher resolution was selected. This protein had 4 chains. Next, we removed the unsuitable chain of the protein using Chimera 3 software, and water molecules and solvents were also removed. Then, hydrogen ions and charge flow were performed on the A chain, and this protein was stored for the docking process Then we downloaded the three-dimensional structure of melphalan and hesperetin from PUBCHEM site in SDF format. Specifications of hesperetin: Molecular formula: $C_{16}H_{14}O_6$ Molecular Weight: 302.28 Specifications of Melphalan: Molecular formula: $C_{13}H_{18}Cl_2N_2O_2$ Molecular weight: 305.20 We docked using pyrx software, determined the coordinates of the drug in the protein using the deepsite site, and then docked. center_x = 25.2347 center_y = 25.5802 center_z = 25.742

Result: After docking with pyrx software, we had 10 proposed models, of which 3 models were the best docking results according to the table below. Rmsd Binding affinity kcal/mom Model 0.0 -4.7 kcal/mol 1 2.98 -4.6 kcal/mol 2 2.46 -4.5 kcal/mol 3 Rmsd Binding affinity kcal/mol Model 0.0 -6.3 kcal/mol 1 2.35 -6.3 kcal/mol 2 7.64 -6.1 kcal/mol 3 According to Docking results, due to the more negative binding energy of hesperetin than melphalan, it has a better effect on p53 protein.

Keywords: p53, docking, melphalan

A-10-983-2

The critical role of competing endogenous RNA networks in the pathogenesis of the metabolic synome: A systematic review

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Introduction: RNA transcripts including mRNAs, non-coding RNAs, pseudogene transcripts, and circular RNAs are examples of competing endogenous RNAs (ceRNAs) that can control one another by competing for the same miRNA pool. In this systematic review article, we aimed to evaluate the involvement role of ceRNA networks in the pathogenesis of metabolic synome.
Methods: An electronic search of the literature was conducted using PubMed, Web of Science, Scopus, and Google Scholar. Key search terms were "Diabetes Mellitus, Type 2," "MicroRNAs," "long non-coding RNA", "circular RNA"; and "ceRNA". Without regard to language, all studies published between January 1, 2000, and November 30, 2021, were included.
Results: The majority of ceRNA research is still at the bioinformatics prediction stage. There have been few cellular or animal studies investigating the relationship between ceRNA and metabolic synome, which includes obesity, type 2 diabetes, and non-alcoholic fatty liver disease (NAFLD). Furthermore, clinical practice has failed to incorporate strong evidence for ceRNA's function in metabolic diseases. CeRNAs are unique regulatory molecules that are found in many different stages of biology and clinical situations. It is true that the disruption of ceRNA networks (ceRNETs) has an impact on gene development and causes various changes that result in the emergence of metabolic diseases.
Conclusion: ceRNAs have been validated to function in obesity, diabetes, and NAFLD. To properly carry on ceRNA studies, researchers should have a grasp on factors impacting ceRNA activity and the main processes of doing ceRNA research in metabolic synome. The development of new therapies for the metabolic disorder is aided by the functional identification of non-coding RNAs and the non-coding roles of mRNAs in -cell function provided by ceRNA studies.

Keywords: Competing endogenous RNAs, obesity, diabetes, non-alcoholic fatty liver disease (NAFLD)

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Evaluation the effect of combined treatment of metformin and morin on skeletal muscle inflammation in C57BL/6J mice fed high-fat diet

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Introduction: Inflammation in skeletal muscle plays an important role in the pathogenesis of insulin resistance. Medicines and strategies that can improve inflammation and obesity in muscle are very important in the treatment of type 2 diabetes. In this study, the effect of combined treatment of metformin with morin on the improvement of inflammation and insulin resistance in muscle has been investigated. Method: Fifty C57BL/6 male mice were fed on an HFD for 12 weeks. The mice were categorized into five groups, control, HFD, HFD + MET (0.23%), HFD + morin (0.1%), and HFD + MET + morin for 10 weeks.
Results: Treatment with metformin and morin, either alone or in combination, led to reduced weight gain ($p<0.05$), fasting blood glucose ($p<0.05$) and Area Under the Curves (AUCs) in ipGTT ($p<0.05$). Plasma and skeletal muscle triglycerides and intra-myocellular lipid deposition were reversed by treatment with MET and morin, alone or in combination ($p<0.05$).
Conclusion: These results imply that the combination therapy of MET and morin may have therapeutic potential for decreasing obesity-induced skeletal muscle inflammation in the HFD-fed model.

Keywords: Metformin, Morin, Skeletal muscle inflammation, Insulin resistance

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Combination treatment of genistein and metformin displays negative downstream effects on insulin resistance and lipid deposition in HFD-fed c7BL/6 mice

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Introduction: Although the pharmacological activities of genistein and metformin on diabetes and lipid metabolism have been clarified, their combined impacts, especially on skeletal muscle, have not been clearly understood. This study aimed to examine the beneficial effects of genistein in combination with metformin on glucose, lipid and insulin concentration in a high-fat diet (HFD) fed C57BL/6 mice.

Methods: Fifty C57BL/6 male mice were fed on an HFD for 10 weeks. The mice were categorized into five groups, control, HFD, HFD + metformin (0.23%), HFD+ genistein (0.2%), and HFD+ metformin + genistein for 12 weeks.

Result: The findings presented that combination therapy with metformin and genistein caused significant reduction in the plasma TG and muscle TG compared to those in either compound alone. The results of H&E staining indicated that metformin and genistein, alone or in combination, improved intramuscular lipid deposition. metformin or/and genistein intervention decreased weight gain, FBS, plasma insulin, HOMA-IR levels, and AUCs in ipGTT in the HFD group. Also, combination of them led to further reduction in these parameters.

Conclusion: These results indicate that the combination therapy of metformin and genistein may have therapeutic potential for improving Insulin Resistance and fat accumulation in the HFD-fed model.

Keywords: Metformin, Genistein, Insulin, lipid, glucose

A-10-1004-2

The effect of the glycolipoprotein extract (G-90) from earthworm Eisenia foetida on the wound healing process in alloxan-induced diabetic rats

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Introduction: Diabetes is now regarded as a major public health problem. One of the severe problems in diabetic patients is impaired wound healing and foot ulcer. Estimated that approximately 15% of diabetic cases suffer from ulcers of the end organs The earthworm Eisenia foetida glycolipoprotein (as known G-90) is a blend of macromolecules with some biological properties. Given the biological properties of G-90, this study was conducted to investigate the effect of (G-90) on the wound healing process in diabetic rats.

Methods: Thirty adult albino Wistar rats weighing 150–200 g were selected. After induction of diabetes in rats, they were all given anesthesia and circular wounds (2 cm in diameter) were created on the nap region. Then animals were divided into 5groups (n=6). Group (A), the positive control, and Group (B) were treated with an injection of G-90. Group (C) treated with G-90 on site of a wound. Group (D) diabetic rats were left without any treatment, and Group (E) healthy rats were untreated. The period of treatment was as long as 21 days and on the 0,3,6,9,12,15,18,21 the diameter of the wound was measured and histological, and microbiological analysis was measured.

Results: The results revealed that treatment by using G-90 can speed up the wound healing process in diabetic rats. These findings also demonstrated that G-90 treatment decreases the risk of infection in the wound site compared. In addition, the histological analysis indicated that a better extracellular matrix formation with increased fibroblast proliferation, neovascularization, collagen synthesis, and early epithelial layer formation was observed in G-90 treated group.

Conclusion: the results from the wound closure rate and epithelialization evaluation were in agreement with the microbiological and histological studies. Therefore, the G-90 could be considered a new wound healing agent introducing promising therapeutic approaches in both human and veterinary medicine.

Keywords: foot ulcer, diabetic rat, Eisenia foetida, earthworm, wound healing, G-90

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Hypermethylation of brain-derived neurotrophic factor is related to the severity of coronary heart disease

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Introduction: Brain-derived neurotrophic factor (BDNF) plays a pivotal role in cardiovascular homeostasis. However, there is no data regarding to the association between BDNF methylation status and the risk of coronary heart disease (CHD). The aim of the present study was to assess the association of BDNF methylation status and its serum level with the severity of CHD.

Methods: A total of 84 non-diabetic CHD participants with at least 50% stenosis in one of the major coronary arteries were selected as the CHD group and 62 non-CHD subjects were selected as control group according to the angiography report. Furthermore, subjects were categorized according to the Gensini Score. Genomic DNA isolation from blood samples was performed and methylation status of the BDNF gene in exonic region was determined with methylation-specific polymerase chain reaction (MS-PCR) method and serum BDNF levels were measured using ELISA.

Results: Hypermethylation of BDNF gene was observed in the CHD group comparing to the non-CHD group ($p < 0.05$). BDNF gene hypermethylation increases the risk of CHD in the total population (OR = 2.769; 95% CI, 1.033–7.423; P = 0.043) after adjustment for confounding factors e.g. age, gender, smoking, and lipid profile. Moreover, BDNF gene hypermethylation was higher in patients with severe CHD than patients with mild CHD based on Gensini Scoring system. Additionally, the serum BDNF levels were not statistically different between non-diabetic CHD and control groups.

Conclusion: Our observations revealed that BDNF hypermethylation was associated with increased CHD risk, which may help identify subjects being at the risk of developing CHD. In addition, BDNF hypermethylation shows a significant correlation with the CHD severity.

Keywords: Brain-derived neurotrophic factor, Coronary heart disease, DNA methylation

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Cytotoxic Activity of Citrullus colocynthis (L.) Schrad. (Bitter Apple) Pulp Extract in HepG2 cells

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Page | 247

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Introduction: Anticancer, anti-diabetes, anti-lipid, anti-microbial, and insecticidal effects are a few of the medicinal properties of Citrullus colocynthis (C. colocynthis). Nevertheless, there are reports of its toxic side effects. This study investigated the plant's antiproliferative effect in the human hepatocarcinoma cell line (HepG2).

Methods: After preparing the ethanolic extract of C. colocynthis pulp, we determined the extract's antiproliferative/cytotoxic activity against the HepG2 cell line using the MTT and Neutral Red Uptake (NRU) assay methods. Briefly, twenty-four hours after seeding (25×10^3 cells/well), the media were replaced by 200 µl of serum-free media for 2 h and then replaced by 200 µl of fresh media containing 5% serum and different concentrations (0, 0.5, 1.0, 2.0, 4.0 mg/ml) of the extract in quauplicate. We performed the MTT assay after 24, 48, and 72 h and measured NRU after 24 h exposure. The optical density was recorded at 570 nm. Percent cell viability was determined against a control group.

Results: The ethanolic extract of C. colocynthis pulp showed inhibitory effects on HepG2 cell proliferation (Fig. 1). The IC50 values were calculated as IC50 (24 h) = 1957.79 µg/ml, IC50 (48 h) = 733.72 µg/ml, and IC50 (72 h) = 839.20 with MTT; and IC50 (24 h) = 1762.08 µg/ml with NRU. MTT assay and NRU method produced slightly different yet comparable results. **Conclusion:** C. colocynthis may be toxic to liver cells. This plant may be a potential chemotherapeutic ug to treat hepatocellular carcinoma.

Keywords: Citrullus colocynthis, HepG2 cell line, MTT assay, NRU, Antiproliferative

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Cytotoxic Activity of Cichorium intybus (L.) Leaf Ethanolic Extract on HepG2 Cells

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Introduction: Cichorium intybus Linn (chicory) is a plant of the Asteraceae family used by the ancients as a medicine to enhance metabolism. We evaluated the cytotoxic effect of the ethanolic extract of chicory leaves on the human hepatocarcinoma (HepG2) cell line.

Methods: The leaves (5 g) were extracted with EtOH (96%) by maceration. After separating the chlorophyll, the extract was ied to yield 0.17 g. HepG2 cells were seeded (2.5×10^4 cells/well) in DMEM (low glucose) supplemented with 10% FBS and 1% penicillin/streptomycin and incubated in a humidified atmosphere of 5% CO_2 at 37 °C. After adherence, different concentrations of the extract (0.25, 0.5, 1.0, and 3.0 mg/ml) were added after filtering to sterilize. After 24 h, 48 h, and 72 h exposure, the cytotoxic activity of the extract against HepG2 cells was determined using the MTT and neutral red uptake (NRU) assays. The absorbances were measured at 570 nm and 540 nm. The percent cell viability in both tests was calculated using the following formula: Cell viability (%) = (A test – A blank/A control – A blank) × 100.

Results: Statistical analysis showed that the extract significantly decreased HepG2 cell viability (Fig. 1). The IC50s obtained from 24, 48, 72 h MTT assay were 924.5, 684.2, and 675.6 µg/ml, respectively; IC50 by 24 h NRU assay was 658.7 µg/ml.

Conclusion: These data show that the ethanolic extract of chicory leaves shows toxicity in HepG2 cells and may be used to treat liver cancer.   Figure 1: Cytotoxic effect of different concentrations of ethanolic extract of chicory leaves on HepG2 cells by MTT assay (A) and NRU assay (B).

Keywords: Chicory, cytotoxicity, HepG2 cells, MTT and NRU assay

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Amelioration of STZ-induced nephropathy in diabetic rats by Scrophularia striata ethanolic extract

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Introduction: One of the major complications of diabetes is diabetic nephropathy (DN), which these patients suffer from. That is why it is important to find the mechanisms that cause nephropathy and its treatment. The present study was conducted to examine antidiabetic effects of Scrophularia striata ethanolic extract [S.striata] and evaluate its effects on oxidative stress markers and the expression of RAGE, S100A8 genes in the kidney of type 1 diabetic rats.

Methods: 36 rats (weight 200-250 g) were randomly assigned into six groups as follows: Cnt, Cnt+S.striata100 and Cnt+S.striata200 that received normal saline, 100 and 200 mg /kg.bw of ethanol extract of S.striata, respectively. Group Dibt, Dibt+S.striata100 and Dibt+S.striata200 that received normal saline, 100 and 200 mg/kg.bw of ethanol extract of S.striata, respectively. Type 1 diabetes was induced in rats by a single injection of streptozotocin (55 mg/kg.bw). After 60 days of treatment, biochemical factors and oxidative stress markers (SOD and A) were measured using spectrophotometric methods. Gene expression of RAGE and S100A8 were analyzed using real-time PCR.

Results: Diabetes significantly impairs the serum and urine fasting blood glucose (FBG), lipid profile, creatinine, urea and albumin parameters. After the treatment with S.striata extract, these parameters are close to the normal range. It was shown the S.striata extract significantly decrease the kidney expression levels of RAGE and S100A8 genes and improve oxidative stress markers (SOD and A) in the kidney tissues when compared to diabetic control group. Also, it was found that the beneficial effects of the S.striata were dose-dependent.

Conclusions: Ethanolic extract of S.striata has beneficial anti-diabetic effects. Moreover, S.striata by reducing the expression of RAGE and S100A8 genes and improving oxidative stress might be used as adjuvant treatment for diabetic complications.

Keywords: SOD, A, histopathology, lipid profile, diabetic nephropathy

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Formononetin reduces the miRNA-21 expression and inhibits the cell proliferation and Invasion in HepG2 cells

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Page | 250

Introduction: Hepatocellular carcinoma (HCC) is the third leading cause of cancer-related death yearly. The late-diagnosed setting of HCC exacerbates the mortality. Formononetin (FMN), a naturally occurring isoflavone stemmed from Red Clover, has shown to own pleiotropic effects against cancerous cells. This study aimed to assess the FMN efficacy of HCC cells.

METHODS: qRT-PCR was used to assess the effect of FMN on miR-21, PTEN, Bcl-xL, P21, VEGF, and MMP-2 expression. The efficacy of FMN on cell growth of HepG2 cells was determined using trypan blue and MTT assays, respectively. Colony-forming ability and migration of HepG2 cells were tested using wound healing and Clonogenic assays, respectively. Apoptosis was illustrated by Hoechst 33342 staining.

RESULTS: We found that FMN [60, 80 (IC50), and 100 μM] were strikingly downregulated the miR-21, MMP-2, VEGF, and Bcl-xL, and upregulated PTEN and P21, and inhibited the cancer cell growth, relative to blank and solvent control ($p < 0.05$). Results of FMN by wound healing and colony formation assays on HepG2 cells demonstrated a mean reduction in both migration and colony-forming ability ($p < 0.05$). Hoechst 33342 staining illustrated that FMN can induce apoptosis.

CONCLUSION: Our data implying that FMN plays a leading role in the inhibition of HepG2 cell proliferation, survival, migration, metastasis and invasion, colony-forming ability, and apoptosis induction together with altering genes expression. Hence, FMN might be a promising therapeutic candidate for the treatment of advanced HCC, which worthwhile for further studies.

Keywords: Hepatocellular carcinoma, Formononetin, Cancer therapy, miR-21

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Targeting anti-apoptotic proteins by a combination of miRNA-15a and miRNA-16-1 enhances the therapeutic efficacy of fludarabine and ABT-199 in CLL cells

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INTRODUCTION: Down-regulation of miRNA-15a and miRNA-16-1 is associated with Bcl-2 and Mcl-1 expression and chemoresistance in tumor cells. In this study, the combination effect of miRNA-15a and miRNA-16-1 on apoptosis and sensitivity of the CLL cells to fludarabine and ABT-199 was investigated.

METHODS: The expression levels of Bcl-2 and Mcl-1 was measured using RT-qPCR. The effect of treatments on cell growth and survival was measured by trypan blue staining and MTT assay, respectively. Apoptosis was measured using caspase-3 activity and ELISA cell death assays.

RESULTS: Transfection of miRNA-15a or miRNA-16-1 significantly suppressed the expression of Bcl-2 and Mcl-1 in a time-dependent manner (*$p<0.05$ versus negative control miRNA or blank control). Other experiments showed that up-regulation of each of miRNA-15a or miRNA-16-1 decreased cell growth, induced apoptosis, and synergistically lowered the IC50 value of fludarabine and ABT-199 in CLL cells. Moreover, simultaneous transfection of two miRNAs showed a greater effect on cells survival, apoptosis and ug sensitivity, relative to single transfection.

CONCLUSION: Our study shows that the miRNA-15a and miRNA-16-1 can efficaciously enhance the anticancer effects of fludarabine and ABT-199 in CLL cells, and may offer a new promising therapeutic strategy for CLL resistant patients.

Keywords: ABT-199, apoptosis, Bcl-2, fludarabine, Mcl-1, miRNA-15a, miRNA-16-1

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Evaluation the anti-diabetic effect of resistance and endurance training in streptozotocin-nicotinamide diabetic rats

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Introduction: Physical inactivity are the major risk factors for type 2 diabetes. The present study was conducted to investigate the effects of resistance training and endurance training on diabetic related metabolic parameters in diabetic rats.

Methods: Male Wistar rats (Twenty-four) randomly assigned them to four groups of six rats: control group (C), diabetic group (D), resistance training group (RES), endurance training group (END). Type 2 diabetes induced by nicotinamide (120 mg/kg) and streptozotocin (STZ, 65 mg/kg) intraperitoneally. The training period was 70 days. The irisin, betatrophin, insulin, FBG and lipid profiles were measured in serum of all rats.

Results: Diabetes significantly increased serum levels of FBG ($p < 0.001$), which were decreased significantly after administration of training ($p < 0.001$). Training administration had a significant effect in normalizing serum lipid profile ($p < 0.001$) and it was shown to increase the serum levels of irisin, betatrophin ($p < 0.001$) and insulin (endurance training: $p < 0.001$ and resistance training: $p < 0.05$). It was also found that the endurance training was more effective in improve this parameters when compared with resistance training ($p < 0.05$). In addition, the irisin revealed a significant positive association with betatrophin (endurance training: $p < 0.01$ and resistance training: $p < 0.05$) and insulin (endurance training: $p < 0.01$ and resistance training: $p < 0.05$) values in diabetic training groups.

Conclusion: This study demonstrated that endurance training could more effective diabetic related metabolic derangement compared resistance training. This effect is probably due to better regulation of irisin, betatrophin and insulin relative to resistance training.

Keywords: Diabetes mellitus, fibronectin type III domain containing protein 5 (FNDC5), Angiopoietin-like protein 8 (ANGPTL8), endurance training, resistance training

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Nanocrystalline cellulose is a biomedical application in cancer target therapy

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Introduction: Cancer therapy has become one of the major challenges in the biomedical field of the entire world. Traditional cancer therapies have severe side effects which impair normal tissue in addition to the tumors. In current years, the use of nanostructured systems for biomedical applications has been widely expanded. The implementation of Nanocrystalline cellulose (CNCs) may bring great benefits because of their considerable availability, absolute renewability, physicochemical properties, and moderately low price of production. The absence of noticeable toxicity and untargeted cellular uptake of CNC could prospect these nanoparticles as appropriate carriers in drug delivery applications. In this review, we concentrate on some significant properties and applications of NCC, procedures for the preparation of nanoscale cellulose, numerous surface conversions which improves the effectiveness of drug delivery, targeting cancer cells based on NCC, and chemical modifications that happen at the surface of NCC for controlled release of drugs in an acidic situation of cancer cells and numerous other biomedical characteristics of NCC.

Methods: By literature review from 2010 to 2022 including Medline, PubMed, Scopus, and Google scholar, 130 articles were reviewed.

Results: Special properties of NCC such as the absence of immune reaction in the body, lower cytotoxicity, biodegradability, and hydrophilic character caused by hydroxyl groups, improve the possibility of this nanoscale material as a drug delivery system. By Hydroxyl groups the surface of NCC becomes very flexible for adding various chemical groups, leading to expanded drug release in tumor cells. It also drives NCC very valuable in targeted drug delivery to cancer cells and boosts the abruption of conjugated drugs with NCC.

Conclusion: Normally, cancer target therapy based on CNCs is a new type of therapy that guarantee the low invasive localized therapy of cancerous tissue, with even little to no side effects.

Keywords: Nanocrystalline cellulose, Biomedical applications, Nanocarrier, Cancer

A-10-2100-1

Improvement of NRF2 gene expression and antioxidant status in patients with type 2 diabetes mellitus after supplementation with omega-3 polyunsaturated fatty acids: A double-blind randomised placebo-controlled clinical trial

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Introduction: Nrf2 is a transcription factor that induces the expression of several proteins with antioxidant properties such as sestrin2 (Sesn2) and is therefore considered as the major regulator of anti-oxidative defence system. Objectives: The aim of this research was to study the effect of supplementation with n-3 PUFAs on the antioxidant status and the gene expression of Nrf2 and Sestrin2 (Sesn2) in patients with type 2 diabetes mellitus (T2DM).

Methods: Sixty patients with T2DM were enrolled in a placebo-controlled, double-blind, randomised clinical trial. Intervention and design: The participants were randomly allocated to two intervention groups receiving either n-3 PUFAs (2,700 mg/day) (n = 30) or placebo soft gels containing 900 mg of edible paraffin (n = 30). The main outcome measures were the expression of Sesn2 and Nrf2 genes which were assessed in peripheral blood mononuclear cells (PBMCs) after RNA extraction and cDNA synthesis by real-time PCR. Total antioxidant status in plasma samples was also measured based on the ferric reducing ability of plasma.

Results: NRF2 gene expression was significantly increased in n-3 PUFA-supplemented subjects, compared with the placebo group. Plasma total antioxidant status was also significantly augmented in n-3 PUFA-supplemented subjects. SESN2 gene expression was not significantly affected by n-3 PUFA supplementation although a slight up-regulation was observed.

Conclusion: Supplementation with n-3 PUFAs enhanced NRF2 gene expression and improved overall antioxidant capacity and thus might be considered beneficial in the amelioration of oxidative stress and prevention of T2DM complications.

Keywords: diabetes, sestrin,nrf2,oxidative stress, omega 3, n3-pufa

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Promising effects of Persian shallot extract on the serum markers and blood pressure of patients with metabolic syndrome: A double-blinded randomized controlled trial

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Background: Persian shallot is an endemic herb of Iran with several therapeutic properties, including antioxidative potentials. In this randomized controlled trial, we evaluated the effect of Persian shallot extract on the serum markers and blood pressure of patients with metabolic syndrome (MetS).

Methods: Fifty patients with MetS diagnosis were randomly assigned to the intervention (Persian shallot extract) and the control (placebo) group. Both groups received treatment for three months. Before the study and at the end of the study, 5ml peripheral blood was taken from each patient. Outcome measures were total antioxidant capacity (TAC), superoxide dismutase enzyme (SOD), malondialdehyde (MDA), oxidized low-density lipoprotein (Ox-LDL), Apolipoprotein H (Apo-H), FBS, cholesterol, triglycerides, HDL and LDL, as well as systolic and diastolic blood pressure.

Results: At baseline, evaluated parameters were not significantly different between the intervention and control groups. At the end of the study, the mean serum levels of malondialdehyde and oxLDL were significantly lower in the intervention group (P=0.003 and P=0.026, respectively). The mean FBS, Cholesterol, triglycerides, and LDL were significantly lower in the intervention group (P=0.027, P=0.045, P<0.001, and P=0.007, respectively), as well. The mean TAC and HDL were significantly higher in the intervention group)P<0.001 and P=0.006, respectively). Moreover, systolic and diastolic blood pressure were significantly reduced in the intervention group (P<0.001 and P=0.041, respectively). No other significant association was observed.

Conclusion: Persian shallot extract has several beneficial effects in MetS patients, including optimizing oxidative balance and reducing blood pressure, fasting blood sugar, and blood lipid profile

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Molecular-based detection of Leishmania species among resistant patients treated with Meglumine Antimoniate

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Introduction: Cutaneous Leishmaniasis (CL) is a major health problem in different areas of Iran. The standard treatment is pentavalent antimonial used in the world as a first-line drug. However, resistance to pentavalent antimony has increased dramatically in Iran. Mashhad is known as one of the most important endemic centers of anthroponotic cutaneous leishmaniasis (ACL). Many patients with resistant lesions from endemic regions of zoonotic cutaneous leishmaniasis centers (ZCL) have been referred to Mashhad for further proceedings. In this study, we aimed to investigate the Leishmania species among the resistant people referred to the Parasitology laboratory in the school of medicine of the Mashhad university of medical sciences.

Methods: According to the patients' clinical history, 50 patients with resistant Leishmania lesions to Meglumine Antimoniate (Glucantime®) were selected from October of 2018 to August 2022. After microscopic examination, dermal scrapings and stained slides prepared of skin lesions were used for morphological diagnosis. DNA extraction and PCR amplification were optimized to identify Leishmania species.

Results: Amastigote forms were seen in 31 of 50 slides in direct examination. In PCR, of 50 patients with resistant CL, 40 individuals were infected with Leishmania tropica while Leishmania major was found in 10 patients. L. major was detected by molecular approach. All the patients with L. tropica and 4 individuals with L. major lived in Mashhad, while 6 of the 10 infected people with L. major lived in the surrounding cities of Mashhad, which were known as ZCL center.

Conclusions: Due to the high sensitivity of the molecular method, it is recommended for diagnosis of CL in resistant cases with low parasite load. Contrary to the belief that the L. tropica strains cause resistant CL in Mashhad, L. major were also found in these patients. More molecular studies on resistant strains in each species are recommended.

Keywords: Molecular detection ،Leishmania species ،resistant patients ،Meglumine Antimoniate

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Recombinant CD137-Fc, its synthesis, and applications to reduce the inflammation due to the novel coronavirus

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Introduction: CD137 (ILA/4-1BB), a member of tumor necrosis factor receptor superfamily, is one of the most important T cell costimulatory molecules. Interaction of this molecule with its ligand transmits a two-way signal that activates both T lymphocyte and antigen presenting cells. The soluble form of CD137 (sCD137) reduces the activity of its membrane isoform and is associated with T lymphocyte activation-induced cell death. Recombinant CD137-Fc may be used to treat cancers, autoimmune disorders and viral infections. It may also be useful for the management of coronavirus infection.

Methods: The 1276 bp DNA sequence encoded CD137-Fc recombinant protein was prepared and subcloned into the lentiviral vector and expressed in transduced CHO-K1 eukaryotic cells. Western blot analysis and enzyme-linked immunosorbent assay tests were performed. The IL-6 and IL-8 levels as inflammatory cytokines were measured using the ELISA kits.

Results: Different assay results demonstrated that the expression of the 70-kDa CD137-Fc molecule was detectable without any degradation. IL-6 and IL-8 decreased significantly in the sample exposed to CD137-Fc protein.

Conclusion: This study helps to confirm previous research suggesting the use of this recombinant protein as a promising solution for the treatment of virus infections. This product is widely used in novel medical treatments, including cell-based immunotherapy such as dendritic cell, CAR T and CAR NK therapy. This product also is useful in the treatment of the 2019 coronavirus disease pandemic Because of its effect on reducing cytokine-induced inflammation.

Keywords: Autoimmune disorders, cancer immunotherapy, coronavirus inflammation, recombinant protein CD137-Fc, sCD137.

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Evaluation of indexes related to megaloblastic anemia: a conducted study on megaloblastic anemia patients

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Introduction: Megaloblastic anemia is a disorder caused by lack of folate and cobalamin, genetic susceptibility and use of methotrexate, cytosine, and arabinose. It has high prevalence among people with 40-49 years.

Methods: Here, we investigated the hematological and biochemical parameters as well as bone marrow cell line in eighteen-one Iranian megaloblastic anemia patients.

Results: The results showed that megaloblastic anemia is related to increase of LDH, hyperplasia of erythroid cell line. In addition, it occurred following to age increase. The increase of MCV and MCH are indicated macrocytes with high content of hemoglobin. Finally, it was found that age increase along with RBC reduction and peripheral blood macrocytosis that indicate megaloblastic anemia.

Conclusion: Given that, this disease commonly occurred in old ages therefore, should be a special attention to people with the disease.

Keywords: megaloblastic anemia, genetic susceptibility, erythroid cell line, RBC

17th National Congress of Biochemistry & 8th International Congress of Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

Page | 259

Poster Presentations

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TEHRAN UNIVERSITY OF MEDICAL SCIENCES

A-10-1785-2

Evaluation of the antioxidant activity of eugenol on the toxicity induced by bisphenol A in the liver and serum of male rats

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Introduction: Bisphenol A (BPA) is a chemical toxicant that used in many synthetic materials such as water bottles. Hepatotoxicity caused by oxidative stress is one of the major side effects of BPA. Studies suggest that the use of antioxidants may reduce the progression of oxidative stress-related disorders. This study was designed to evaluate the antioxidant effect of eugenol against BPA-induced toxicity in the liver and serum of rats.

Methods: Forty male Wistar rats were randomly divided into 5 groups: control group, DMSO group (as a vehicle), Olive oil group (as a vehicle), BPA (50mg/kg) group, Eugenol group (50mg/kg BPA+10.7mg/kg). In the last group, the animal received Eugenol 1 h after administration of BPA. All groups underwent oral gavage for four weeks. After sacrificing the rats, serum and liver samples were collected to measure oxidative stress markers. One-way ANOVA with Tukey post hoc test was used to determine the difference in the experimental variables between the studied groups.

Results: BPA-treated rats showed significantly increased total oxidant status (TOS) and malondialdehyde (MDA) levels as well as a significant decrease in the glutathione peroxidase (GPX), superoxide dismutase (SOD) activities and glutathione (GSH) and total antioxidant capacity (TAC) levels in the liver and serum compared to control group. In addition, BPA meaningfully increased the activities of serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) compared with the control group. Eugenol-treated rats showed a significant decrease in MDA and TOS levels and a significant increase in GSH and TAC levels in liver and serum compared to the BPA group. Eugenol had no significant effect on SOD and GPx activities compared to the BPA group. However, it significantly reduced serum activities of AST and ALT compared with the BPA group.

Conclusion: The results of this study show that Eugenol significantly reduces BPA-induced hepatotoxicity in rat liver and serum by attenuating oxidative stress.

Keywords: oxidative stress, Bisphenol A, antioxidant, Eugenol

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Quercetin synergistically potentiates the anti-metastatic effect of 5- Fluorouracil on MDA-MB-231 breast cancer cell line

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Page | 261

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Introduction: Breast cancer (BC) cells' ability to metastase to other tissues increases its mortality. The Matrix metalloproteinase 2 and 9 (MMP-2 and MMP-9) facilitate cancer cells' migration. 5 Fluorouracil is a frequently applied chemotherapeutic agent in cancer treatment with destructive side effects on normal tissues. Hence, researchers have focused on finding a way to reduce the dose of chemotherapeutic drugs. Quercetin, a natural polyphenolic compound, has inhibitory effects on the proliferation and migration of tumor cells. This study evaluated the effect of the combination of Quercetin and 5 Fluorouracil on the migration of MDA-MB-231 breast cancer cell line. Materials and

Method: The effect of Quercetin,5 Fluorouracil, and their combination on MDA-MB-231 breast cancer cell proliferation was investigated through MTT assay. Inhibition of tumor cell migration was examined by wound healing assay. Finally, the effect of treatments on the gene expression of MMP-2 and MMP-9 was evaluated by quantitative real-time PCR.

Results: The IC50 value for Quercetin and 5 Fluorouracil after 48h treatment was 295μM and 525μM, respectively. The combination index (CI) for Quercetin and 5 Fluorouracil was <1, indicating synergy between them. The combination of Quercetin plus 5 Fluorouracil resulted in a significant reduction in migration rate and MMP-2 and MMP-9 gene expressions of MDA-MB-231 cancer cells compared to the individual application of 5-FU.

Conclusion: Quercetin enhances the suppressory effect of 5 Fluorouracil on the migration of breast cancer cells. The combination of Quercetin and 5 Fluorouracil can be an attractive field for future studies.

Keywords: Quercetin, synergism, anti-metastatic effect, 5- Fluorouracil, breast cancer

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Quercetin Enhances the Suppressive Effects of Doxorubicin on the Migration of MDA-MB-231 Breast Cancer Cell Line

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Page | 262

Introduction: Cancer cell metastasis is facilitated by matrix-metalloproteinases through degradation of extracellular matrix (ECM) proteins and is a major cause of mortality. One of the most common remedies for cancer is chemotherapy, which has many side effects. Therefore, it seems necessary to find a way to reduce the side effects of these drugs while maintaining their anticancer effects. Quercetin (que) is a natural substance that has been reported to have anticancer activities. Objectives: This study aims at evaluating the effect of que in combination with doxorubicin (dox) on the migration of the MDA-MB-231 breast cancer cell line.

Methods: The effects of que and dox on cell viability in 24h and 48 h was assessed by MTT assay. Also, the effects of the same drugs on the cancer cells migration were evaluated, using the wound healing assay. Lastly, the effects of que and dox were assessed on the expression of MMP-2 and MMP-9 genes.

Results: The combination of 50 µM of que with 32 nM of dox was selected by CI comparison. The viability and migration of cancer cells and the gelatinases genes expression were decreased after treatment with individual drugs. The migration and the expression of MMP-2 and MMP-9 genes after treatment with the combination of que and dox was significantly reduced compared to the treatment with que and dox alone.

Conclusions: Que inhibits the viability and migration of MDA-MB-231 cancer cells and synergistically enhances the effects of dox on the survival and migration of these cells. Hence, we propose this drug combination as a path for further research on breast cancer therapy

Keywords: Quercetin, Enhance, Anti-migratory Effect, Doxorubicin, Breast Cancer Cell Line

A-10-1013-1

Quercetin potentiates chemosensitivity of MCF-7 breast cancer cells to 5-fluorouracil

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Introduction: Breast cancer is one of the leading cause of cancer mortality worldwide.5-fluorouracil (5-FU) is one of the chemotherapy drugs to treat breast cancer، but it is associated with several side effects. combination therapy is a way to increase the effectiveness of chemo drugs and decrease their usage dose. Quercetin (Quer) is one of the natural polyphenols with anti-cancer properties. This study investigated the apoptotic effect of 5-fu in combination with Quer compared with 5-FU alone on MCF-7 breast cancer cells.

Methods: Different single and combined concentrations of 5-FU and Quer were applied to MCF7 cells for 48h.Cell viability، apoptosis، gene expression of Bax، Bcl2، p53 ،caspase activity، and colony number were assessed using MTT assay ،flow cytometry، quantitative real-time PCR، enzyme-linked immunosorbent (ELISA) ،and colony formation assay، respectively.

Results: The combination of 5-FU and Quer compared to 5-FU alone improved apoptosis by increasing the gene expression of Bax and p53 and caspase-9 activity and decreasing the Bcl2 gene expression. colony formation in MCF7 cells significantly decreased in the combined state compared to 5-FU alone.

Conclusion: Quer potentiates the sensitivity of breast cancer to 5-FU so that this combination may be proposed as a treatment for breast cancer. Therefore, ،this combination can be suggested for future in vivo studies.

Keywords: Quercetin، Potentiate, Chemosensitivity, 5-Fluorouracil, Breast cancer

Enhancement of BAX/BCL2 Ratio and Induction of Apoptosis with Combination Therapy in HT29 Colon Cancer Cells

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Introduction: Cancer is the third cause of death following accidents and heart diseases in Iran. During the treatment protocol of colon cancer - one of the most common cancers - several drugs are used which have severe side effects. Combination therapy is a new strategy that minimizes resistance to chemotherapy and reduces drug toxicity. For the first time, we investigated the effect of combination therapy on cell survival and BAX/BCL2 gene expression ratio in HT29 colon cancer cells. In this study we used gamma-tocopherol as an adjuvant in addition to the 5-fluorouracil to increase the drug efficacy.

Methods: The proliferation of cancer cells was determined via colony formation assay. BAX/BCL2 ratio was evaluated after incubation with concentrations of 5-Fluorouracil and Gamma Tocopherol via real-time-PCR.

Results: The average number of colonies in the cells treated with 5-Fluorouracil, Gamma Tocopherol and their combination of them was 63 ± 4, 78 ± 3, and 28 ± 2, respectively which significantly decreased in the combination group. In contrast with the control group, the BAX/BCL2 ratio remarkably increased when the cells underwent combinational treatment ($p<0.05$).

Conclusion: 5-Fluorouracil and Gamma Tocopherol reduced HT 29 cell proliferation. Our results suggest that combination therapy with 5- Fluorouracil and Gamma Tocopherol can be considered as a strategy for induction of apoptosis via increasing the BAX/BCL2 ratio.

Keywords: Colon cancer, Apoptosis, 5-fluorouracil, Combination Therapy, γ-tocopherol

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Dermatoglyphic patterns on fingers and gynecological cancers diagnosis

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Introduction: Fingerprints have so far been used for determining the basis of certain malignant diseases, with positive outcomes. Considering the high rates of cancer-related mortality in Iran, this study was conducted for the purpose of examining the dermatoglyphic pattern of fingers in patients with gynecological cancers as compared to healthy people.

Methods: The present study was conducted on 151 women with gynecological cancers as the case group and 152 healthy women with no history of such cancers as control group. The dematographic details of participants from both control and case groups were collected using a checklist, and the pattern of their fingerprints was prepared and examined. The data were analyzed for their significance using chi-square test and t- test. Odds ratio with 95% confidence intervals were calculated.

Results: Dermatoglyphic analysis showed that arch and loop patterns significantly changed in cases group as compared to control. However, the odds ratio suggested that loop pattern in 6 or more fingers might be a risk factor for developing gynecological cancers.

Conclusion: Our results showed that there is an association between fingerprint patterns and gynecological cancers and so, dermatoglyphic analysis may aid in the early diagnosis of these cancers.

Keywords: Dermatoglyphic pattern, Ovarian cancer, Uterine cancer

A-10-1029-1

Lactoperoxidase Enzyme Stabilization with Betaine

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Introduction: Enzymes have widespread usage in hygiene and different industry. The enzymes' processes' stabilization is necessary Because of their high valence to increase the half-life and features like sensitivity, instability toward environmental conditions, the existed stress, and high cost. betaine is one of the compatible solutes which doesn't affect enzymes' chemical constructions and causes the stabilization of the enzyme toward environmental stress such as temperature, PH, time, different salt concentrations also protect the enzyme even in its low concentrations.

Methods: the 75 microliter amount of lactoperoxidase enzyme with 1 cc of betaine solution 0.5 molars prepared by potassium phosphate buffer 6.8 ph is stabled for 72 hours; then the stabled lactoperoxidase enzyme and free lactoperoxidase enzyme as a control sample were exposed to pH the 5.3, 6.8, 9. Finally, the stabled and free Lactoperoxidase enzymes' function and stability were measured by spectroscopy UV-VIS 2600.

Results: after the examinations and measurement the function results have shown that the stabled and free Lactoperoxidase enzymes' remainder in pH: 5.3, 6.8, and 9. The stabled enzyme with betaine's remainder function areas 46.3%, 91.05%, and 52.95% respectively; whiles, the free enzyme stabled its remainder function in mentioned degrees which areas 30.62%, 46.74%, and 37.29% respectively. Also, the betaine-stabilized sample was able to maintain 50% of its activity after 72 hours compared to the control sample, while the control samples lost more than 50% of their activity.

Conclusion: the examination showed that the stabilization with compatible samples like betaine caused the enzyme's stability in tough conditions and increased its remainder activity.

Keywords: Betaine, Stability, Stabilization, Compatible solute, Lactoperoxidase

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Anti-proliferative effect of ethanolic, and polysaccharide fractions of Astragalus ovinus against MCF-7 cancer cell line

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Page | 267

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Introduction: Astragalus has considered in traditional Chinese medicine, and the root of this plant has anti-tumor and anti-cancer properties. In this study, the effects of ethanolic extract and polysaccharide fraction of Astragalus ovinus (PFA) root on the MCF7 cell line were investigated.

Methods: MTT test was used to evaluate cytotoxicity. Cell cycle and cell apoptosis were assessed using flow cytometry. The expression of genes related to extrinsic and intrinsic apoptotic pathways (caspases 8 and 9) was also examined by real-time PCR.

Results: The results of cytotoxicity showed that extracts and PFA inhibited the proliferation of MCF-7 cancer cells in does dependent manner. The IC50 value of extract, PFA and cisplatin were 560.9, 961.2 and 22.42µg/ml respectively. Also, cell cycle analysis showed that the extract and PFA arrested the cell cycle in G1 phase, and the cell percentage of the SubG phase also increased. Examination of apoptotic effects shows that both treatments (extract and PFA) induced apoptosis in MCF-7 cancer cells, which is less than cisplatin. Expression of caspase 8 and 9 genes is increased in both cisplatin and PFA treatments; however, ethanolic extract only affects caspase 8 expression.

Conclusion: Our results confirmed that ethanolic extract and PFA ant- proliferative activities in MCF-7 cell line by inhibiting cell proliferation and inducing apoptosis. Taken together, it can suggest that the ethanolic extract and PFA has a potential   therapeutic agent for breast cancer.

Keywords: Astragalus polysaccharide, Apoptosis, cell cycle, Breast cancer, Caspase 8, Caspase 9

The rs4808793 polymorphism of GDF-15 associates with significantly elevated Ferritin in both thalassemia major and thalassemia intermedia

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Introduction: Previous studies have proposed the rs4808793 polymorphism of the GDF-15 as a potent inducer of hypertension, cardiovascular disease and renal failure. The current study was performed to investigate the role of rs4808793 polymorphism in the pathogenesis of iron overload in patients suffering from major or intermedia beta-thalassemia.

Methods: The study included 69 major thalassemia patients and 25 intermedia thalassemia patients as a control group. The study was conducted on 69 major thalassemia patients and 25 intermedia thalassemia who were referred to Baqa'i Hospital 2 in Ahvaz, Iran. Five ml of blood was collected and DNA was extracted. After DNA amplification by use of PCR, the rs4808793 polymorphism was detected by AlwNI restriction enzyme application and RFLP.

Results: Mean serum ferritin in patients with beta-thalassemia major (3490.41 ± 169.22 ng / ml) was significantly higher than those with thalassemia intermedia (677.16 ± 388.80) (P-value <0.05). The frequency of mutation showed no statistically significant difference between cases and controls (41% vs 32%) (p-value > 0.05). Both cases and controls with rs4808793 polymorphism showed significantly elevated serum ferritin concentrations compared to patients without mutations (P <0.05).

Conclusion: Incidence of rs4808793 GDF-15 polymorphism can be considered an effective factor in iron overload and predisposing people to thalassemia both in thalassemia major and intermediate groups.

Keywords: GDF-15, rs4808793 Polymorphism, ferritin, β-Thalassemia

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Human Colon Cancer HT29 Cell Line Treatment with High-Dose L-Ascorbic Acid Results to Reduced Angiogenic Proteins Expression and Elevated Pro-Apoptotic Proteins Expression

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Introduction: Some studies have shown anticarcinogenic effects of high dose L-Ascorbic Acid. However, there are controversies around the therapeutic administration of Ascorbic acid as an anticancer medicine. We conducted a case-control study to investigate the role of pharmacologic concentration of Ascorbic acid on viability and angiogenesis of human colon cancer (HT29) cell line.

Methods: The HT29 cells were cultured in DMEM-HG and treated with 10 mM ascorbic acid for 3h. The culture medium was exchanged, and after incubation at 37 ˚C for 24 h, the cells were collected and utilized to evaluate viability, ROS production, gene expression, and protein expression levels. The control group consisted of untreated HT29 cells. The viability of the cells was determined using the MTT method. Moreover, Nitro Blue Tetrazolium (NBT) was used to detect the ROS production capacity. The mRNA transcript's level and protein expression were evaluated by Real-time PCR and Western blotting, respectively.

Results: The ascorbic acid-treated group showed a significant increase in ROS production and a noticeable reduction in viability compared to the control group. The treated group showed significantly increased early apoptotic markers (Bax, Cyt C, Caspase3, and Caspase 9) and late apoptotic markers (Caspase 8). Bcl2 expression showed significantly decreased levels relative to the control group. Ascorbic acid therapy substantially reduced the expression of bFGF, bFGFR, PDGF, PDGFR, and PLC- γ compared to the control group.

Conclusion: The results confirm that high-dose L-ascorbic acid reduces HT29 cell line viability in vitro.

Keywords: Ascorbic acid, human colon cancer cell line, angiogenesis, apoptosis

A-10-1064-3

Manipulation of Sonic Hedgehog Signaling Pathway in Maintenance, Differentiation and Exocrine Activity of Insulin Producing Cells: A Scoping Review

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Introduction: Shh signalling pathway can be regarded as an important determinant of pancreatic morphogens. Some studies evaluated Shh signalling pathway manipulation to achieve more efficient Insulin-producing cells. However, the exact role of Shh in the production and functionality of mature IPCs is controversial. Here we reviewed the studies of Shh overexpression or inhibition in production, differentiation, maintenance, and endocrine activity both in vitro and in vivo.

Methods: A systematic review was performed using all available experimental studies to determine the role of the Shh manipulation effect on the differentiation of stem cells toward IPCs and IPCs functionality. Search protocol was performed across the electronic databases, including Scopus, Medline/PubMed, EMBASE, Web of sciences (WOS), and Cochrane library, several databases using all MeSH words regarding Sonic hedgehog Insulin-producing cells.

Results: Many types of research confirmed the usefulness of Shh inhibition in the definitive endoderm stage for functional Insulin-producing cells production. Some studies showed the importance of Shh reactivation in the late stages of differentiation toward efficient Insulin-producing cells. Researches propose a significant baseline concentration of Shh in mature pancreatic β cells affecting Insulin secretion and endocrine activities of the cells. However, Shh overexpression in pancreatic β cells ultimates to in-proper endocrine functionality and inadequate glucose-sensing Insulin secretion.

Conclusion: Shh manipulation can be regarded as an effective manner in producing and maintaining functional Insulin-producing cells.

Keywords: Sonic Hedgehog, Hedgehog signaling regulation, Pancreatic β-cells, Insulin-producing cells, Stem cells

A-10-1073-1

Effective drug design to increase dopamine release based on methamphetamine structure

Introduction: Alzheimer's disease is a type of brain dysfunction in which the patient's mental abilities gradually decline. A protein such as VMAT2 is involved in increasing the release of dopamine in the synaptic space of neurons. Various plant compounds, such as methamphetamine, increase dopamine levels by acting on the VMAT2 protein. Due to the side effects of this substance, the aim of this study was to design an effective drug to increase dopamine levels with an effect on VMAT2.

Methods: The sequence of this protein was extracted from the Uniprot site and a three-dimensional structure was created with I_TASSER server. Based on three pdb files, 4xp6, 4gqp and 3gkz, methamphetamine pharmacophores were extracted using a Pharmit server. The best ligands were docked with VMAT2 protein using PyRex software. Five ligands with the lowest binding energy were selected. One of the ligands with the closest binding energy to the Pharmit server was kinetically investigated using Gromex software.

Results: The results of RMSD and Rg showed that the presence of ligand in the active site of the protein increased the fluctuation in the structure of the protein so that the structure is opened and decompressed. RMSF analyzes also confirmed that these fluctuations were related to amino acid residues in active site of the protein structure that have a turn configuration, and this was confirmed in the second structure analysis by the Stride server.

Conclusion: The present study showed that the designed drugs contain pharmacophores on methamphetamine and are equivalent to the compounds of the methamphetamine family in terms of Lipinski's rule. For the first time, these drugs are focused on VMAT2 protein. According to the simulation results, after comparing the simulation data of other designed ligands, the best ligand can be selected for synthesis and analyzed in vitro and in situ.

Keywords: Alzheimer's, methamphetamine, dopamine, VMAT2 protein

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A-10-1077-1

Selenium Effects on Oxidative Stress-Induced Calcium Signaling Pathways in Parkinson's Disease

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Parkinson's disease (PD) is a neurological disorder in which oxidative stress and reactive oxygen species productions are proposed to be involved in its pathogenesis. Despite considerable advancement in Selenium's (Se) molecular biology and metabolism, we do not know much about the cell type-specific pattern of Se distribution in the brain of PD humans and experimental animals. Although, there is plenty of evidence around the role of Se deficiency in PD's pathogenesis impacting lipid peroxidation and reducing glutathione (GSH) and glutathione peroxidase (GPX). It has been suggested that Se has an inducible role in selenium-dependent GPX activity in PD animals and humans. However, calcium as a second messenger regulates the neuron cells' essential activities, but its overloading leads to cellular oxidative stress and apoptosis. Therefore, Se's antioxidant role can affect calcium signaling and alleviate its complications. There are signs of Se and Selenoproteins incorporation in protecting stress oxidative in various pathways. In conclusion, there is convincing proof for the crucial role of Se and Calcium in PD pathogenesis.

Keywords: Parkinson's disease, Calcium signaling, Selenium, Oxidative stress, Glutathione peroxidase (GPX)

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Role of PEAR1 Polymorphisms in Idiopathic Thrombocytopenic Purpura: Is There an Association?

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Introduction: Genetic risk factors are implicated in the etiology and pathogenesis of immune thrombocytopenic purpura (ITP). Platelet endothelial aggregation receptor 1 (PEAR1) plays an important role in regulating megakaryopoiesis and thrombopoiesis. rs12041331 and rs12566888 single-nucleotide polymorphisms of PEAR1 are associated with megakaryocyte differentiation and platelet function.

Methods: To conduct this study, 68 peripheral blood samples of patients with ITP (56 acute and 12 chronic) were collected. The amplification refractory mutation system-polymerase chain reaction (ARMS-PCR) was used to detection of rs12041331 and rs12566888 PEAR1 polymorphisms.

Results: Statistically significant differences were not seen between rs12041331 and rs12566888 genotypes in acute and chronic groups (P = 0.778, P = 0.844). The frequency of rs12041331 AG/AA genotypes and the rs12566888 GT genotype was more in acute ITP patients; on the other hand, the rs12566888 TT genotype was more in the chronic group. The highest platelet counts and platelet distribution width (PDW) were related to the rs12041331 AG allele. GT and TT of rs12566888 had more PDW and platelet count, respectively. Mean platelet volume values between alleles of both the polymorphisms were constant and did not differ much. In general, no statistically significant differences were observed between genotypes of polymorphisms and platelet parameters.

Conclusions: There was no association between rs12041331 and rs12566888 with platelet parameters in ITP patients and the severity of this disease. Further investigation with a larger size is recommended.

Keywords: Genotype, immune thrombocytopenic purpura, megakaryocyte, platelet endothelial aggregation receptor 1, platelet, polymorphisms

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A-10-1078-2

The potential similarities of COVID-19 and autoimmune disease pathogenesis and therapeutic options: new insights approach

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Page | 274

Cytokine pathways and their signaling disorders can be the cause of onset and pathogenesis of many diseases such as autoimmune diseases and COVID-19 infection. Autoimmune patients may be at higher risk of developing infection due to the impaired immune responses, the use of immunosuppressive drugs, and damage to various organs. Increased secretion of inflammatory cytokines and intolerance of the patient's immune system to COVID-19 infection are the leading causes of hospitalization of these patients. The content used in this paper has been taken from English language articles (2005–2020) retrieved fromthe PubMed database and Google Scholar search engine using "COVID-19," "Autoimmune disease," "Therapeutic," "Pathogenesis," and "Pathway" keywords. The emergence of COVID-19 and its association with autoimmune disorders is major challenge in the management of these diseases. The results showed that the use of corticosteroids in the treatment of autoimmune diseases can make diagnosis and treatment of COVID-19 more challenging by preventing the fever. Due to the common pathogenesis of COVID-19 and autoimmune diseases, the use of autoimmune drugs as a possible treatment option could help control the virus.

Keywords: Autoimmune disease. COVID-19. Pathogenesis. Pathway. Therapeutic

A-10-1091-1

The potential role of Acetyl-Coa Acetyltransferase 1 in histone acetylation

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Introduction: Acetyl-CoA acetyltransferase 1 (ACAT1) is involved in the ketone body metabolism and catalyzes reversible formation of acetoacetyl-CoA from two molecules of acetyl-CoA during ketogenesis and ketolysis respectively. Additionally, recent studies have reported the novel acetyltransferase activity of ACAT1 and its oncogenic role through acetylation of mitochondrial pyruvate dehydrogenase complex (PDC). However, the potential role of ACAT1 in histone acetylation remains elusive.

Methods: In this study, we investigated the role of ACAT1 in acetylation of histone H4 lysine 5 (H4K5ac). HepG2 and HEK293 cell lines were transfected with siRNA. The effect of ACAT1 knockdown on the level of H4K5ac was investigated by western blotting using specific antibody against acetylated histone H4 lysine 5 (H4K5ac) on extracts of ACAT1-KD HepG2 and HEK293 cell lines.

Results: Knock down of ACAT1 resulted in reduced H4K5ac level. This H4K5ac reduction was observed only in HepG2 cell line.

Conclusion: Our findings provide new insight into the role of ACAT1 and suggesting that ACAT1 may mediate histone acetylation. However, future studies are needed to establish this concept.

Keywords: Histone modification, ACAT1, Metabolism, Cancer

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The effect of starvation on lysine acetylation in the liver of mice

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Introduction: The emerging link between metabolism and epigenetics suggests that control of gene expression by epigenetics can be sensitive to the environment through cell metabolism. Lysine acetylation is a highly conserved post-translational modification that plays a critical role in regulating diverse cellular processes. In this study, the effect of starvation on lysine acetylation in an animal model was investigated.

Methods: In this study, C57BL/6 mice were divided into control group with free access to food and water and starved group with only access to water. After 48 hours, the mice were sacrificed. Immunohistochemistry was performed using K-Ac antibody to evaluate the effect of 48-hours starvation on lysine acetylation. Data were analysed by one-way analysis of variance.

Results: Hepatocytes are heterogeneous respect to acetylation, meaning that not all hepatocytes are Kac-positive (Kac+). The level of acetylation in the liver of female C57BL/6 control mice was higher than male mice. Starvation significantly increased acetylation in the liver of male mice ($P < 0.05$), changes in lysine acetylation in the liver of female mice were not significant ($P < 0.05$).

Conclusion: The findings of the present study confirmed the heterogeneity of hepatocyte lysine acetylation and showed that starvation increases the level of lysine acetylation only in the liver of male mice.

Keywords: Starvation, Metabolism, Epigenetics, Histone acetylation

A-10-1091-3

The mRNA expression of HDAC3 in Iranian patients of Oral Squamous Cell Carcinoma

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Introduction: Histone modifications have been demonstrated to play a significant role in epigenetics regulation of oral squamous cell carcinoma (OSCC). Histone deacetylases (HDACs) are enzymes that are operative in the remodeling of chromatin and have a significant role in the epigenetic regulation of gene expression.

Methods: In this study we quantitatively evaluated the mRNA gene expression level of HDAC3 by quantitative reverse transcription polymerase chain reaction (RT-PCR) in OSCC and compared it with oral normal mucosa tissue. Total RNA was extracted from tumour and normal oral tissues of 15 samples patients (including 10 OSCC and 5 normal tissue) by the TRIzol reagent according to the manufacturer's instructions. Next, 500 ng of RNA was used for the cDNA synthesis by PrimeScript 1st Strand cDNA Synthesis kit (Takara, Japan). Quantitative Real-time PCR was performed using Ampliqon Real-Time PCR Master Mix (For SYBR Green I). The $2^{-\Delta\Delta CT}$ method was used to calculate the relative gene expression in tumour tissues of OSCC patients compared to normal oral tissues.

Results: Our findings did not show significant changes in gene expression levels of tumoural HDAC3 in comparison with normal oral tissue (P=0.27)

Conclusion: In the results of this study, no notable changes was observed in the level of HDAC3 in Iranian OSCC patients compared to normal oral tissues.

Keywords: Histone deacetylases HDAC3, OSCC, epigenetics

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Designing a Logistic Regression Model for a Dataset to Predict Diabetic Foot Ulcer in Diabetic Patients

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Page | 278

Introduction: Although the risk factors for diabetic neuropathy and diabetic foot ulcer have been detected, there was no practical modeling for their prediction. We aimed to design a logistic regression model on an Iranian dataset to predict the probability of experiencing diabetic foot ulcers up to a considered age in diabetic patients.

Methods: The present study was a statistical modeling on a previously published dataset. The covariates were sex, age, body mass index (BMI), fasting blood sugar (FBS), hemoglobin A1C (HbA1C), low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglyceride (TG), insulin dependency, and statin use. The final model of logistic regression was designed through a manual stepwise method. To study the performance of the model, an area under receiver operating characteristic (AUC) curve was reported. A scoring system was defined according to the beta coefficients to be used in logistic function for calculation of the probability.

Results: The pretest probability for the outcome was 30.83%. The final model consisted of age (β_1 = 0:133), BMI (β_2 = 0:194), FBS (β_3 = 0:011), HDL (β_4 = −0:118), and insulin dependency (β_5 = 0:986) (P < 0:1). The performance of the model was definitely acceptable (AUC = 0:914).

Conclusion: This model can be used clinically for consulting the patients. The only negative predictor of the risk is HDL cholesterol. Keeping the HDL level more than 50 (mg/dl) is strongly suggested. Logistic regression modeling is a simple and practical method to be used in the clinic.

Keywords: HDL, Foot Ulcer ,Diabetic Patients

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TEHRAN UNIVERSITY OF MEDICAL SCIENCES

A-10-1100-2

Small Ubiquitin-Like Modifier 4 Gene M55V Polymorphism and diabetic nephropathy

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Page | 279

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Introduction: Many factors may be associated with the pathogenesis of diabetic nephropathy, a leading cause of end-stage renal disease, in individuals with type 2 diabetes. It is suggested that genetic susceptibility plays an important role in the development and progression of diabetic nephropathy. SUMO4 protein is encoded by the SUMO4 gene located at chromosome 6q25. A common single nucleotide polymorphism encoding a methionine-to valine substitution at codon 55 (M55V) has been recently identified in SUMO4 gene. Recent reports showed that the SUMO4 M55V polymorphism is associated with increased susceptibility to type 2 diabetes and diabetic nephropathy in several populations, whereas our pervious study indicated not association of the SUMO4 M55V polymorphism with the susceptibility of type 2 diabetes in Iranian population. We studied the impact of SUMO4 M55V polymorphism on susceptibility to diabetic nephropathy in Iranian type 2 diabetes patients.

Methods: The patient group consisted of 100 Iranian type 2 diabetes patients with nephropathy, and the control group consisted of 100 Iranian type 2 diabetes patients without nephropathy. Genotyping was performed using polymerase chain reaction restriction fragment length polymorphism (PCRRFLP) method. PCR was used to amplify the fragments of SUMO4 that contained the site of 163 A/G polymorphism.

Results: this study indicates that the M55V polymorphism of SUMO4 gene is associated with diabetic nephropathy in Iranian type 2 diabetes patients The frequency of SUMO4 AA, AG, and GG genotypes were 48%, 36%, and 16% in the patient group and 20%, 52%, and 28% in the control group. There was a significant increase in frequency of SUMO4 AA genotype in type 2 diabetes patients with nephropathy compared to type 2 diabetes patients without nephropathy (48% vs 20%, P=0.003).

Conclusion: These findings indicate that SUMO4 M55V Polymorphism is associated with diabetic nephropathy in Iranian type 2 diabetes patients.

Keywords: sumo 4, diabetes patients, nephropathy

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Saccharomyces boulardii attenuates lipopolysaccharide-induced anxiety-like behaviors in rats

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Page | 280

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Introduction: Anxiety is the brain's response to dangerous or stressful situations. Exposure to stressors can activate the hypothalamic-pituitary-adrenal (HPA) axis and lead to the secretion of glucocorticoids associated with anxiety. A growing body of evidence has also shown that stressors can result in disrupted intestinal microbiota. Recent studies have reported that probiotics can alleviate anxiety-like behaviors via reconstructing the gut microbiota. The present study aimed to investigate the effects of Saccharomyces boulardii (Sb) administration on anxiety-like behaviors induced by lipopolysaccharide (LPS) in rats.

Methods: Rats were randomly divided into four groups (Control, LPS, Sb + LPS, and Sb). All animals were orally treated with saline or S. boulardii (1010 CFU/ml/rat) for 28 days. They were also injected with saline or LPS (250 µg/kg/day) intraperitoneally from day 14 until day 22. Anxiety-like behaviors were assessed using the elevated plus-maze and open-field tests. Besides, the serum levels of cortisol, corticosterone, and serotonin were measured.

Results: The results indicated that S. boulardii could alleviate LPS-induced anxiety-like behaviors. The findings also showed that oral administration of S. boulardii significantly reduced the elevated levels of cortisol and corticosterone in the LPS-induced model. Moreover, S. boulardii attenuated the decremental effect of LPS on the serum serotonin level.

Conclusion: The present findings revealed the anxiolytic effect of S. boulardii in an LPS-induced rat model of anxiety-like behaviors, probably through modulation of the HPA axis and the intestinal microbiota.

Keywords: Probiotic, Hypothalamic-Pituitary-Adrenal axis, Anxiety, Corticosterone, Cortisol, Serotonin

17th National Congress of Biochemistry & 8th International Congress of Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

TEHRAN UNIVERSITY OF MEDICAL SCIENCES

Cloning and purification of inhibitory peptide (P-99B) of SARS-Cov-2 's spike receptor

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Page | 281

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Introduction: In 2019, a virus called SARS-COV-2 caused the global epidemic of COVID-19. Among the various proteins of the virus, the spike protein plays an important role in the inflow of the virus into the cell. This protein is being located at the surface of virus and has 2 main domains, the N terminal domain and receptor binding domain(RBD). The RBD domain makes the cell entry path by interacting with Angiotensin-converting enzyme 2 (ACE2) thus interrupting it is the key to stopping the virus from entering the cells. There are several ways to how we can interrupt this interaction.

Methods: In this study, a peptide was designed with the help of bioinformatical studies called P-99B. The gene sequence was ordered with the appropriate tag. Expression, purification, tag separation and peptide purification were performed and structural characterization was made by the Circular dichroism technique (CD) and Mass spectrometer.

Results: this peptide in bioinformatic investigation has a high bond free energy while interacting with the virus's RBD and RBD has more affinity towards it rather than ACE2.This peptide's expression and purification is easy and straightforward and it has a low toxicity towards body cells in invitro assay. Also this peptide will prohibit the cell entry ability of virus in low drug dosage. Datas of CD spectroscopy has shown that it has the desired secondary structure (alpha helix) like the first alpha helix of N terminal of ACE2 which has a key role in ACE2-RBD interaction.

Conclusion: At the end we can conclude that this peptide can successfully repulse the disease caused by SARS-CoV-2 and inhibit the virus. With attention to the inhibitory characteristic of the peptide towards the RBD, it can be expected that we can use the peptide in various forms for prevention and curing the disease in near future.

Keywords: COVID-19 ،Syndrome Coronavirus2 (SARS-CoV-2(،Spike protein ،Angiotensin converting enzyme 2 (ACE2) ، Inhibitory Peptide

A-10-1110-1

Effect of L-serine on oxidative stress markers in the kidney of STZ-induced diabetic mice

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Introduction: Background: Recently, a potential role of L-seine in the improvement of diabetic complications has been suggested by some studies. L-serine supplements enhance glucose homeostasis, mitochondrial function, and reduce neural death. Moreover, L-serine declines the occurrence of autoimmune diabetes in NOD mice. This study aimed to evaluate effects of daily L-seine intake on oxidative stress markers in the kidney of STZ-induced diabetic mice.

Method: Eighteen C57BL/6 male mice (weight 20–25 g) were randomly divided into three groups. Two of the groups were induced with diabetes by a single intraperitoneal injection of freshly prepared streptozotocin. A group of diabetic mice was treated with 300 mg/day of L-serine in water for 4 weeks. Oxidative stress markers (protein carbonyls, malondialdehyde, glutathione peroxidase, superoxide dismutase, and catalase) were measured in the kidney tissue using spectrophotometry. Finally, all the data has been analyzed with the ANOVA test.

Results: The result indicates that the amount of protein carbonyl which had raised in the diabetic group with no treatment, declined significantly in the group treated with L-seine. Also, the amount of malondialdehyde was reduced in the L-serine treated group ($p=0.051$). However, the levels of glutathione peroxidase, superoxide dismutase, and catalase showed no significant difference between the groups.

Conclusion: Based on the results of this study it seems that L-serine has a moderate protective effect against oxidative stress in the kidney of STZ-induced diabetic mice.

Keywords: L-serine, Protein carbonyl, STZ, glutathione peroxidase, superoxide dismutase, catalase, malondialdehyde

In-silico analysis to predict the effect of miR-1256 single nucleotide polymorphisms on the incidence of non-small cell lung cancer

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Introduction: Non-small cell lung cancer (NSCLC) is a frequent type of lung cancer. Considering the low 5-year survival (26%) and high relapse after treatment (55%), it is highly crucial to predict the incidence of NSCLC. MicroRNAs are a type of non-coding RNAs with 18-22 nucleotides that participate in the regulation of mRNA translation. As microRNAs are small functional units, single-base changes, such as single nucleotide polymorphism (SNP) may result in the evolution of new microRNAs by altering their biological function. The relation between structural changes and ectopic expressions of miRNA, and the incidence of NSCLC has been previously proven. Here, in-silico analyses were employed to predict whether the miR-1256 rs1048084045 (A>G) and rs781376916 (A>C) polymorphisms affect the susceptibility to NSCLC.

Methods: To validate the expression profile of miR-1256 in NSCLC, "miRCancer" database was employed. By recruiting "miRbase" webserver, the sequence of the microRNA was obtained. Visualization of the molecular interaction network of miR-1256 and its targets was carried out through the "miRTargetLinkHuman" webserver. To observe the effect of this SNP on stem-loop structure and determination of the minimum free energy (MFE) of the polymorphic and non-polymorphic variants, the "ViennaRNA" webservice was used.

Results: While the MFE of the non-polymorphic sequence of mir-1256 was -1.94 kcal/mol, the MFE for rs1048084045 and rs781376916 was -1.46 and -1.93 kcal/mol, respectively.

Conclusion: Studies have demonstrated that miR-1256 plays a suppressing role in the progression of NSCLC by regulating TCTN1. Therefore, we conducted bioinformatics to investigate the impact of SNPs (rs1048084045 and rs781376916) on miR-1256 secondary structure. The MFE of these two given SNPs were compared to the non-polymorphic miRNA. Considering the difference detected between the MEF of SNPs and the non-polymorphic miR-1256, it can be concluded that SNPs can affect the secondary structure of miR-1256.

Keywords: Non-small cell lung cancer, microRNA, Single nucleotide polymorphism

Effects of Salvia officinalis essential oil on induction of apoptosis in SKOV3 prostate cancer cells

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Prostate cancer is the second most common cancer in men in the world (with an incidence rate of 29.3 and a death rate of 7.6 per 100,000 people). Salvia (Salvia officinalis) is one of the most important genus of dark mint that most species of this genus have medicinal properties and have many applications in traditional medicine. The aim of the present study was to evaluate sage essential oil on growth inhibition and apoptosis of prostate cancer cells in SKOV3. Salvia miltiorrhiza was prepared from the National Center for Genetic and Biological Resources of Iran and was identified by gas chromatography and components by gas chromatography. Concentrations (100, 200, 300, 400, 500, 600 µg / ml) were then applied to SKOV3 ovarian cancer cells and the bioavailability of the cells by trypan blue uptake (colorimetry), MTT in three time intervals 24, 48 and 72 hours were evaluated. The rate of induction of cell apoptosis was evaluated by flow cytometry. The greatest effect of essential oil was related to the concentration at 72 hours with a concentration of 600 µg / ml. The IC50 level of sage essential oil for 48 hours was determined to be equal to 400 µg / ml. Induction of apoptosis was dose-dependent and the concentration of treatment with a dose of 600 essential oils caused a significant increase in apoptosis index. Based on the results, it can be seen that sage essential oil can reduce the biological ability and increase the apoptosis of prostate cancer cells of SKOV3 category.

Keywords: prostate cancer- Salvia officinalis- SKOV3 cells

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Study of biofilm formation in Acinetobacter baumannii isolates collected from intensive care units

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Page | 285

Introduction: Acinetobacter baumannii has the potential to form biofilms and survive in unfavorable conditions in hospitals, especially intensive care units. Pathogens with biofilm, are ten to a thousand times more antibiotic resistance than planktonic cells. Treatment of the corresponding infections is one current challenges facing the clinical community. The purpose of this study was to evaluate the biofilm formation of A. baumannii isolates collected from sputum of patients admitted to intensive care units.

Methods: Eighty-one A. baumannii isolates were extracted from sputum samples of intensive care unit patients of Rasoul-E-Akram Hospital in Tehran and after confirmed identification, their ability to produce biofilms was examined using the Microtiter plate method.

Results: Isolates were assorted into four groups of strong, medium, weak and negative biofilms based on their ability to form biofilms. In this study, there were 2 strong biofilm isolates, 42 medium, 32 weak and 5 negative biofilm isolates.

Conclusion: Based on these results, A. baumannii isolates have different biofilm production abilities. Bacteria producing biofilm can withstand adverse conditions such as antibiotic use, leading to the emergence of multidrug-resistant strains, particularly in the intensive care unit. Hence, periodic monitoring of intensive care units is extremely important for microbial resistance management.

Keywords: Acinetobacter baumannii, biofilm, intensive care

A-10-1122-1

Investigation of biofilm production in Klebsiella pneumoniae isolates isolated from the intensive care unit

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Introduction: Klebsiella. pneumoniae through its ability to create a thick layer of biofilm, is considered as one of the most important pathogenic agents, especially in intensive care units, and by creating resistance to antibiotics, it can lead to infection in all wards of the hospital, and intensive care unit in particular. Considering that biofilm production results in a much harder Klebsiella pneumoniae infection clearance, the goal of this study was to evaluate the production of biofilm in Klebsiella pneumoniae isolates isolated from the sputum of patients admitted to intensive care units.

Methods: 105 samples of Klebsiella pneumoniae isolated from the sputum of patients admitted to the intensive care units of the Rasoul-E-Akram Hospital in Tehran were collected and the identity of all samples were confirmed using specific differential cultures. Then, in vitro biofilm production ability of isolates was investigated by the Microtiter plate method.

Results: The biofilm production ability of Isolates was classified into four groups of (1) strong (2) medium (3) weak and (4) negative. Based on this classification, in the current study, 6 isolates were strong biofilm producers, 19 were moderate, 48 were weak, and 32 were negative biofilm producers.

Conclusion: Based on the results of this study, the capacity for biofilm production varies in each strain of K.pneumoniae. As biofilm production is one of the main reasons for resistant infections, particularly in intensive care units therefore, finding suitable approaches against these phenomena is vital.

Keywords: Klebsiella pneumoniae, biofilm, intensive care

A-10-1132-1

Humanin as the cardioprotective mitochondrial-derived peptide

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Introduction: Humanin is a new peptide related to 24 mitochondrial amino acids, best known for its protective effects on heart disease, shown through interference, with pro-and anti-apoptotic proteins such as Bid, Bax, ceramide and IGFBP-3. The protective mechanism of HN is not yet fully understood. The laboratory work has shown that Humanin is expressed in both vascular endothelium and unstable carotid plaque. In addition, humans entering cultured endothelial cells repel the damage caused by the production of reactive oxygen species (ROS), which is usually caused by the inflammatory stress of low-density oxidized LDL (Ox-LDL) lipoproteins.

Methods: We search about the Humanin cardioprotective effect, by using of two-word consisting of Humanin and heart disease in NCBI advanced search. Finally, we obtain 12 related articles about this subject. ·

Results: We reported that Humanin has a cardiac protective effect mediated by activation of the G protein-coupled receptor (GPCR) and PLCβ. This activation, in turn, activates two pathways, one involving PKC and ATP-sensitive potassium channels and the other involving PI3K and Akt.

Conclusion: Data from previous studies suggest that human levels may be negatively correlated with microvascular function and have a beneficial effect in inhibiting myocardial fibrosis in myocardial dysfunction. However, the mechanical consequences of this finding remain unclear and require further investigation.

Keywords: Humanin, cardiovascular, mithocondria

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The role of bioinformatics in the therapeutic development of Covid-19

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Page | 288

Introduction: The greatest battle of the 21st century against the Covid-19 virus has led to the unprecedented use of bioinformatics tools in deciphering the molecular properties of infectious pathogens. Because SARS-COV-2 viral genome data became available only a few weeks after the outbreak, bioinformatics platforms have become a vital tool for gaining time to combat the epidemic. Therefore, the study of different pipelines can lead to the development of useful therapeutic candidates using the knowledge of existing genomic data.

Methods: The present study is a review study that has been compiled using electronic resources in reputable databases such as PubMed, Scopus, Google Scholar, ISI, and Science Direct related from 2019 to 2022.

Results: Reports of in silico approaches such as molecular docking, molecular dynamics simulation, network-based identification, and homology modeling suggest that researchers are moving toward reuse strategies for drugs that have already been validated and used against pathogens. This is because identifying potential drugs by screening existing drugs and examining protein interactions is relatively cheaper and more time-efficient than traditional drug design approaches. Also, the expertise gained in selecting antigen targets as well as the use of adjuvants and delivery systems to shape the immune response to the vaccine help, which in turn influences the requirements for building and forming a clinical trial. Understanding the molecular and evolutionary origins of SARS-CoV-2, the basic mechanisms of virus-host binding interaction, and identifying potential antiviral peptides and epitope vaccine candidates as potential treatment options for coronavirus has enhanced our knowledge of coronavirus pathogenesis.

Conclusion: Bioinformatics has not only strengthened research strategies to prevent Covid-19 but also the goal of aggregating large volumes of genomic data and related research observations on centralized open access platforms for dissemination to the wider scientific community worldwide. And can play an important role in predicting potential therapies.

Keywords: Coronavirus disease 2019 (Covid-19), Bioinformatics, Genetics, Treatment, Vaccine.

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Exosomes and breast cancer

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Almost all living cells secrete a set of extracellular vesicles (EVs). The naming of EVs depends on various factors, including their origin cells, function, and size. Extracellular vesicles(EVs) were first observed 50 years ago in plasma. Since then, all biological fluids tested have been shown to contain vesicles, and also in vitro grown cell lines have been shown to release vesicles to different extent. Extracellular vesicles (EVs) are classified into three groups typically based on their size and biogenesis: exosomes (30–200 nm), micro vesicles (MVs) (100–1000 nm) and apoptotic bodies (> 1000 nm). Exosomes with a size range of 40–160 nanometers in diameter (averaging 100 nanometers), and the density is between 1.13 and 1.19 g·mL−1, are a subset of extracellular vesicles (EVs).EVs are natural carrier systems that can transfer nucleic acids, proteins, and lipids between donor and recipient cells in an autocrine, paracrine, and endocrine manner. tumor cells possess more exosomes-releasing properties when compared to normal cells. Tumor-derived exosomes (TEX) have been widely studied in various types of cancer, such as renal cancer, hematological cancer, breast cancer and melanoma. Growing evidence suggests that tumor-derived exosomes (TEXs) play critical roles in Breast Cancer (BC). BC is extremely predominant illness. In This review discusses the potential clinical application of exosomes in BC by summarizing how exosomes participate in BC proliferation, metastasis, drug resistance, therapeutic effect and other biologic progress. Moreover, we propose exosome as a candidate biomarker in predicting and monitoring the therapeutic drug response of BC and as a potential target or carrier to reverse the drug resistance of BC.

Keywords: Exosomes, breast cancer, Extracellular vesicles, Tumor-derived exosome (TEX)

A-10-1097-1

Study of a Predicted 4-amino acid peptide as MMP-2 and MMP-9 Inhibitor in human monocyte- differentiated macrophages

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Page | 290

Introduction: Matrix metalloproteinases (MMPs) are involved in the tissue remodeling pathways and cellular migration process. In this study, we predicted a motif of TIMP family and investigated the activities of MMP-2 and MMP-9 secreted from human differentiated macrophages.

Methods: First, the monocytes were isolated from healthy individuals by RosetteSep kit. Then, they were differentiated into macrophages, which were done using growth factors such as M-CSF. A 4-amino acid motif (TCAP) was predicted using bioinformatics tools and was the subject for the interventional studies. For the measurement of MMP activities, the Zymography technique was applied. Also, the docking studies were evaluated between MMPs, tetrapeptide (TCAP), and Batimastat.

Results: The macrophage MMP-2 and MMP-9 activities were inhibited by TCAP tetrapeptide (p = 0.0001 and p = 0.01, respectively). The docking results showed that several amino acids are involved with both tetrapeptides (TCAP) and Batimastat. In addition, the MMP-2 activity was inhibited effectively by the TIMPs (TCAP) motif.

Conclusion: The study showed that the TCAP motif of TIMPs inhibits the MMP2 activity. Furthermore, this tetarapeptide may suggested as a drug target for clinical aims such as vessel varicose.

Keywords: MMP-2 ‹MMP-9 ‹macrophage ‹TIMP ‹prediction ‹motif.

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Association between vitamin D levels and routine laboratory tests in infants

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Introduction: The normal growth of infants depends on optimal levels of vitamin D. The benefits of vitamin D supplementation in the prevention and treatment of pediatric diseases have been widely discussed. However, the association between vitamin D status and blood biochemical parameters in a healthy neonatal population has been virtually ignored. This study examined the relationship between vitamin D status and biochemical parameters in 449 healthy infants (0-24 months) who were breastfed.

Methods: Based on the questionnaire response to vitamin D supplementation, we divided the participants into three groups: regular vitamin D supplementation users (1 ml per day), irregular vitamin D supplement users (1 ml on some days of the week). Less than 1 ml), and non-consumers of vitamin D supplements - Consumers according to vitamin D levels, infants in the groups of vitamin D deficiency (VDD), vitamin D deficiency (VDI) and vitamin D deficiency (VDS) class Are classified. Participants were also categorized into low weight, normal weight and overweight groups. We assessed blood concentrations of -25 (OH) of vitamin D, calcium, phosphorus, glucose, lipid markers, inflammatory markers and liver and kidney function indices.

Results: Serum levels of vitamin D were higher in normal consumers who had lower weight, creatinine and RDW / Plt ratio than in non-consumers. Higher vitamin D in childhood was more associated with cholesterol, ALT, urea, uric acid, bilirubin, LHR and WBC, while it was associated with lower PLR. VDS infants in the overweight group had higher levels of total urea, uric acid, and bilirubin than VDD infants in the same group.

Conclusion: The present findings show that cholesterol, urea, PLR, and WBC counts are independently associated with vitamin D levels in breastfed infants.

Keywords: Keywords: Infants, weight, Vitamin D, blood biochemical parameters, metabolic markers, breastfed

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The impact of preeclampsia on offspring pancreatic function

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Introduction: Preeclampsia is a common pregnancy complication. Previous epidemiological studies suggest that it can exert long-lasting adverse effects on offspring by increasing the risk of developing metabolic diseases such as diabetes. However, the exact underlying mechanism remains unclear. The aim of this study was to investigate pancreatic function in offspring born to reduced uteroplacental perfusion (RUPP) rats.

Methods: Thirty timely pregnant Wistar rats were randomly allocated into three groups: control (n=8), sham (n=10) and RUPP (n=12). RUPP or sham procedures were performed on day 14 of gestation. After parturition, the litter size of all groups was adjusted to 6 pups per dam. At postnatal day 60, circulatory insulin and glucagon levels, intraperitoneal glucose tolerance test (IPGTT) and insulin immunohistochemical staining of pancreatic islets were investigated. Moreover, pancreatic islets were isolated, and their insulin secretion activity was investigated in different glycemic conditions.

Results: Compared to the sham group, offspring born to RUPP dams exhibited no difference in fasting blood glucose and glucagon, but they had impaired IPGTT and lower circulatory insulin (258.03 vs. 410.85 ng/L, p=0.005) levels. Despite the non-significant difference in pancreatic islet area between the studied groups, the insulin immunoreactivity of the RUPP group was significantly lower than the sham group. The isolated islets of the RUPP group also exhibited lower insulin secretion, especially in supra-physiologic glucose concentration (16.7 mM).

Conclusion: These results indicate that preeclampsia has a negative impact on pancreatic islets in offspring and that, as adults, maybe functionally less responsive to glucose.

Keywords: Preeclampsia, Offspring, Metabolic diseases, Diabetes, Pancreas

A-10-1113-2

Rat offspring born to preeclamptic dams exhibit an increased cortisol response to stress at adulthood

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Introduction: In preeclampsia, the fetus is exposed to high circulating cortisol levels due to insufficient placental 11β-hydroxysteroid dehydrogenase type 2 (11β-HSD2) levels. It has been proposed that this overexposure may influence fetal hypothalamic-pituitary-adrenal axis programming, which may increase vulnerability to mood disturbances in later life. Hence, this study aimed to investigate cortisol response to stress in adult rats born to preeclamptic dams.
Methods: The surgical model of reduced uteroplacental perfusion (RUPP) was established in pregnant Wistar rats at gestational day 14; meanwhile, Sham rats were operated on in a fashion similar to that performed in RUPP rats but without micro-coils applying. Unmanipulated pregnant rats were also allocated as control group. After parturition, the litter size of all groups was adjusted to 6 pups per dam. On postnatal day 60 and after the implantation of the vein catheter, acute immobilization stress was performed by placing animals in restrainers and securing their heads and tails end for 6-h. Blood samples were collected at baseline, 1-h, 3- h, and 6-h of the immobilization. The cortisol levels were assessed using the heat-inactivated corticosteroid-binding globulin plasma samples and a rat cortisol ELISA kit.
Results: No significant difference in plasma cortisol level was found between the studied groups at baseline. During the course of stress, plasma cortisol levels of RUPP born rats were significantly higher than the sham group at 1-h (492.36 vs 381.32 ng/mL, p<0.001), 3-h (406.49 vs 329.01 ng/mL, p<0.001) and 6-h (427.41 vs 339.71 ng/mL, p<0.001)] post immobilization stress.
Conclusion: Our study demonstrates for the first time that rat offspring born to RUPP dams exhibit an increased cortisol response to stress in adulthood.

Keywords: Preeclampsia, offspring, cortisol, stress

A-10-1154-1

Evaluation of the presence of Epstein-Barr virus (EBV) with thyroid cancer in patients of East Azerbaijan

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Introduction: Papillary thyroid cancer (PTC) is the most common thyroid cancer. EBVK is one of the most important viruses associated with different types of malignancies. In this study, we examined the association between the EBV virus and papillary thyroid cancer.   In this study, the presence of Epstein-1 nuclear nuclear antigen gene in papillary thyroid cancer tissues was investigated by PCR

Method: In this study, 60 cases of thyroid cancer tissue blocks in which paraffin was implanted were used DNA was extracted from all samples and then the samples were evaluated for the presence of EBV.

Results: In 60 samples, the Epsin 1 nuclear antigen gene was detected in 55.8% of patients with papillary thyroid cancer, which was increasingly more common at younger ages.

Conclusion: The significant presence of the AVD genome of papillary thyroid carcinoma suggests that the virus may be involved in this cancer, especially at younger ages. As a result, monitoring of patients with latent EBV for papillary thyroid cancer, it can be very important.

Keywords: Epstein-Barr virus (EBV)-thyroid papillary carcinoma

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Evaluation of Antibacterial activity of aluminum oxide (Al2O3) nanoparticle on Staphylococcus aureus

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Introduction: Recently, nanotechnology has received much attention, because of versatile applications products which are used in industry. One of the important characteristic of the nanoparticles is antimicrobial activity. (Al2O3) nanoparticles represent an important class of commercially viable product with unique antimicrobial activity. Since the Staphylococcus aureus is one of the most common causes of bacterial infections in the intensive care unit (ICU) and is a gram-positive bacterium that is prevalent worldwide.

Methods: To count suspension colonies of bacteria of unknown concentration and obtain CFU, dilutions are usually made so that at least one countable plate is available. And we have to find the right plate to count the colony. The different concentrations between (10-400 µg/ml) were prepared in PBS buffer. After characterization with Transmission Electron Microscopy (TEM). The Staphylococcus aureus treated with these nanoparticles. And the MTT assay was performed in according to enzymatic reduction of the lightly colored tetrazolium salt to its formazan of intense purple-blue color, which can be quantified spectrophotometrically.

Results: In this study, we evaluated the toxicity of Al2O3 against microorganisms in different concentration on Staphylococcus aureus. Al2O3 nanoparticles causing irregular holes on membrane surfaces, causing irregular effects such as cell death. According to MTT assay the IC50 for Al2O3 is approximately 49 µg/ml and while this IC50 for cefazolin is nearly 56 µg/ml This is an important cause of nosocomial infections which leads to increased morbidity and mortality and health care costs with skin, wound and soft tissue infections.

Conclusion: Al2O3 nanoparticles act as an effective antibacterial agent against Staphylococcus aureus. The Al2O3 nanoparticles, adhere to the bacterial cell wall and penetrate through the cell membrane. Break the permeability of the outer membrane and lead to leakage of cellular material. This inhibited the growth and proliferation of bacterial cells.

Keywords: Antibacterial activity, aluminum oxide (Al2O3), nanoparticle, Staphylococcus aureus

A-10-998-1

Investigation of purified Survivin interaction with Caspase 9 using Native-PAGE

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Introduction: Survivin is one of the smallest members of the IAP family. Improper expression of this protein is found in much human cancer, which inhibits caspases and creates resistance to therapies. Survivin protein is shown as a cancer marker due to its expression is higher in cancer cells compared to normal tissues. Since IAP proteins have the potential to interact with caspase 9 and so for no interaction between survivin and caspase 9 has been investigated by purified proteins. In this study, the interaction of these proteins was analyzed using Native-PAGE gel.

Methods: The vectors carrying the caspase 9 wild-type and Survivin genes from non-expressive DH5α bacteria were extracted separately, and transferred independently to the BL21(DE3) expression strain. Both proteins were expressed by IPTG and lactose inducers in 2xYT medium and then purified. Two proteins were mixed together in a 1:1 ratio (v/v) and incubated for 20 min at 4 and 50°C and cross-linked by glutaraldehyde. This process was stopped by Tris 1M and estimated by Native-PAGE gel.

Results: The results of SDS-PAGE gel showed that a significant amount of both purified proteins were obtained. It was also observed from the result of Native-PAGE gel that survivin protein interacted with caspase 9 as XIAP-BIR3.

Conclusion: Because survivin has an alpha helix instead of a RING-finger domain, it binds zinc ions to the BIR domain. Native-PAGE gel showed survivin interacted with caspase 9. Adding a chelating agent like EDTA can be found whether the detach zinc ion from survivin destroy the possible interaction with caspase 9 or not, which needs to be investigated.

Keywords: Keywords: Survivin, Caspase 9, Native-PAGE, Protein interaction

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Association of FOXO1 rs17592236 polymorphism and tumor size in Papillary thyroid carcinoma

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Page | 297

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Introduction: A group of transcription factors involved in several cellular processes like cell growth, proliferation, cell cycle, differentiation and apoptosis which are critical to the cell biology of cancer is Forkhead Box O (FOXO) family. FOXOs are known as putative tumor suppressors. FOXO1 is a member of FOXO family which its abnormal expression or function has been indicated to promote cell proliferation and tumorgenesis. The probable effects of FOXO1 rs17592236 polymorphism on Papillary thyroid carcinoma (PTC) and its clinical findings were evaluated.

Methods: In total, 156 PTC patients and 158 healthy subjects were participated in the study. Genotyping of FOXO1 rs17592236 polymorphism was carried out using RFLP-PCR method.

Results: There was no association between the FOXO1 rs17592236 polymorphism and PTC in codominant, recessive, dominant, overdominant and log-additive models. The frequency of rs17592236A allele was 13% in PTC and 17% in control group and were not statistically significant (P=0.15). The analysis of the relationship between FOXO1 rs17592236 polymorphism and clinical specifications of papillary thyroid carcinoma demonstrated no significant relationship between rs17592236 polymorphism and PTC in different ages (<40 and ≥40), gender (male/female), extrathyroidal expansion, N stage, vascular invasion and capsular invasion in PTC patients. There was a relationship between FOX1 rs17592236 polymorphism and a larger tumor size (≥1 cm) only in log-additive model (OR=2.96, 95% CI=0.88-9.98; P=0.04).

Conclusions: FOXO1 rs17592236 polymorphism was not associated with PTC; however, this variant was associated with a larger tumor size (≥1 cm) only in log-additive model.

Keywords: FOXO1, Papillary thyroid carcinoma, polymorphism, Tumor size

A-10-1130-1

Beneficial implication of calorie restriction and quercetin on oxidative stress status and liver function in high-fat diet mice

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Introduction: Obesity causes oxidative stress, liver toxicity and dysfunction. Some strategies, such as dietary intervention, calorie restriction (CR), and the use of antioxidant compounds, have been propounded to reduce oxidative stress induced by obesity. This study aimed to investigate the impacts of quercetin plus CR on liver function in high fat diet mice.

Methods: to this end, 30 8-weeks-old BALB/c mice were divided into five groups: normal diet as healthy control, high-fat diet (for 10 weeks) as obese control, high-fat diet and quercetin (15 mg Kg-1, IP) (4 Weeks), high-fat diet and CR (2 fasting days per week with an interval of 2 days), and high-fat diet with quercetin and CR. At the end of the treatment, the activity of antioxidant enzymes, liver enzymes and lipid profile were measured.

Result: High-fat diet reduced activity of catalase and paraoxonase. The use of both quercetin and CR increased the activity of catalase and paraoxonase. Elevated levels of triglyceride and cholesterol were observed in high-fat-fed group. Quercetin decreased LDL and total cholesterol and augmented HDL. Compared to quercetin, CR had a greater impact on lipid profiles. The simultaneous use of quercetin and CR led to significant changes ($P < 0.05$). To be more precise, this treatment lessened total cholesterol, triglycerides, and LDL and increased HDL. An increase in liver enzymes was detected in the high-fat-fed group. Quercetin decreased ALT and ALP; however, this reduction was not statistically significant. The use of both quercetin and CR significantly reduced liver enzymes.

Conclusion: Based on the results, quercetin, CR, and particularly their combination has the potential to reduce the destructive effects of a high-fat diet by improvement of oxidative stress status. Accordingly, CR and quercetin, are deemed appropriate strategies for improving liver function and antioxidant enzymes in obese people.

Keywords: Obesity, High-fat diet, Calorie restriction, Quercetin, Catalase, Paraoxonase

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The expression of proinflammatory genes dorsal, unpaired3 and eger in the offspring of Drosophila melanogaster flies developed under high glucose conditions

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Page | 299

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Introduction: Type 2 diabetes is characterized by hyperglycemia with effects that could persist as a metabolic memory even after appropriate treatment. In this study, we used the fruit fly Drosophila melanogaster to address the effect of glucose riche diet on the expression of inflammatory genes, known to be involved in type 2 diabetes pathogenesis.

Methods: Fruit flies were bred in low (0.86 g/dl), medium (2.66 g/dl) and high (5.7 g/dl) glucose conditions. Males and females were then separated and mated with flies bred in the same medium or in a medium with a different glucose levels. The expression of three genes dl, upd3 and egr, orthologs of human IL-6, TNFα and RELA, respectively, were examined using RT-qPCR. Mann-Whitney U test was carried out for data analysis

Results: Our results show that, in comparison to the offspring of flies bred in medium glucose, the expression of dl was 1.97 times increased, upd3 1.35 folds decreased and egr 1.69 times decreased (p=0.0005) in the offspring of flies bred in high glucose. In the offspring of flies bred in low glucose, dl was increased 3.68 times (p=0.005), upd3 was decreased 7.69 folds and egr was decreased 2.12 folds (p=0.0005). In the offspring of males bred in high glucose and females in low glucose, the expression of dl was 2.21 times increased (p=0.0005), the expression of upd3 was 2.08 times decreased and egr was 2.32 folds decreased. The expression of dl was 2.6 times increased (p=0.0005), the expression of upd3 was 9.1 times decreased and egr was 1.85 times decreased (p=0.0005) in the offspring of females bred in high glucose and males in low glucose.

Conclusions: Glucose rich diet affects the expression of inflammatory genes.

Keywords: Epigenetic Inheritance, Proinflammatory genes, type 2 diabetes, Metabolic memory

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Anti-apoptotic effect of Sambucus ebulus extract on SH-SY5Y neuroblastoma cells as in vitro model of Parkinson disease.

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Introduction: Parkinson's disease is the second most common neurodegenerative disorder which affecting the senile population with manifestation of motor disability and cognitive impairment. Sambucus ebulus is a plant with traditional uses which might confer neuroprotective effects most probably according to its anti-oxidative stress activity but there are no studies around its role in Parkinson diseases so far. Hence, this study has aimed to investigate the neuroprotective effect of total extract of fruits and aerial parts of Sambucus ebulus in a neurotoxin-induced model of Parkinson.

Methods: In vitro model of Parkinson disease has generated by exposing SH-SY5Y neuroblastoma cells to neurotoxin: 6-hydroxydopamine (6-OHDA) 100μM/well.Total extract of fruits and aerial parts of Sambucus ebulus extracted by tow solvents of methanol and ethyl- acetate by maceration method. Cytotprotective effect of methanol and ethyl acetate extracts in five concentrations on cell viability by using MTT assay. Apoptotic assay was done with route of Annexin V-propidium iodide method by flow- cytometry.

Results: According to MTT assay analysis, both methanol and ethyl acetate extracts have shown protective effect against 6-OHDA induced cytotoxicity in SH-SY5Y neuroblastoma cells especially at concentrations of 30 and 60 μg/ml $P<0.05$ but apoptetic analysis has shown at IC50 Conct, only methanolic extract of the heeb had anti-apoptic effect $P<0.05$.

Conclusion: We can introduce aerial parts of sumbacus ebulus extract as a cytoprotective co-trearment in Parkinson disease

Keywords: Sambucus ebulus, Apoptosis, SH-SY5Y, 6-OHDA, Neurodegenerative disorder, Parkinson's disease, Neuroprotection

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Resveratrol and brain tumors: Where do we stand?

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Page | 301

Introduction: Resveratrol (a.k.a 3,4',5-tri-hydroxy-trans-stilbene), a naturally-occurring phytoalexin, demonstrates well-described anti-inflammatory, anti-oxidative, cardioprotective, and analgesic properties, as well as antitumor and chemopreventive capacities. This phytoalexin has been found to affect cellular proliferation by affecting the initiation and progression of several types of tumors such as leukemias, prostate cancers, breast cancers, and colon cancers. In the case of brain tumors, resveratrol's anti-carcinogenic mechanisms comprise pathways such as repressing oxidative stress, inflammation and blocking cellular proliferation, while promoting apoptotic mechanisms.

Methods: In the current study, the MEDLINE®/PubMed database, as well as the Scopus were searched to achieve relevant publications. In this context, "Resveratrol", "Brain neoplasms", "Glioma", "signal transduction", and "Molecular mechanisms" were used as keywords. For a more efficient search, inclusion and exclusion criteria were considered as follows; all related controlled clinical trials, in vitro evaluations, and in vivo studies were included, while Meta-analyses were excluded.

Results: It has been revealed that resveratrol undermines cancerous brain cells by targeting several signaling pathways such as Wnt and STAT3. This compound suppresses tumorigenesis in vitro and in vivo. In this regard, 100 micromolar of resveratrol has been reported to inhibit cell growth and induce cell apoptosis in primary CD133-positive glioblastoma multiforme (GBM) tumor-initiating cells (TIC) by suppressing STAT3 activity, and also reducing tumorigenicity in mouse models of GBM and enhances the sensitivity of GBM-TIC to radiotherapies through the STAT3 pathway. Resveratrol could also sensitize brain cancer cells to drug-induced growth inhibition by targeting multiple molecular signaling pathways involved in carcinogenesis, an important advantage due to cancers' inherent heterogeneity.

Conclusion: It can be concluded from this study that resveratrol could be considered a potential therapeutic agent against brain tumors. However, further research is needed to overcome the pharmacokinetic limitations of resveratrol before its introduction into brain malignancies' clinical management by developing optimized delivery systems.

Keywords: Resveratrol, Brain neoplasms, Glioma, Glioblastoma, Signal transduction

A-10-1167-2

Association of AXIN1 and CTSB polymorphisms and Papillary thyroid carcinoma and clinical/ pathological features: a case-control study

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Introduction: Papillary thyroid cancer (PTC) is the most common type of thyroid cancer which its precise etiology remains unknown. However, environmental factors and genetic causes, contribute to the etiology of PTC. Axis inhibition protein 1 (AXIN1) is a scaffold protein that plays a tumor suppressor role via negative regulation of the Wnt signaling pathway. In addition, Cathepsin B (CTSB) is a cysteine protease enzyme with higher expression in several types of tumors. In the present study, the possible effect of AXIN1 rs12921862 and rs1805105 and CTSB rs12898 polymorphisms on PTC susceptibility.

Methods: 156 PTC patients and 158 sex- age- and BMI- matched control subjects were enrolled in the study. AXIN1 rs12921862 and rs1805105 and CTSB rs12898 polymorphisms were genotyped using the PCR-RFLP method.

Results: There was a relationship between AXIN1 rs12921862 polymorphism and increased risk of PTC in all genetic models except the overdominant model. The frequency of AXIN1 rs1805105 CT genotype was higher in PTC patients, and rs1805105 polymorphism was associated with increased PTC risk only in codominant and overdominant models. The frequency of AXIN1 Ars12921862 Trs1805105 haplotype was higher in the PTC group and this haplotype was associated with an increased risk of PTC. Moreover, the AXIN1 rs12921862 polymorphism was not associated with PTC findings, but, AXIN1 rs1805105 polymorphism was associated with near to three folds of larger tumor size (≥1 cm). There was no association between CTSB rs12898 polymorphism and PTC and its findings.

Conclusion: The AXIN1 rs12921862 and rs1805105 polymorphisms were associated with PTC. AXIN1 rs1805105 polymorphism was associated with higher tumor size.

Keywords: AXIN1, CTSB, Papillary thyroid cancer, polymorphism, tumor size

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Circulating levels of CCN3 protein in polycystic ovary syndrome: a case-control study

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Introduction: Polycystic ovary syndrome (PCOS) is a heterogeneous syndrome that involves several cardiometabolic and endocrinologic disorders. Studies showed that its pathogenesis coincides with some underlying mechanisms of recurrent pregnancy loss (RPL). Cellular communication network (CCN)-3 protein is a vastly studied adipokine that plays a role in tumorigenesis, organogenesis, inflammation, fibrosis, and glucose metabolism. The current study, for the first time, aims to determine the association of CCN3 levels with a number of parameters involved in PCOS pathogenesis.

Methods: This is a case-control study involving 120 PCOS patients (60 RPL and 60 infertile) and 60 healthy non-PCOS controls. Circulating levels hs-CRP and homocysteine were measured using commercial kits. The serum levels of CCN3 were assessed using ELISA kit.

Results: Circulating levels of CCN3 were significantly elevated in PCOS-RPL and PCOS-Inf subgroups when compared to the control group (7.61 ± 3.03 and 6.85 ± 2.54 vs. 3.12 ± 0.82, $P < 0.001$). Serum CCN3 positively correlated with fasting insulin and HOMA-IR in the control group ($P < 0.05$) and PCOS group ($P < 0.001$). CCN3 significantly associated with PCOS (OR 4.808, 95% CI [2.744—8.423], $P < 0.001$).

Conclusion: Our results show that CCN3 might be involved in the pathogenesis of PCOS. Future studies are needed to test the possibility to utilize CCN3 in the diagnosis and therapy of the disease.

Keywords: Polycystic ovary syndrome, Nephroblastoma overexpressed gene product, Metabolic syndrome, Recurrent pregnancy loss, Homocysteine, C-reactive protein.

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Circulating levels of C1q/TNF-α-related protein 6 (CTRP6) in polycystic ovary syndrome

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Introduction: Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders affecting females of reproductive age. It has been associated with cardiometabolic disorders including diabetes mellitus and cardiovascular disorders, and increases the risk of developing fecundity pathologies including recurrent pregnancy loss (RPL) and infertility. C1q/tumor necrosis factor- α-related protein-6 (CTRP6) is a novel adipokine involved in glucose and lipid metabolism, host inflammation, and organogenesis. In the present study, we aimed to determine the association of serum CTRP6 levels with some components of metabolic syndrome in PCOS patients (infertile PCOS [inf-PCOS] and PCOS-RPL).

Methods: This case–control study included 120 PCOS patients (60 inf-PCOS and 60 PCOS-RPL) and 60 healthy controls. Serum high-sensitivity C-reactive protein (hs-CRP) and homocysteine were measured using commercial kits, while adiponectin and CTRP6 levels were assessed using ELISA technique.

Results: Inf-PCOS and PCOS-RPL individuals had higher levels of serum CTRP6 than controls (546.15 ± 125.02 ng/ml and 534.04 ± 144.19 ng/ml vs. 440.16 ± 159.24 ng/ml; both $p < .001$). Moreover, serum adiponectin levels were significantly reduced, while fasting insulin, homeostasis model assessment of insulin resistance, free testosterone, and hs-CRP levels were significantly elevated in PCOS group, when compared with controls. Furthermore, serum CTRP6 positively associated with body mass index in all subjects. It showed an inverse correlation with adiponectin in PCOS group and subgroups. However, it had a direct association with hs-CRP in PCOS group and inf-PCOS subgroup, but not PCOS-RPL subgroup.

Conclusion: These findings unravel a probable role of CTRP6 in PCOS pathogenesis, which poses a possibility to be a good diagnostic target. However, further investigation is needed.

Keywords: adiponectin, C1q/TNF-α-related protein 6, C-reactive protein, homocysteine, metabolic syndrome, polycystic ovary syndrome, recurrent pregnancy loss

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Aberrant expression profile of miR-32, miR-98 and miR-374 in chronic lymphocytic leukemia

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Introduction: Leukemia is a malignant and progressive disease of hematopoiesis. The disease arises due to abnormal proliferation and development of white blood cells and their precursors in the blood and bone marrow. Chronic lymphoblastic leukemia (CLL) is a subtype of blood cancers, with the origin of B lymphocytes and the involvement of bone marrow, blood and lymph nodes. MicroRNAs (miRNAs) are small non-coding RNAs with pivotal roles in cellular and molecular processes related to different malignancies, including CLL. In this way, we aimed to evaluate the expression of miR-32- 5p, miR-98- 5p, and miR-374b-5p in CLL patients. We also investigated the signaling pathways regulated by the studied miRs and also frequently disturbed miRs in CLL. **Methods:** Blood samples were collected from 32 CLL patients from Kermanshah province, Iran and 34 age and sexmatched healthy individuals. RNA was extracted from PBMCs and then was subjected to cDNA synthesis. Using specifically designed primers and Real-Time PCR method the expression of miRNAs was detected and was statistically analyzed. Using mirPath v.3, systematic pathway enrichment analysis was performed for the three studied miRNAs here along with the frequently disturbed miRNAs in CLL.
Results: The experiments indicated a significant reduction in the expression of all three miRs (p-value<0.0001) in CLL patients compared with healthy individuals. ROC analysis suggested that the three studied miRs can serve as potential biomarkers for early diagnosis of CLL. The in silico analysis suggested proteoglycans in cancer as a pathway regulated by the studied miRs and frequently dysregulated miRs in CLL.
Conclusion: The observed reduction in expression of miR-32- 5p, miR-98- 5p, and miR-374b-5p in treatment naïve CLL patients here might be suggestive of their modulatory protective role in CLL progression. Moreover, the candidate peripheral miRNAs could potentially serve as diagnostic biomarkers which warrant further investigation in a larger sample size.

Keywords: CLL miR-32 miR-98 miR-374 Signaling pathways

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selection signatures study among European and Middle Eastern sheep breeds

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Abstract Natural and artificial selection leaves patterns on the genome during the domestication of animals and leads to changes in allele frequencies among populations. Detecting genomic regions influenced by selection in livestock may assist in understanding the processes involved in genome evolution and discovering genomic regions related to traits of economic and ecological interests. In the current study, genetic diversity analyses were conducted on 34,206 quality-filtered SNP positions from 450 individuals in 15 sheep breeds, including nine breeds from Europe, namely East Friesian Sheep, Ile de France, Mourerous, Romane, Swiss Mirror, Spaelsau, Suffolk, Comisana and Engadine Red and six indigenous breeds from the Middle East, namely Iranian Balouchi, Afshari, Moghani, Qezel, Karakas and Norduz Sheep. The SNP genotype data generated by the Illumina OvineSNP50 Genotyping BeadChip array was used in this analysis. We applied two complementary statistical analyses, FST (fixation index) and xp-EHH (cross-population extended haplotype homozygosity), to detect selection signatures in Middle Eastern and European sheep populations. FST and xp-EHH detected 629 and 256 genes indicating signatures of selection, respectively. Genomic regions identified using FST and xp-EHH contained the CIDEA, HHATL, MGST1, FADS1, RTL1, and DGKG genes, which were reported earlier to influence a number of economic traits. Both FST and xp-EHH approaches identified 60 shared genes as the signatures of selection, including four candidate genes (NT5E, ADA2, C8A and C8B) that were enriched for two significant Gene Ontology (GO) terms associated with the adenosine metabolic procedure. The candidate genomic regions under selective pressure in sheep breeds may facilitate identification of the underlying genes and enhance our understanding on these genes role in local adaptation.

Keywords: selection signatures, sheep genome, xp-EHH test, FST test

A-10-1202-1

Investigation and comparison of the effect of several methods on quitting opioid addiction

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Introduction: Addiction is one of the major problems of society. Opioids are the chemical and industrial housing compounds similar to Morphine. Codeine and Methadone, are also among the opioids group, so we need to suggest medications and methods so that they can inhibit the dependence on opioids without complications of physical and psychological dependence.

Methods: we used the mature male mice of the Wistar breed. Mice were infused with Morphine sulfate to cause dependence. At the end to prove the dependence on morphine, a Naloxone injection was performed once. Subsequently, for 25 days, morphine related mice were treated with Methadone, Codeine, Liposomal CBD C1 (Is a phytocannabinoid derived from plants and has no effect of psychedelic) and exercise. After 25 days, the blood of mice was extracted. The level of thyroid hormones was measured by ELISA method.

Results: The results showed that the use of morphine causes changes in the level of thyroid hormones. We used exercise and different drugs to reduce the negative effects of morphine on the level of thyroid hormones. Fortunately, exercise and drugs have the ability to reduce the negative effects of morphine on thyroid hormones.

Conclusion: The present study aims to propose a solution to prevent and quit addiction, according to the results of thyroid tests, the Liposomal CBD C1 edible drops, Methadone, Codeine and exercise have been able to inhibit the effects of Morphine on thyroid hormones.

Keywords: Addiction, Opioids, Morphine, Liposomal CBD C1, Exercise

Expression of inflammatory and growth factors in Androgenetic alopecia (AGA) after treatment with minoxidil and enriched media

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Page | 308

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Introduction: Male androgenetic alopecia is a type of concentrated hair loss which affects many people, and is influenced by several factors such as testosterone level, the number and quality of its receptors and dihydrotestosterone. Inflammatory factors are the main causes of this disease. According to the mechanism of the disease, numerous treatments including Finasteride, surgery, Minoxidil, and Regenerative medicine have been proposed. This study was performed to investigate the effect of independent and simultaneous injection of umbilical cord stem cell enriched media and minoxidil on the expression of inflammatory, hair follicle growth and survival genes during an animal study of male pattern hair loss.

Method: Testosterone dissolved in the thermo-sensitive gel based on poloxamer 407 was injected subcutaneously into 4-weeks-old mice for 6 weeks (once every 4 days) to induce male pattern hair loss. Then, 5% Minoxidil was used topically to first group and subcutaneous injection of enriched media was performed to second group and third group was injected by Minoxidil and enriched media. After Two months rat skin tissue samples were used for RNA extraction. Gene expression was evaluated by real time PCR method using TNF, IL-1a, IL-B, PTC-1, Ver and LEF primers.

Results: Results showed treatment with minoxidil couldn't significantly reduce inflammatory factors expression or increase growth and survival genes' expression. However, treatment with conditioned media or simultaneous treatment with conditioned media and minoxidil significantly increased hair follicle growth-related genes expression and decreased inflammatory factors.

Conclusion: Therefore, treatment with conditioned media may be a more comprehensive and effective treatment for androgenic hair loss that eliminates the need for other treatments.

Keywords: Androgenic Alopecia, Minoxidil, conditioned media, Gene expression

A-10-1130-2

Effect of calorie restriction and quercetin on oxidative stress status in rats: age-related evaluation

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Introduction: Aging is caused by the progressive accumulation of various changes in the body, which is associated with an increase in oxidative stress and related disease. Free radicals are directly responsible for the damage and defects during the aging process. In this study, we aimed to evaluate potential of calorie restriction and flavonoid quercetin to reduce the destructive effects of aging in male wistar rats.

Methods: Two age groups of rats (8 and 20 weeks) were included in the study and subdivided to normal diet, normal diet with quercetin (15 mg Kg-1), normal diet with calorie restriction, and normal diet with quercetin and calorie restriction groups. Activities of catalase, paraoxonase, liver enzymes, and lipid profile were measured.

Result: The level of liver enzymes and lipid profile in 20-week-old rats were higher than those in 8-week-old rats, and administration of quercetin and calorie restriction returned these values to the normal range. The paraoxonase activity of older rats was lower than that of young rats. The use of both quercetin and calorie restriction increased paraoxonase activity in 20-week-old rats. In both age groups, the simultaneous use of quercetin and calorie restriction significantly reduced total cholesterol, triglycerides, and liver enzymes, while increased HDL ($P < 0.05$).

Conclusion: Collectively, it can be concluded that quercetin and calorie restriction together decrease the destructive effects of aging by increasing the level of antioxidants. These results incline us to utilize calorie restriction and flavonoids in life style to benefit from their anti-aging potential.

Keywords: Aging, Calorie restriction, Quercetin, Catalase, Paraoxonase

A-10-1205-1

Evaluation of the effects of synbiotic supplementation (lactobacillus acidufilus and cinnamomum) on inflammatory condition and lipid profile in diabetic type 2 patients

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Introduction: Cardiovascular disease is more prevalent in patients with diabetes mellitus type 2 (DMT2). Regarding the role of Probiotics and cinnamon in control of inflammation and modulating the lipid profile, this study assesses the effect of probiotic and Cinnamon on lipid profile and inflammatory markers in type 2 diabetic patients.

Methods: In this randomized crossover double-blind controlled clinical trial 120 subjects with DMT2 referred to diabetes clinic in Karaj were randomly assigned to four groups. Patients in group1 received one capsule of probiotic and cinnamon, group 2 one capsule of probiotic, group 3 one capsule of cinnamon and group 4 one capsule of rice powder (placebo) daily for three months, Inflammatory markers and lipid profile were evaluated at the end of intervention. One-way variance and Tukey Analysis were performed by SPSS software for statistical analyses

Results: Compared with control group, Cholestrol, tumor necrosis factor alpha (TNFα), C- reactive protein (CRP) in group cinnamon, probiotic and synbiotic have a significant decrease ($p < 0.05$). Heigh density lipid (HDL) has a significant increase in group cinnamon, probiotic and synbiotic. Low density lipid (LDL) in group cinnamon and probiotic have a significant decrease ($p < 0.05$).

Conclusion: Consumption of synbiotic improved lipid profile and some inflammatory biomarkers in patients with DMT2

Keywords: DMT2, Lactobacillus, Cinnamon, Inflammatory factor, Lipid profile

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Effects of anti-diabetic herbs on the insulin-degrading enzyme in the human colon cancer Caco-2 cell line

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Page | 311

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Introduction: Type 2 diabetes mellitus (T2DM) is a condition characterized by insufficient insulin production or insulin resistance. The insulin-degrading enzyme (IDE) is responsible for degrading insulin and is a potential drug target for T2DM treatment. Numerous mechanisms have been proposed for plant extracts, but research on the effects of plant extracts on IDE expression and activity is riddled with drawbacks.

Methods: We investigated the effect of Phaseolus vulgaris, Allium cepa, Portulaca oleracea, Cinnamomum verum, and Citrullus colocynthis extracts on the expression and activity of IDE in the Caco-2 cell line.

Results: Findings of the RT-PCR gene expression test showed that IDE gene expression was reduced in treatment with P. vulgaris, C. colocynthis, and C. verum extracts. The results of IDE activity with fluorogenic peptide substrate V also indicated that P. vulgaris, C. colocynthis, and P. oleracea extracts reduced IDE activity in a significant and concentration -dependent manner.

Conclusion: The hydroalcoholic extracts studied, except for A. cepa, can prevent insulin degradation by reducing the expression and activity of the IDE enzyme. This new insight into the effects of herbal medicines on IDE activity can help advance future studies.

Keywords: Phaseolus vulgaris, Allium Cepa, Portulaca oleracea, Cinnamomum verum, Citrullus colocynthis

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Paraquat-alginate particles as a possible chemotherapeutic agent

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Introduction: Paraquat (PQ) is a bi-quaternary nitrogen cationic compound, generally known as a promising contact herbicide. The mode of action for this chemical agent is mainly based on the mitochondrial electron transfer and the production of reactive oxygen species (ROS). The radicals generation is followed by DNA damage and eventually cell death. Recently an increasing interest has been thriving in introducing anticancer propeties of well-known compunds and accordingly the application of encapsulation of antitumors in particles, mainly to offer specific delivery to tumor and safety for healthy organs.

Methods: The paraquat particles (PP) were prepared by applying ion gelation method, using alginate as a generally safe polyanionic polymer, and paraquat itself as a positive-charged crosslinker since it bears tertiary amines in its structure. The hydrodynamic size, polydispersity index (PdI) and zeta petential of the particles were evaluated by dynamic light scattring method. The encapsulation efficiency (EE%) and loading capacity (LC%) of particles were evaluated by UV-Vis spectrophotometry. The morphology of the particles was assayed by scanning electron microscope (SEM).

Results: The size, zeta potential and PdI of particles were approximately 127 nm, 5 mV, and 0.5, respectively. EE% was 16 and LC% was about 6. SEM presented spheric particles with noticeable size variations.

Conclusion: PP were prepared successfully and the physicochemical characterictics are promising. Further studies are being conducted to evaluate and compare PP possible inhibitory effects on cancerous and normal cell lines.

Keywords: Paraquat, Anticancer Agent, Alginate, Nanoparticles.

Evaluation of the relationship between parathyroid hormone and vitamin D3 in people undergoing weight loss

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Page | 313

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Methods: Obesity is one of the most common nutritional problems in the world. Obese people are prone to metabolic and endocrine disorders. Due to the fact that the parathyroid hormone (PTH), which is responsible for regulating serum calcium levels, we face an increase in parathyroid hormone when the serum calcium level decreases. On the other hand, intestinal absorption of calcium can be decrease due to a reduction in serum levels. Therefore, it can be concluded that people with low vitamin D and especially obese can develop secondary hyperparathyroidism.

Methods: In this study, 70 people from the age of 20 to 70 years old who have had gastric sleeve surgery for their obesity.in the recent years, have come to the laboratory. Their blood samples were taken to measure calcium, parathyroid hormone Vitamin D. The levels of vitamin D and parathyroid hormone were measured using ELISA method and monobind kits. And the serum calcium level was measured using the device Biolysis 24 and pars azmoon kit. According to the information forms of these people and reviewing the level of calcium, parathyroid hormone and vitamin D before and after surgery, it was found the parathyroid hormone level is still high.

Results: low calcium intake which cause low level of it in serum, and increase of parathyroid hormone level can increase obesity.

Conclusion: In this study, there was no significant difference between increased parathyroid hormone before and after obesity treatment. However, decreased calcium level was found in both state. It seems that if you take vitamin D tablets and re-measure parathyroid hormone and calcium, you may be able to find a way to control the increase in parathyroid hormone to prevent re-obesity.

Keywords: Parathyroid hormone - Obesity - Calcium - Vitamin D.

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Synthesis and characterization of a peroxidase-like two-dimensional anionic nano-clay and its application for catalytic removal of malachite green from aqueous solutions

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Page | 314

Introduction: Nanozymes are nanomaterials with inherent enzyme-like characteristics that have recently gotten much attention because of their high catalytic activity, low cost, and high stability grades.

Methods: in this work, two-dimensional anionic nano-clay were synthesized and characterized using different methods such as Fourier-transform infrared spectroscopy (FTIR), Field emission scanning electron microscopy (FE-SEM), and powder X-ray diffraction technique (XRD). The peroxidase-mimetic catalytic activity of nanoparticles was measured using a colorimetric method based on the oxidation of 3,3', 5,5'-tetramethylbenzidine (TMB) in the presence of hydrogen peroxide (H_2O_2) and the production of a blue-colored product. The effects of different parameters, including pH, temperature, TMB, and H_2O_2 concentrations, on nanoparticle catalytic activity, were assessed.

Results: Kinetic parameters (K_m and V_{max}) were found to be 0.01 mM and 0.87×10^{-3} mM/min (for TMB), 0.05×10^{-3} mM and 0.69×10^{-3} mM/min (for H_2O_2), respectively. Compared to natural horseradish peroxidase (HRP), Cu/Al LDH showed a high affinity for H_2O_2 and TMB. In addition, catalytic decolorization of MG was performed using the peroxidase-mimic activity of the prepared nanoparticles. The results showed that the nanoparticles could decolorize malachite green (MG) by 73% in 21 minutes. The high decolorization efficiency was obtained under the optimum conditions of pH=4, 1.37mM MG,1 mg/mLnanoparticles, and 60 seconds of incubation at 50 °C.

Conclusion: results confirm that two-dimensional anionic nano-clay with intrinsic peroxidase-mimic activity could be helpful for decolorizing and detoxifying MG from industrial wastewater.

Keywords: Peroxidas-like activity, Two-dimensional anionic nano-clay, Dye Removal.

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Systemic profiling of miRNAs and genes involved in IBD using GO enrichment and signaling pathways

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Introduction: Inflammatory bowel disease (IBD) is a long-term inflammatory immune-mediated gut illness with several extra-intestinal complications. The aim of this study was to identify a novel network-based meta-analysis approach on the combination of the differentially expressed genes (DEGs) from microarray data, to enrich the functional modules from human protein-protein interaction (PPI) and gene ontology (GO) data, and to profile the miRNAs on the functional genes.
Methods: Four datasets (GSE75214, GSE126124, GSE87473 andGSE95095) were found on the searching IBD disease in Gene Expression Omnibus (GEO) andh Array Express databases. Genes (n=309) with different expression values between the two groups of healthy and IBD patients were determined and entered into the R program using the LIMMA package after the gene normalization process. A gene network (node =163, edge =382) was determined based on the gene expression values >1 log FC and STRING score > 0.7 and finally, was visualized in Cytoscape software. Then, the gene network was enriched by GO database and KEGG signaling pathway. A hub was obtained on the impact of inflammatory and stimulatory pathways and the gene function so that it annotated with the miRWalk server.
Results: After dataset normalization process, the high-expressed genes (n=309) were identified significantly (P 0.01). More analysis was carried out to discover more key genes in the network (n=94) based on the node and edge percentiles (75th). A gene hub (including 4 genes) was found on the GO combination and the KEGG pathway crosses (n=3). Furthermore, the hsa-miR-711, has-miR-6133, has-miR-6746-5p, has-miR-5002-5p, and has-miR-6728-5p were predicted to modulate the expression of gene profile.
Conclusion: The network-based meta-analysis suggested that five miRNAs, hsa-miR-711, has-miR-6133, has-miR-6746-5p, has-miR-5002-5p, and has-miR-6728-5p, may control the gene expression levels in IBD, so that it may be a new approach in the biological drug findings for treatment of patients.

Keywords: IBD, Gene network, Microarray, Gene ontology, miRNA prediction

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Selenium Nanoparticles as Emerging Strategy to Cure Breast Cancer

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Introduction: The synthesis of nanoparticles has generated tremendous interest due to their remarkable optical, chemical, electrical, and magnetic properties. Selenium (Se) is a trace element necessary nutritionally for functioning living cells in mammals and animals. Selenium nanoparticles (SeNPs) are appealing therapeutic agents due to their high bioavailability, biological activity, and low toxicity compared to inorganic and organic Se molecules.

Methods: We searched the keywords " Selenium nanoparticles," " Breast Cancer," " MCF7," and "MDA-MB-231" in PubMed, NCBI, Scopus, and Google Scholar for updated articles.

Result: Nowadays, Conjugation or surface modification of SeNPs are employed to overcome the lower cellular intake and enhances the anticancer capability. Many research has revealed that Se might be a viable chemo-preventive option for breast cancer. So validated the cytotoxic effects of Se and nano-Se on MCF7 and MDA-MB-231 malignant cell lines. Underlying Se's anticancer chemo-preventive actions also regulate the nuclear factor kappa B (NF-kappaB) pathway, which induces the production of anti-apoptotic and pro-inflammatory genes such as IL-6, MCP1, and NOS, which have an essential role in cancer. They help maintain the equilibrium between superoxide anions and nitric oxide and govern the production of sticky cell molecules and cell death.

Conclusion: Se and nano-Se show promise in treating and chemoresistance breast cancer cells because of their antioxidant and anti-apoptotic properties. In these articles, we found that MCF7 is susceptible, but MDA-MB-231 malignant cell lines are resistant to Se and nano-Se. Furthermore, nano-Se as a medication carrier boosted their chemo-preventive effects overlapping cancer drug resistance to new therapeutic cures. These findings rely on malignant cell lines and the modulation of cell death by Se formulations, showing the new era in curing Breast Cancer.

Keywords: Selenium nanoparticles, Breast Cancer, MCF7, MDA-MB-231

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The biocatalytic activity of an OV-serpin metal complex: Synthesis, characterization and kinetics study

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Introduction: Enzymes are a principal component of all biological cells that speed up the rate of reactions. Regarding their critical importance in the body, the chemical and food industries, and medicine, they have some serious drawbacks, such as short half-life, high cost, and time-consuming purification. Also, poor temperature adaptability, instability in harsh environments, and highly selective activity, which limit their technical applications. To overcome these difficulties, nanoparticle-based enzyme mimics have received considerable attention due to their fundamental and technological interest, unique electrical, chemical, and mechanical features, tunable catalytic activities, ease of storage, and high stability.

Methods: In this work, hen egg white ovalbumin (OVA) was extracted and then a soluble biopolymer was prepared by conjugating OVA with a transition metal ion (Zn^{2+}). The synthesized OVA-Zn complex w:as characterized using different methods, including UV-vis absorption, fluorescence, and ATR-FTIR spectroscopies. The catalytic activity of the prepared complex was investigated using a colorimetric method based on the oxidation of 3,3', 5,5'-tetramethylbenzidine (TMB) in the presence of H_2O_2. Michaelis–Menten and Lineweaver–Burk plots were plotted and kinetic parameters (K_m and V_{max}) were calculated. Results: All characterization studies confirmed the successful synthesis of the OVA-Zn complex. Furthermore, the kinetic analysis indicated the peroxidase-like activity of the prepared complex. The results showed that the peroxidase-mimic activity of the OVA-Zn complex was H_2O_2 and TMB concentration-dependent. Kinetic parameters (K_m and V_{max}) were calculated to be 65.6 mM and 0.46 mM/min (for H_2O_2) and 0.118 mM and 0.31 mM/min (for TMB), respectively.

Conclusion: Compared with natural horseradish peroxidase, the OVA-Zn complex showed a higher K_m value. So, the prepared complex can be used as an alternative to natural enzymes.

Keywords: Keywords: Peroxidase-mimic activity, Colorimetric assay, Kinetic parameters

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The effect of Saffron and its active compounds on oxidative stress markers in diabetes rats: A Systematic Review and Meta-analysis of animal studies

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Introduction: The study aimed to assess the influence of Saffron and its active component on oxidative stress markers in diabetic rats.

Methods: The databases were searched until December 24, 2021. The quality of the included articles was assessed using the SYRCLE's Risk of Bias tool. To estimate the effects of Saffron and its active component, SMD with 95% confidence intervals were pooled using the random-effects model. Subgroup analysis and meta-regression were used to explore heterogeneity. Publication bias was assessed using Begg and Egger tests. The results were reported under the PRISMA guidelines.

Results: The meta-analysis comprising of 42 articles revealed that prolonged hyperglycemia leads to increased oxidative markers (MDA, NO, TOS, XO, ROS), and a decrease in antioxidant defense system (GSH, CAT, SOD, GPX, TAS, SH, TAC) Treatment of diabetic rats with saffron, crocin, and safranal decreased oxidant markers and increased the antioxidant markers.

Conclusions: Saffron, Crocin, and Safranal condense the oxidative stress by reinforcement of the antioxidant defense system and plummeting the oxidant markers. Hence, we opine that saffron and its active ingredients can be a favorable option for the management of diabetes and its complications, albeit further human studies are desirable to draw definite conclusions.

Keywords: Diabetes, Oxidative Stress, Saffron, Crocin, Safranal, Meta-analysis.

Evaluation of changes in the inflammatory process on the adipogenesis of mesenchymal stem cells (MSCs) under the influence of apigenin as an anti-inflammatory flavonoid

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Introduction: The effects of inflammation on the process of adipogenesis are conflicting. Consequently, in the present study, we investigated the impact of inflammation on adipogenesis. We also looked at how the anti-inflammatory compound, apigenin affects this mechanism. **Methods:** MSCs which were isolated from human adipose tissue was differentiated into adipocyte. They were also treated by LPS/PA. To evaluate the impact of apigenin, another group was treated concurrently with apigenin. Then, using Oil Red O staining the level of differentiation was assessed. Eventually, the expression of the NF-KB gene was examined by Real-time PCR and the protein expression of IL-6 by the ELISA method. **Results:** LPS/PA induced inflammation in MSCs, as shown by increased expression of the NF-KB gene and the IL-6 protein. Oil Red O staining revealed that the inflammation promoted adipogenesis. Apigenin was able to reduce the expression of NF-KB and IL-6 (p<0.001), indicating that it might control inflammation. Apigenin was also effective to diminish the adipogenesis differentiation of cells affected by inflammation. **Conclusion:** The results indicate the increasing effect of inflammation on the adipogenesis of MSCs. Furthermore, the inflammatory effect of inflammation on the adipogenesis process can be prevented by employing the anti-inflammatory capabilities of flavonoids like apigenin.

Keywords: Mesenchymal stem cells, Adipogenesis, Inflammation, Apigenin.

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Trehalose administration reduces oxidative stress and inflammation though upregulation of SIRT1 in aged kidneys

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Introduction: Aging is a physiological phenomenon in which a progressive decrease occurs in the function of various organs of the body, such as kidneys. Sirtuin1 (SIRT1) plays an important role in combating aging-related kidney damage and has been reported to be reduced in aged rodents. Trehalose, a non-reducing disaccharide protects cells against various cellular damage. In addition, trehalose has anti-inflammatory and antioxidant effects. In this study, we investigated the effect of trehalose on SIRT1 level, and some indicators of oxidative stress, and inflammation in the kidneys of aged rats.

Methods: In this study, 23 male Wistar rats were used which were divided into three groups including young control group, old control group and old trehalose group. The last group received oral administration of 2% trehalose for one month. Then animals were sacrificed and kidneys were removed. mRNA level of SIRT1 and TNFα were measured by Real-Time PCR in the kidney tissue. In addition, SIRT1 and TNFα protein levels were measured by ELISA. The level of malondialdehyde (MDA) and total antioxidant capacity (TAC) was measured by spectrophotometric methods.

Results: According to our data, the level of SIRT1 gene expression and its protein increased in the old group treated with trehalose compared to aged control group ($p<0.01$). Administration of trehalose led to a significant reduction in TNFα at both gene and protein levels and also MDA in the old treated group compared to aged control group ($p<0.01$). In addition, the level of TAC in the old trehalose group was significantly increased compared to aged control group ($p<0.01$).

Conclusion: Collectively, these findings showed that trehalose treatment increased the levels of SIRT1 and TAC but decreased TNFα and MDA levels in renal tissue. In other words, treatment with trehalose reduced the level of oxidative stress and inflammation through upregulation of SIRT1 in aged kidneys.

Keywords: Aged kidney, Trehalose, Oxidative stress, Inflammation

The effect of amyloid beta on the expression of microRNA-96 and HMGCR and ABCA1 genes in astrocytes isolated from the brain of C57BL/6J mice

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Introduction: Impaired cholesterol homeostasis of the brain causes the accumulation of amyloid plaque protein deposits in the hippocampus. Accumulation of these deposits eventually leads to neuronal death, memory impairment, and Alzheimer's disease. MicroRNAs are a type of regulatory molecule that can be manipulated to alter cholesterol synthesis pathways. The aim of this study was to investigate the effect of beta amyloid on the expression level of mir-96, which regulates HMGCR and ABCA1 genes and play a very important role in cholesterol synthesis and homeostasis.

Methods: Astrocyte cells were isolated from the brains C57BL/6J mice and cultured in culture medium containing 10% FBS. The cells were then treated with 0.5 µM beta amyloid and the expression of ABCA1, HMGCR and mir-96 was measured by Real time-PCR. IRNdb, TargetScan and RNAhybrid software were used to evaluate InSilico.

Result: The results of analyzing the data obtained from the expression of mir-96 as a positive regulator of HMGCR protein, as well as a negative regulator of ABCA1 protein, showed a significant decrease (* $P < 0.02$) in the treatment group. Also, the expression of HMGCR and ABCA1 genes showed a non-significant decrease ($p < 0.5$) and a significant increase (** $P < 0.007$), respectively.

Conclusion: The expression level of HMGCR and ABCA1 genes change in mice astrocytes treated with amyloid beta via their regulatory miRNAs. So, amyloid beta can alter the expression of major genes in the cholesterol homeostasis pathway. Further in vitro and in vivo studies are needed to investigate regulatory role of miRNAs in neurodegenerative disease like Alzheimer.

Keywords: Cholesterol homeostasis, amyloid beta, HMGCR, ABCA1, mir-96

In Vitro Characterization of a chimeric structure comprising VEGF-derived dipeptide and Hydroxyapatite-binding domain

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Introduction: A major challenge in tissue engineering that led to its few clinical applications is the lack of proper angiogenesis in implanted tissues. Therefore, the induction of appropriate angiogenesis to nourish the implant tissues is very important. Introducing a delivery system for specific growth factors to the site is a technique to solve this issue. This study aimed to investigate the in vitro characterization of a chimeric structure composed of a dipeptide derived from VEGF and a hydroxyapatite-binding domain in the presence of a collagen-hydroxyapatite scaffold. **Methods:** We completed bioinformatics studies, cloning, and purification of the peptide earlier. At this stage, we performed cell proliferation and migration assays; and a peptide release test from scaffolding in the presence of SBF.

Results: The chimeric peptide showed proliferative effects in the MTT assay. Scratch repair started in the first hours of scratching, and after 24 hours, the scratch was closed completely. The peptide release test indicated good bioavailability of the peptide through scaffold binding.

Conclusion: The results of the present study showed that the hydroxyapatite-binding sequence in this construct helped with tethering to the collagen-hydroxyapatite scaffold and sustaining the release properties of the peptide. The peptide affected the proliferation and migration properties of cells efficiently.

Keywords: Tissue Engineering, Vascular Endothelial Growth Factor

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Synthesis of aldopentose derivative of curcumin and evaluation of its inhibitory effect against α-amylase and α-glucosidase

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Page | 323

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Introduction: Over the past twenty years, the prevalence of diabetes as one of the most common metabolic diseases has become a public health problem worldwide. Blood glucose control is an important factor in delaying the onset and progression of diabetes-related complications. Inhibition of starch-degrading enzymes is a suitable alternative method to reduce the rate of starch digestion. Treatment of diabetes mellitus by oral α-glucosidase inhibitors is currently confined to acarbose, miglitol and voglibose marred by efficacy problem and unwanted side effects. Recent research has shown curcumin can prevent the postprandial hyperglycemia due to the inhibitory effects on α-glucosidase. Therefore, in this study, an aldopentose (ribose) derivative of curcumin was synthesized and characterized by FT-IR and MS. Then their inhibitory properties examined against two carbohydrate-hydrolyzing enzymes α-glucosidase (α-Glu) and α-amylase (α-Amy) which are known to be significant therapeutic targets for the reduction of postprandial hyperglycemia. The inhibitory of aldopentose derivative of curcumin against α-glucosidase and α-amylase were investigated by enzyme kinetic analysis. The inhibition modes of α-amylase and α-glucosidase were determined from the Lineweaver-Burk plot. Result indicated that this curcumin derivative inhibited α-amylase (IC50: 17/7 ± 0/9μM) and α-glucosidase (IC50: 14/4 ± 0/3 μM) by mixed and competitive mechanisms, respectively. It is concluded that the synthesized compound could be an appropriate candidate for further study through the rational drug design to the exploration of a new class of anti-hyperglycemic drugs.

Keywords: Curcumin derivatives, antioxidants, diabetes, α-amylase, α-glucosidase

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Quercetin attenuates bile duct Ligation -induced hepatic fibrosis by increasing Sp1 transcription factor

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Introduction: The paraoxonase 1 (PON1) is synthesized in liver and secreted into blood, where it is associated exclusively with high density lipoproteins (HDLs) and, by its antioxidant activity, is involved in reducing oxidative stress. Several transcription factors and signaling pathways influences the expression of PON1 such as SpecificityProtein1 (Sp1), a ubiquitous mammalian transcription factor, which enhances the expression of PON1. Quercetin, as an anti-inflammatory, hepato-protective and antioxidant, has been shown to increase paraoxonase 1 expression in liver fibrosis. Bile Duct Ligation (BDL) is a common model for analyzing of hepatic injury caused by bile duct obstruction which induces the production of free radicals leads to inflammation. According to the properties of quercetin on hepatic fibrosis and PON1 as well as the relationship between PON1 expression and SP1 transcription factor, we investigated the effects of quercetin on the expression of Sp1 gene in hepatic tissue of BDL rats.

Methods: The rats were categorized into the four groups: Sham, sham+quercetin, BDL and BDL+quercetin. The effect of quercetin (30 mg/kg/day) was assessed on gene expression of Sp1 with qPCR method. Statistical significance was determined using one-way analysis.

Results: The aim of this study is to evaluate the effect of quercetin on upregulation of Sp1 gene in BDL rats. A significantly reduction in Sp1 gene expression was showed in liver tissue of BDL rats compared with the sham group ($p < 0.05$). Moreover, the results of our study showed that that quercetin treatment increased the expression of Sp1 in the liver tissue of BDL+ quercetin group compared with the BDL group ($p < 0.05$).

Conclusion: Our study indicates that quercetin may be improving hepatic fibrosis via up-regulation of Sp1, a regulatory gene in PON1 gene expression, and the results suggest that it can be used as a therapeutic option.

Keywords: Bile duct ligation, Quercetin, Sp1 Transcription Factor, Oxidative stress, Paraoxonase 1

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the effect of hydroalcoholic seed extract of securigera securidaca on serum homocysteine levels and paraoxonase phenotypes in diabetic animal model treated by streptozotocin

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Introduction: Reactive oxygen and nitrogen species (RONS) have been implicated in the pathophysiology of various disease states, including diabetes mellitus (DM). Enzymatic antioxidant such as paraoxonase and non-enzymatic antioxidants such as total thiol are capable of stabilizing, or deactivating RONS before they attack cellular components. On the other hand, natural antioxidants such as phenolic and flavonoid compounds protect body from oxidative damage by removing free radicals, and thereby indicating anti-carcinogenic, anti-atherogenic, anti-ulcer, anti-thrombotic, and anti-inflammatory properties. In this experimental study, total phenol and flavonoid contents of Securigera securidaca (S. securidaca) and antioxidant effects of the hydroalcoholic extract of S. securidaca seeds (HESS) were determined on diabetic rats.

Methods: Diabetes was induced in rats through an intraperitoneal injection of streptozotocin (STZ) (55 mg/kg.BW). Eight animal group were considered: two normal and diabetic control groups, three HESS treated groups given orally at doses of 100, 200 and 400 mg/kg.BW, glibenclamide treated group and two glibenclamide plus HESS treated groups (glibenclamide plus 200 and 400 mg/kg.BW, respectively) for 35 days. The PON1 phenotype was determined using double-substrate method. Cholesterol, triglyceride and HDL were assayed by colorimetric method. Serum biochemical profile, total antioxidant activity (FRAP), ROS, lipid peroxidation and were estimated.

Results: The value of total phenolics total flavonoids were 93.3 ± 1.5 mg (GAE)/g (D.W.) and 46 ± 1.7 mg (QE)/g (D.W.), respectively. Reduction in blood glucose levels in groups treated with HESS shows a dose dependent manner. Three phenotypes were determined: AA (low activity), AB (intermediate activity) and BB (high activity). FRAP, ROS and MDA levels were ameliorated by increase in HESS dose and synergistically in combination with glibenclamide.

Conclusion: Securigera Securidaca seed consumption as a supplement for the blood sugar-lowering drugs such as glibenclamide may ameliorate oxidative stress complications in diabetic cases.

Keywords: paraoxonase, Reactive oxygen and nitrogen species, securigera securidaca, total thiol, flavonoid, phenolics, streptozotocin

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The effect of hydroalcoholic seed extract of Securigera Securidaca on the hepatic renin-angiotensin system in thestreptozotocin-induced diabetic animal model

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Introduction: The plant S. securidaca (L.) Degen & Dorfl (Bitter Lentils) is widely used as a medicinal plant in traditional Iranian medicine. Previous studies demonstrated the antihyperglycemic, antioxidant and antiatherogenic properties of the herbal extract. The aim of the study was to investigate the effect of hydroalcoholic seed extract of Securigera securidaca (S. securidaca) (HESS) on liver local reninangiotensin system (RAS) in streptozotocin-induced diabetic rats.

Methods: Three groups of diabetic male Wistar rats were treated with different doses of HESS (100, 200, 400 mg/Kg-BW), and the results were compared with diabetic and healthy control groups. To test the effects of HESS on liver local RAS as well as its alternative pathway, the tissue levels of renin, angiotensin-converting enzyme (ACE), ACE2, angiotensin-II (Ang-II), and Ang-(1-7) were measured. The oxidative state of liver tissue was evaluated by biomarkers of malondialdehyde (MDA), total oxidant status (TOS), and total antioxidant status (TAS). Due to the association between local RAS activity and tissue inflammation, the production of interleukins (IL) IL-1, IL-6, tumor necrosis factor alfa (TNF-a), and IL-10 in the liver was assayed in the experimental group.

Results: Dose-dependent effects of HESS showed that the highest dose of the extract had a reducing effect on the hepatic levels of local RAS components including angiotensinogen, ACE, and Ang-II. Surprisingly, despite the decrease in tissue level of ACE2, an increase in Ang-(1-7) tissue concentration was observed. Decreased local RAS activity through treatment with the highest dose of HESS was associated with decreased tissue levels of proinflammatory cytokines (IL-1, IL-6, TNF-a), and increased anti-inflammatory cytokine (IL-10). Most of the effects of the extract are attributed to its antioxidant properties.

Conclusions: S. securidaca seed can be suggested as a suitable drug supplement to prevent hepatic complications of diabetes.

Keywords: local renin-angiotensin system (RAS), angiotensin-converting enzyme, renin, angiotensin-II, angiotensin-(1–7), angiotensinogen

A-10-1261-1

The effect of yttrium oxide nanoparticles on the mitochondrial biogenesis in streptozotocin treated rats

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Introduction: Alzheimer's disease (AD) is the most common neurodegenerative disorder. Mitochondrial dysfunction, especially a defect in mitochondrial biogenesis, is an early and prominent feature of AD. Many studies indicated reduced mitochondrial number in susceptible hippocampal neurons in the brain of AD patients. Yttrium oxide nanoparticles (Y2O3NPs) have recently gained attention for their anti-apoptotic, anti-inflammatory and antioxidant effects in the central nervous system. In the current study, we investigated the protective effect of Y2O3NPs against mitochondrial biogenesis impairment in streptozotocin (STZ)-treated rats.

Methods: In this study, male Wistar rats weighing 200-250 g were used, which were divided into 4 groups as follows: 1) control 2) Alzheimer 3) Alzheimer+Y2O3NPs 4) Y2O3NPs. Alzheimer's rats received STZ (3 mg/kg, 3µl, bilaterally) intracerebroventricularly and the expression of factors involved in mitochondrial biogenesis (PGC-1α, NRF-1 and TFAM) was measured in the hippocampus of these animals using quantitative polymerase chain reaction (qPCR). The effect of Y2O3NPs (0.5 mg/kg/day, for 21 days, 24 h after STZ injection) treatment on the mitochondrial biogenesis was assayed in STZ-treated rats.

Results: The results showed that intracerebroventricular injection of STZ decreased mitochondrial function by reducing the expression of factors involved in mitochondrial biogenesis. Treatment with Y2O3NPs increased the expression of these agents and improved mitochondrial biogenesis in the hippocampus of Alzheimer's rats.

Conclusion: Taken together, our results suggest that increased mitochondrial biogenesis may represent a potential pharmacological approach for the treatment of AD and introduce Y2O3NPs as potential candidates for the reduction of AD disturbances.

Keywords: Yttrium oxide nanoparticles, Alzheimer, Streptozotocin, Mitochondrial biogenesis

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Anti-Cancer Effects of Telmisartan in Prostate and Breast cancer cells: Inhibition of N-Cadherin

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Page | 328

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Introduction: We studied the influence of Telmisartan as a novel N-cadherin antagonist, analogous to ADH-1, and Docetaxel on cell migration and metastasis in prostate and breast cancer cells.

Methods: Human cancer cell lines including PC3, DU145 and MDA-MB468 were selected and the anti-proliferative effects of Telmisartan, Docetaxel, and ADH-1 were studied using MTT assay. Cell migration and apoptosis were examined via wound healing assay and flow cytometry assay, respectively. The effects of ADH-1 and Telmisartan on cell adhesion in PC3, DU145, and MDA-MB468 cell lines using recombinant human N-cadherin were studied. AKT-1 mRNA expression was assayed by Real time PCR.

Results: The results showed Telmisartan, Docetaxel, and ADH-1 significantly reduced the survival of cancer cells and induced apoptosis after 48 h incubation. We observed that the treatment of PC3 and MDA-MB468 cells (N-cadherin positive) with Telmisartan (0.1 µM) and ADH-1 (40 µM) resulted in 50% and 58% reduction in cell adhesion to N-cadherin coated plate respectively (p<0.001). Whereas, the same treatment for DU145 cells (N-cadherin negative) resulted in 20% reduction in cell adhesion (P<0.05). Therefore, the adhesion of PC3 and MDA-MB468 cells to N-cadherin appeared to be more sensitive than that of DU145 cells to the telmisartan and ADH-1. Also, Telmisartan and Docetaxel significantly reduced cell migration in PC3 and MDA-MB468 cell lines compared to the control group. Using Real time PCR, we found that Telmisartan, Docetaxel and ADH-1 had significant influence on the AKT-1 mRNA level.

Conclusion: The results of this study for the first time suggest that, Telmisartan exerts anti-proliferation and anti-migration effects by targeting antagonistically N-cadherin. Also, these data suggest that Telmisartan as a less expensive alternative to ADH-1 could potentiate Docetaxel anticancer effects.

Keywords: Cancer, Cell adhesion, Docetaxel, N-cadherin, Telmisartan

A-10-1272-1

Ferroptosis related genes in cancer- systematic review

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Introduction: Ferroptosis is a completely novel form of cellular death which is characterized by a considerable quantity of lipid peroxidation and an accumulation of iron throughout the cell death process. Factors which induce ferroptosis can influence glutathione peroxidase through direct or indirect ways by several mechanisms, leading to a reduction in antioxidant capacity and an accumulation of lipid reactive oxygen species (ROS) into cells, eventually contributing to stress oxidative death. According to the latest research, ferroptosis has been linked to the pathophysiological processes of several disorders, including cancers, ischemia-reperfusion injury, nervous system diseases, blood diseases, and kidney injury. In this study, we aimed to find characteristics of ferroptosis and its regulatory gene status in cancers.

Method: Since July 2021, abstracts of publications and titles of works indexed as systematic reviews in PubMed have been used to identify search phrases. Methylation of DNA and somatic copy number changes (SCNA) correlated to the abnormal expression were acquired based on research from The Cancer Genome Atlas. The ferroptosis potential index (FPI) was created to elucidate the essential functions of ferroptosis.

Results: We discovered that in most malignancies, the FPI was increased in tumours compared with normal samples. Some metabolic pathways were adversely associated with the FPI, although several critical metastasis-related and immune-related pathways were strongly correlated. Across several cancers, a large FPI indicated a poor prognosis, but both FPI and FRGs influenced treatment sensitivity.

Conclusions: Our study looks into a systematic search for ferroptosis and related regulatory genes, with an emphasis on the therapeutic benefits of ferroptosis in cancer therapy.

Keywords: Ferroptosis, Regulatory Genes, Oxidative Cell Death, Cancer Therapy

Investigation of Occult Hepatitis C Infection among Iranian Hemophilia Patients

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Introduction: Hemophilia is a hereditary bleeding disorder in which patients need to use specific blood or plasma derivatives. This may cause various chance of infections transmitted through the bloodstream. Hepatitis C virus (HCV) is one of the high-risk blood borne viruses. Occult HCV (OCI) is a form of HCV that defined as the presence of HCV genome (HCV RNA) in liver biopsy and/or peripheral mononuclear cells (PBMCs) specimen, and undetectable levels or absence of HCV RNA in serum. The aim of this study was to investigate the presence of HCV RNA in PBMCs samples of serum HCV RNA negative hemophilia patients receiving anti-viral drugs.

Methods: At first, the levels of liver enzymes (alanine aminotransferase (ALT) and aspartate aminotransferase (AST)) were measured in one hundred Iranian hemophilia patients involved in this study. Then, plasma and PBMCs were separated by Ficoll separation method. Total RNA was extracted from PBMCs and plasma samples using extraction kit. After quantitative and qualitative assessment of the extracted RNA using NanoDrop spectrophotometry and gel electrophoresis, respectively, HCV RNA detection was tested by one step PCR. Next, the HCV genotypes of specimens were analyzed by RT-PCR assay. Finally, analysis of all data was performed by SPSS 22.0 software.

Results: The results revealed that out of 100 Iranian hemophilia patients, three patients were positive for OCI (3%). No significant changes were observed in the levels of ALT and AST in these patients. In addition, a genotype difference was observed between plasma and PBMC samples of 1% (1/100) of patients.

Conclusion: Generally, some viruses are capable to secretly remain in peripheral mononuclear cells even though the virus RNA cannot be detected in serum of the recovered patients. Thus, it is critical to study occult viral infection in patients.

Keywords: Hemophilia, Occult HCV, RT-PCR, Anti-viral drugs

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The evaluation of cytotoxicity and multi-drug resistance (MDR) reversal activity of Fucoxanthin on cisplatin-resistant ovarian cancer cells

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Introduction: The development of multidrug resistance (MDR) is a major barrier to achieving effective chemotherapy in cancer. Studies have shown that epithelial ovarian cancer initially responds to platinum-based therapy, however, the recurrent type is often resistant to treatment and is associated with high mortality. Fucoxanthin is a natural component found in marine algae that possesses various pharmacologic properties. The aim of this study was to evaluate the cytotoxicity and MDR reversal activity of fucoxanthin on MRP2-overexpressing, cisplatin-resistant ovarian cancer cells.

Methods: Cell viability of ovarian cancer cell line A2780 and its cisplatin-resistant derivative, A2780/RCIS, were evaluated in presence of different concentrations of fucoxantin or cisplatin or fucoxanthin/cisplatin combination using MTT assay. Propidium iodide staining and subG1 analysis were used to evaluate fucoxanthin potential for cell cycle modification and apoptosis induction in cancerous cell lines.

Results: The result of the study showed that fucoxantin had an inhibitory effect on the proliferation of human ovarian cancer cells. The IC50 values for A2780/RCIS cells following exposure to fucoxantin for 48 and 72 h were 13.133 ± 1.055 and $11.526 \pm 0.501 \mu m$, respectively. The co-treatment of cells with cisplatin (3.125 to 100µM) and nontoxic concentration of fucoxanthin (1 and 2.5µM) did not reverse drug resistance to cisplatin in the resistant cell line. MTT and flow cytometry results showed that fucoxanthin was able to cause similar cell toxicity and death via inducing apoptosis in sensitive and cisplatin- resistance ovarian cancer cells.

Conclusion: Fucoxanthin was not able to modify cisplatin resistance in A2780/RCIS ovarian cancer cells. However, it was highly effective in inducing apoptosis and death in both cisplatin sensitive and resistant ovarian cancer cells.

Keywords: Fucoxanthin, Ovarian cancer, Multidrug resistance (MDR), Cytotoxicity, Apoptosis

17ᵗʰ **National Congress of Biochemistry & 8ᵗʰ International Congress of Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran**

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Nanocrocin is a potential antidote for the treatment of paraquat poisoning

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Page | 332

Introduction: Parquet (PQ) is one of the most common pesticides in agriculture. It is an extremely poisonous material for humans and animals, which leads to rapid beginning of death within days of exposure due to extreme making of reactive oxygen species and the following fulminant inflammatory response. Today, due to antioxidant, anti-inflammatory and anti-apoptotic properties, crocin is used as an antidote. Crocin is a carotenoid and the real active section in saffron. Targeted drug delivery and enhancement of drug properties by nanoparticles can help design the appropriate antidote. Recently, uncharged particles of niosome have been considered for this purpose.

Methods: The nanocrocin (NC) were prepared by applying "surface-active agents film hydration" method. In summary, span-60 surfactant, polyethylene glycol, and cholesterol were dissolved into ethanol by heating at 50 °C. The hydrodynamic size, polydispersity index (PdI) and zeta potential of the particles were evaluated by dynamic light scattering method. The encapsulation efficiency (EE %) and loading capacity (LC %) of particles were evaluated by UV-Vis spectrophotometry. The morphology of the particles was assayed by scanning electron microscope (SEM).

Results: The size, zeta potential and PdI of particles were approximately 140 nm, -23.4 mV, and 0.222, respectively. EE% was 54.66 and LC% was about 1.89 SEM presented spheric particles with noticeable size variations.

Conclusion: NC were prepared successfully and the physicochemical characterictics are promising. Further studies are being conducted to assess and compare NC possible therapeutic effects on cancerous and normal cell lines treated with paraquat.

Keywords: nanocrocin, crocin, niosome, paraquat, oxidative stress

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The effect of aqueous-alcoholic extract of Chamomile on cell proliferation and Gene expression in human malignant melanoma (A-375 cell line)

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Page | 333

Introduction: Malignant melanoma is one of those cancers that have not yet been fully treated, and there is no cure for it except in very early cases, and most remedies are based on relieving the disease. In this study, the effect of total aqueous-alcoholic extract of chamomile extract on the survival of A-375 cells related to melanoma skin cells was investigated. The present study compares the expression levels of P53, CDKN1A (P21), CDKN2A (P16), BRaf as target genes, and GAPDH as reference genes after different concentrations of total chamomile extract treatment.

Methods and Results: After the cell line treatment with different concentrations of chamomile extract by MTT assay, IC50 was determined. RT-PCR data for the expression of the target genes of P53, CDKN1A (P21), CDKN2A (P16), and BRaf were calculated relative to the reference gene for chamomile extract. According to the MTT data, the concentration of 27.3 µg / ml (of luteolin concentration) was determined as IC50 for chamomile extract. The results showed that the treatment of the A-375 cell line with a 50% lethal dose of chamomile extract could decrease P53, CDKN1A (P21), CDKN2A (P16) genes and increase BRaf gene expression.

Conclusions: According to the results of gene expression in the treated samples compared to the control sample, the active substance concentration in the total extract of chamomile that we used is less than we have expected, so the ability to inhibit its cell proliferation is reduced, and overall no promising results were obtained.

Keywords: Melanoma, Chamomile extract, Real-time PCR, BRaf, CDKN1A (P21), CDKN2A (P16), P53

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Evaluation of the effect of berberine, curcumin and luteolin on melanoma cancer cell line (A-375) and simultaneous study of the expression of related cancer genes

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Introduction: Melanoma is a deadly skin cancer that has a high potential for metastatic and incurable. Patients with advanced melanoma are always incurable and have a worse prognosis. This study aimed to investigate the lethality and toxicity of curcumin, luteolin, and berberine in skin melanoma cancer cell line and also to study the expression of P53, Bax, and Bcl2 genes as target genes and the GAPDH gene as Is the reference gene.

Methods and Results: After treating the cell line with different concentrations of active ingredients by the MTT method, the IC50 value for each substance was determined. In the next step, RNA was extracted from cells treated with a lethal dose of 50% for each substance and cDNA was synthesized and its quantity and quality were controlled by nanoparticle and electrophoresis methods. Primer design steps and Real-Time PCR were performed. Real-time PCR data related to the expression of target genes relative to the GAPDH reference gene was calculated by the ΔΔCT method and the gene expression ratio for chamomile extract. According to MTT test data, concentrations of 0.0521, 0.324, and 0.0091 μg / ml were determined as IC50 for curcumin, luteolin, and berberine, respectively. The results showed that treatment of the A-375 cell line with IC50 of each substance could reduce the expression of P53 genes and increase Bax and Bcl2 gene expression for luteolin and berberine, and also reduce the expression of Bax and Bcl2 genes and increase P53 gene expression for curcumin.

Conclusions: The P53 gene is the first gene known to suppress tumors and increases transcription of the Bax gene, which is proapoptotic. The Bcl2 gene is also an anti-apoptotic. According to the results obtained from Real-Time PCR, all three of these substances had the greatest effect on changing the expression of Bax and Bcl2 genes.

Keywords: Skin Melanoma, A-375, Curcumin, Berberine, Luteolin, Real-time PCR, MTT, IC50, PCR, RNA extraction, cDNA synthesis, GAPDH, Bax, Bcl2, P53

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Evaluation and identification of biomarkers involved in the pathogenesis of acute lymphoblastic leukemia (ALL) by in silico method

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Introduction: Today, despite significant advances in the treatment of acute lymphoblastic leukemia (ALL), the long-term survival of ALL patients, especially adult patients, remains low. Therefore, understanding the pathogenesis of ALL and identifying new diagnostic biomarkers and treatment goals is important for ALL.

Method: GSE67684 Raw data were used to identify lncRNAs & Genes involved in ALL diseases. For this purpose, the difference in expression of all genes in day 8 patients compared to day 0 patients was evaluated. Selection criteria | logFC |> 1 and FDR <0.01 were considered. The DELncRNA-miRNA-DEmRNA network was mapped and the hub genes and hub LncRNAs were identified. GO (gene ontology) analysis was performed through the David database.

Result: The analysis showed that out of 1093 DEmRNA detected, 714 mRNA upregulated and 379 mRNA downregulated. On the other hand, the results of differentially expressed lncRNAs showed that a total of 52 lncRNAs had significant expression changes, 21 lncRNAs showed increased expression in day 8 compared to day 0 and 31 lncRNAs showed decreased expression. C5orf56, MCM3AP-AS1, and TRAF3IP2-AS1 were identified as hub LncRNAs and the genes CD44, MCL1, BCL2L11, FOS, BCL6, RUNX2, ETS1, and FOSL2 were identified as hub genes, all of which were unbelievably overexpressed.

Conclusion: GO analysis showed that the predicted DELncRNAs and DEmRNAs were significantly enriched in regulatory biological processes including cellular function regulation and biology, cell death, and programmed death. These results indicate that the obtained mRNAs and lncRNAs can be suitable candidates for disease progression and may be involved in the pathogenesis of the disease

Keywords: Acute lymphoblastic leukemia, Non-coding RNAs, MicroRNA, ceRNA Network

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Determination of reference intervals for hematological parameters in Iranian pediatrics younger than thirty months

Page | 336

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Introduction: The process of accurate age and sex-specific reference intervals (RIs) for hematology parameters, particularly for the medical specialty population, is very important for creating an associate degree acceptable clinical diagnosis. So, we tend to according to age and sex-specific reference intervals (RIs) for eleven hematologic parameters in Iranian pediatric medicine younger than thirty months for the primary time. **Methods:** contemporary blood samples collected from a complete of 344 participants (boys: 158 and girls: 186) ages 3 to thirty months with a mean age of 12.91±7.15 months were recruited from aid centers in Mashhad, Iran from January to March 2021. hematologic parameters as well as complete blood count (CBC) analyzed on the Sysmex auto-analyzer system (KX-21 N). RIs were calculated exploitation direct methodology and supported the CLSI Ep28-A3 guidelines with 90% confidence intervals. **Results:** None of the CBC parameters weren't needed sex partitioning. Of the eleven CBC parameters, all needed age partitioning except five parameters like white blood cell (WBC), corpuscular hemoglobin concentration (MCHC), mean platelet volume (MPV), and red cell distribution width (RDW), and platelet distribution width (PDW). two of the Red blood cell (RBC)-related markers RIs (RBC mass and hematocrit (HCT)) likewise a lower limit of hemoglobin (HGB) raised with age, whereas 2 alternatives of them like mean corpuscular volume (MCV) and mean corpuscular hemoglobin (MCH) likewise as platelet count decreased with age. **Conclusion:** During this study, we tend to establish RI for eleven hematology parameters. Age partition was needed for six parameters that show the hematology changes that occur throughout pediatric's growth and development and necessitate the utilization of pediatric-specific reference standards.

Keywords: Reference Intervals, complete blood count (CBC), CLSI Ep28-A3 guidelines

The Evaluation of Cytotoxicity Fruit Extract of Phytolacca amricana on Human Lung Cancer A549 Cell Line

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Introduction: Lung cancer is the most common cancers and chemotherapy cancer treatment is one of the methods, but because of the lack of selective cytotoxicity, it leads to the occurrence of intolerable side of the screw. Thus recently, natural products extracted from medicinal plants can play an important role in cancer treatment. Based on medicinal effect of the Phytolacca amricana, it was aimed in this study to determine inhibitory effects of fruit crude extract on lung cancer A549 cell line.

Methods: Fruit extract of P. amricana was harvested from the region of Ramsar city and A549 cells line was cultivated and proliferated. Then, the cells exposed to different concentrations of P. amricana fruit extract (31.25 to 4000 μg/ml) were incubed for 24, 48, and 72 hours. After the incubation period, the colorimetric MTT method was used to determine cytotoxicity.

Results: The results of this study showed that different concentrations of P. amricana fruit extract had a significant effect on inhibiting the growth of cancer cells, so that with increasing the concentration of the extract, the viability of cancer cells decreased ($p < 0.05$). The results have also shown that cancer cell growth was dependent on concentration and time and the highest inhibition of cancer cell growth was obtained at the concentration level of 4000 μg/ml which was 93.46 % in 72 hours.

Conclusion: These results suggested that the fruit extract of P. amricana had the strong effect against lung cancer. It seems to come with further research and utilizes its compound in cancer treatment.

Keywords: A549 cells line, Lung cancer, MTT method, Phytolacca amricana

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Dry eye disease and elevated surface MMP-9 Point- Of- Care Test

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Introduction: The aim of this study was the evaluation of diagnostic ability and quality control of tear matrix metallo proteinase-9 lateral flow test point of care test (MMP-9 LFT POCT) as precision, accuracy, specificity and sensitivity on dry eye (DE) patients.

Methods: 60 participants (30 DE patients and 30 healthy participants as control group) were examined. As physician confirmation, the Tear Film Break-Up Time(TFBUT) less than 10 seconds were used for DE diagnosis. 50µl of prepared tear sample were used for MMP-9 LFT POCT. POCT as immuno chromatographic assay with using gold nano- particles conjugated polyclonal antibody for MMP-9 evaluation can diagnose and screen DE patients with their drugs follow- up.

Results: Diagnostic abilities of tear MMP-9 LFT-POC test with cut off value 30 µg/ ml, were estimated as sensitivity of 96.7 %, specificity of 80 %, precission of 91.66 and accuracy of 91 % in total participants.

Conclusion: Our results demonstrated that MMP-9 LFT-POC test can utilized for diagnosis dry eye disease (DED).

Keywords: Keywords: MMP-9, POCT, Dry eye(DE), Gold nano- particles

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The effect of platelet-rich plasma on osteogenic differentiation of mesenchymal cells

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Introduction: MicroRNAs (mirs) are a group of epigenetic factors that play a role in differentiating mesenchymal cells by regulating gene expression. It has been observed that platelet-rich plasma (PRP) can affect the expression of these mirs by the growth factors it releases, leading mesenchymal cells to bone differentiation. The aim of this study was to investigate the effect of PRP10% on the expression change of Mir-31, Mir-30c and Mir-21 during osteogenic differentiation.

Methods: The effect of PRP 10% on the process of osteogenic differentiation was investigated by measuring alkaline phosphatase activity and calcium deposition. Besides, the expression levels of Mir-31, Mir-30c and Mir-21 in mesenchymal cells isolated from human adipose tissue in control, osteogenic induction medium (OM), and PRP10% groups were measured by Real-Time PCR on the third and fourteenth days.

Results: PRP significantly increased alkaline phosphatase activity and calcium deposition. Mir-31 expression did not show a significant change. Mir-30c expression on the third and fourteenth days in PRP10 group showed a significant increase compared to the control group, while Mir-21 expression only on the third day in PRP10 group showed a significant increase compared to the other two groups.

Conclusions: According to the results of our study, PRP can improve and accelerate the process of MSC cell differentiation by affecting the expression of some microRNAs. However, the molecular reservoir released from PRP is very complex and the experimental design for in vitro experiments to achieve significant results is challenging.

Keywords: MicroRNA, mesenchymal cells, platelet-rich plasma

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Mesenchymal stem cell therapy in Amyotrophic lateral sclerosis (ALS) patients. A comprehensive review of disease information and future perspectives

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Amyotrophic lateral sclerosis (ALS) is a rare deadly progressive neurological disease primarily affects the upper and lower motor neurons with the annual incidence rate of 0.6 to 3.8 per 100,000 people. Weakening and gradual atrophy of the voluntary muscles are the first signs of the disease onset affecting all aspects of patients' lives, including eating, speaking, moving and even breathing. Only 5-10% of patients have a familial type of the disease and show an autosomal dominant pattern, but the cause of the disease is unknown in the remaining 90% of patients (Sporadic ALS). However, in both types of disease, the patient's survival is 2 to 5 years from the disease onset. Some clinical and molecular biomarkers, Magnetic Resonance Imaging (MRI), blood or urine test, muscle biopsy and genetic testing are complementary methods for disease diagnosis. Unfortunately, with the exception of Riluzole, the only medically approved drug for the management of this disease, there is still no definitive cure for it. In this regard, the use of Mesenchymal Stem Cells (MSCs) for the treatment or management of the disease has been common in preclinical and clinical studies for many years. MSCs are multipotent cells having immunoregulatory, anti-inflammatory and differentiation ability which makes them good candidate for this purpose. This review article aims to discuss about multiple aspects of the ALS disease and focusing of MSCs role in disease management based on performed clinical trials.

Keywords: Amyotrophic lateral sclerosis, Mesenchymal Stem Cells, neurological disease, motor neurons

Expression of miR-30b-3p in the progression of carbon tetrachloride-induced liver fibrosis in mice

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Introduction: According to WHO reports, each year almost 1.2 million individuals die from cirrhosis worldwide, while the mortality rate from this disease in Iran is about 5000. There is no effective treatment for fibrosis since the mechanism of fibrosis progression is not yet fully understood. Furthermore, microRNAs are known to have a role in molecular mechanisms of various biological processes. A bioinformatics study reported that the miR-30b-3p was downregulated in the liver of fibrosis patients compared to the liver of normal subjects. In this research, we aimed to determine the mentioned microRNA expression alters during the progression of liver fibrosis in experimental model.

Methods: Liver fibrosis was induced in eight week old male C57bl/6 mice by intra-peritoneal administration of diluted carbon tetrachloride in corn oil and the expression of miR-30b-3p was investigated by real-time PCR after 4, 6, and 8 weeks. To evaluate the severity of induced liver fibrosis, the biochemical markers (serum ALT, AST, and ALP), as well as tissue hydroxy-proline alongside histopathology were analyzed.

Results: The serum ALT, AST, ALP and liver tissue hydroxy-proline content (as an indicators of fibrotic tissue) was significantly higher in hepatic fibrosis groups than the control group (p value<0.05). Although AST and hydroxy-prolin significantly increased with the progression of fibrosis (p value<0.05); serum ALP and ALT did not show the same trend. Finally, the expression of miRNA 30b-3p gene was downregulated in the fibrotic group, and this decrease became more pronounced as fibrosis severity increased.

Conclusion: This research finding demonstrated that the expression of the miR-30b-3p gene decreases as liver fibrosis progresses, suggesting that this gene may play a role in liver fibrosis and along with future studies may contribute in the diagnosis of this disease.

Keywords: Liver fibrosis, miRNA, miR-30b-3p

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Targeted delivery of tacrolimus to T cells

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Introduction: The overproduction of inflammatory cytokines is an important feature of graft versus host disease and a direct cause of target organ damage. Tacrolimus (TAC) is a kind of a macrolide lactone immunosuppressant isolated from the fungus Streptomyces tsukubaensis. Nanotechnology has introduced new opportunities to overcome many barriers exist for the development of efficient drug delivery systems. This study introduces a targeted delivery platform via CS-modified PLGA nanoparticles conjugated electrostatically with CD8AP17s Apt to deliver TAC into T cells (MOLT-4 cells), which express CD8 as the target of Apt Also, JURKAT (CD8–) cell line was chosen as nontarget cells to investigate the effects of the designed delivery system in vitro.

Methods: In this study, we aimed to design a targeted delivery platform with poly (lactide-co-glycolide; PLGA) nanoparticles modified with chitosan (CS) and CD8AP17s aptamer (Apt). MOLT-4 cells as CD8 positive and JURKAT cells as CD negative were adopted to investigate the efficacy of the proposed delivery system in vitro.

Result: The particle size and Z potential of the TAC-PLGA-CS-Apt nanocomplex were 345 nm and 13.7 mV, respectively. Release study showed an efficient TAC release from complex in citrate buffer (pH 5.5). The 3-(4,5-dimethylthiazol-2-yl) -2,5-diphenyltetrazolium bromide assay showed that TAC-PLGA-CS-Apt nanocomplex was highly selective toward MOLT-4 cells. Complex increased the cellular uptake of TAC in MOLT-4 cells (target) while reducing its cytotoxicity in JURKAT cells (nontarget).

Conclusion: In summary, a novel noncomplex functionalized with CD8AP17s Apt was designed for the targeted delivery of TAC into CD8-positive cells. The TAC-PLGA-CS-Apt nanocomplex inherited features of simple design and TAC targeting. This targeting platform caused the reduction of the cytotoxicity of the TAC in nontarget cells (JURKAT cells). The developed nanocomplex was effectively internalized into target cells (MOLT-4) and reduced their viability.

Keywords: CD8AP17s aptamer, chitosan, PLGA, tacrolimus

Preparation of a fusion DNA construct harboring HIV-1 accessory and regulatory genes

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Introduction: Development of an effective therapeutic HIV-1 vaccine can help at increasing antiretroviral therapy (ART) efficacy, and/or at substituting the antiretroviral treatment. Two main HIV-1 accessory and regulatory genes include nef and tat genes, respectively. The nef gene encoding Nef protein is essential for viral replication and disease progression in vivo. The tat gene encoding Tat protein plays an important role in viral transcription and replication, and the pathogenesis of the virus. The goal of this study was the design and preparation of a fusion DNA construct harboring HIV-1 nef accessory and tat regulatory genes as a vaccine construct.
Methods: The nef and tat gene sequences were obtained from UniProt and the National Center for Biotechnology Information (NCBI), and synthesized as a fusion construct in a cloning vector. Next, the nef-tat fusion gene was subcloned into the pcDNA3.1 eukaryotic vector using NheI/NotI restriction enzymes. After confirmation of DNA construct by enzyme digestion and agarose gel electrophoresis, the recombinant pcDNA3.1- nef-tat vector was prepared by plasmid purification kit. Finally, its concentration and purity was determined by NanoDrop spectrophotometry.
Result: The recombinant pcDNA3.1-nef-tat vector was confirmed by digestion with NheI/NotI enzymes as the clear bands of ~ 855 bp for nef-tat gene, and ~ 5427 bp for pcDNA3.1 (-) vector. The purity and concentration of the recombinant DNA vector was 1.85 and ~ 483 ng/ µL for 10 mL of culture, respectively.
Conclusion: DNA construct encoding the nef-tat fusion gene can be utilized as a HIV-1 DNA vaccine candidate.

Keywords: HIV-1, Accessory and regulatory genes, DNA vaccine

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Yttrium oxide nanoparticle treatment alleviates cholestasis-induced mitochondrial dysfunction

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Page | 344

Introduction: Cholestasis is a liver disease characterized by the accumulation of toxic bile salts, bilirubin and cholesterol, resulting in hepatocellular damage. Recent findings have revealed several key steps of cholestasis liver injury including mitochondrial dysfunction. Yttrium oxide nanoparticles (Y2O3NPs) have a profound effect on alleviating central nervous system damage. In the present study, we investigated the protective effect of Y2O3NPs on the cholestasis-induced mitochondrial biogenesis impairment.

Methods: In this study, cholestatic model in male Wistar rats (weighing 200-250 g) was induced by bile duct ligation (BDL). Animals were divided into 4 groups as follows: 1) control 2) cholestatic 3) cholestatic +Y2O3NPs 4) Y2O3NPs. Cholestatic rats were treated with Y2O3NPs (0.5 mg/kg; intraperitoneal) 24 h after cholestasis surgery for 21 days. The expression of factors involved in mitochondrial biogenesis (PGC-1α, NRF-1 and TFAM) was assessed in the hippocampus of cholestatic rats using quantitative polymerase chain reaction (qPCR).

Results: Our results indicated that cholestasis surgery significantly reduced the expression of factors involved in mitochondrial biogenesis and in fact impaired mitochondrial function. Treatment cholestatic rats with Y2O3NPs increased the expression of these factors and improved cholestasis-induced mitochondrial biogenesis impairment in the hippocampus.

Conclusion: According to the findings, Y2O3NPs had a protective effect on mitochondrial biogenesis impairment induced by cholestasis.

Keywords: Keywords: Yttrium oxide nanoparticles ،Cholestasis ،Mitochondrial biogenesis

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The Effect of Thymoquine on STAT3 signalling pathway in cancer cell

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Introduction: Thymoquinone (TQ), extracted from Nigella sativa, has been reported to exhibit anti-cancer effects against of cancer cells. The anticancer effects of TQ on cell viability, apoptosis, cell proliferation and generation of ROS have been reported by multiple papers. Its central mechanism of action is not fully comperhended, but It has been proved that TQ can affects some cellular signaling pathways. This review study was designed to assemble evidences of the effect of TQ on STAT3 signaling pathway in various cancer cells.

Method: We searched Thymoquinone, Thymoquinone AND neoplasm AND STAT3, Thymoquinone AND apoptosis AND STAT3 in pubmed and scopus data bases to extract articles to investigate and describe the potential therapeutic role and the mechanism of Thymoquinone in cancers.

Results: The antiapoptotic properties of TQ increases the possibility that this compuand can play a role in cancer treatment. STAT3 dimerization act as a transcription factor and cause expression of genes which involves in pathogenesis of cancer. Studies showed that TQ decreased the phosphorylation of JAK2 and STAT3 (Ser727 and Y705) which leads to inhibition of STAT3 target gene expression. Genes such as Survivin, c-Myc, Bcl-xL and Bcl-2 are some STAT3 target genes which have roles in cell survival and cell prolifration processes. In addtition mentioned genes, some studies have claimed that TQ induces oxidative stress and generation of reactive oxygen spieces. They found a relation between ROS generation and deacrease of p-STAT3. These findings lead researchers to design more studies on anti-apoptotic effects of TQ as aptoential treatment and STAT3 as a thrapuetic target.

Conclusion: TQ plays an anticancer role in different cancer cells by inhibiting apoptosis and interfering phosphorylation of STAT3. It can be a potential treatment for future reaserches.

Keywords: Thymoquinone, STAT3, Cancer

A-10-1286-2

Effects of Resveratrol supplementation on non-alcoholic fatty liver disease management: An updated systematic review and meta-analysis

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Introduction: considering that pro-inflammatory cytokines, fibrogenesis, and oxidative stress have important roles in the non-alcoholic steatohepatitis process and developing metabolic abnormalities in non-alcoholic fatty liver disease (NAFLD), different studies investigated the antioxidant and anti-inflammatory effect of Resveratrol in the management of NAFLD. Given the controversial results reported in these researches, this review aimed to achieve an accurate insight of resveratrol efficacy on NAFLD management.

Methods: A systematic search of PubMed, EMBASE, Scopus, Web of Science, and Cochrane library databases was done until June 2021 for randomized clinical trials which assessed resveratrol supplementation in adult patients with NAFLD in comparison with placebo. A meta-analysis of extracted data was conducted using comprehensive meta-analysis software version 2.0 Six trials, involving 232 participants were included regarding the eligibility criteria.

Results: The meta-analysis results showed that serum triglyceride (p-value=0.04), interlukin-6 (p-value=0.01), tumor necrosis factor-α (p-value=0.02) and systolic blood pressure (p-value=0.04) levels were decreased significantly in resveratrol group compared with the placebo group, while other parameters were not changed significantly following resveratrol supplementation.

Conclusion: Although resveratrol might attenuate NAFLD development partially, more high-quality and large-scale trials are required to discover its exact beneficial effects.

Keywords: Nonalcoholic fatty liver disease, Resveratrol, anti-inflammatory, antioxidant, systematic review, meta-analysis

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Effect of the curcumin and piperine co-administration on the lipid profile in metabolic syndrome and related disorders: a systematic review and meta-analysis of randomized controlled trials

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Introduction: The "metabolic syndrome" (MetS) refers to a condition that is a link between insulin resistance, hypertension, dyslipidemia, impaired glucose tolerance, and is associated with numerous adverse health outcomes. The role of curcumin, a biologically active yellow pigment, in the treatment of MetS has been investigated. It has generally been shown that curcumin can improve lipid profile and reduce lipid peroxidation, but the disadvantage of curcumin is its low bioavailability. Piperine, a bioactive alkaloid, has been suggested to be effective in improving curcumin metabolism. It reduces the activity of glucuronidase enzymes, resulting in improved absorption of curcumin, which suggests a combination therapy of curcumin and piperine.

Methods: RCTs were searched systematically using several electronic databases including PubMed, Cochrane Library, SCOPUS, and web of science up to April 2022. Randomized controlled trials (RCTs) that investigated the potential effects of curcumin plus piperine supplements on lipid profile among patients with MetS and related disorders were included. The meta-analysis was performed using Comprehensive Meta-Analysis (CMA) V3 software (Biostat, NJ).

Results: Eight articles were included in this study. This meta-analysis demonstrated that curcumin plus piperine significantly decreased total cholesterol [WMD: −0.79 mg/dl; 95% CI, −1.51 to -0.07; P = 0.03], triglyceride [WMD: −0.79 mg/dl; 95% CI, -1.43 to 0.03; P = 0.04], LDL concentrations [WMD: −0.93 mg/dl; 95% CI, -1.77 to 0.08; P = 0.03] and increase serum HDL-C concentrations [WMD: 0.78 mg/dl, 95% CI: −0.14, 1.41; P = 0.01] in patients with metabolic syndrome and related disorders.

Conclusion: As a result, the current systematic review and meta-analysis have shown the beneficial effects of curcumin plus piperine on lipid profile in patients with metabolic syndrome and related disorders.

Keywords: metabolic syndrome, curcumin, piperine, lipid profile

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Evaluation of cell proliferation-based and apoptosis studies of the effect of total chamomile extract on ovarian cancer

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Introduction: Ovarian cancer is the fifth most common cancer in women. Ovarian cancer is highly metastatic disease, and in more than twice as many patients, the diagnosis is made at an advanced stage of the disease, which is why the mortality rate is so high. Chemotherapy drugs were usually highly toxic to the body's normal cells. Therefore, the development of new therapies to overcome this resistance and to find low-toxic natural drugs for healthy cells in the body is an urgent need for the successful treatment of ovarian cancer and the recovery of patients. Chamomile (Matricaria recutita) is one of the medicinal plants that have more than 120 active biological compounds, the most important of which are flavonoids such as apigenin and luteolin. Bax, p21, BCL2, and p53 genes are involved in the process of apoptosis in the cell. This study is aimed at determining the effect of hydro-alcohol chamomile extract on the expression of these genes.

Methods and Result: MTT test data showed a dose of 11.466 µg/ml as IC50 for total chamomile extract on the A2780 ovarian cancer cell line. Real-time PCR data indicated that hydro-alcohol chamomile extract has increased expression in the Bax, p21, BCL2, and p53 genes on ovarian cancer cells compared to control culture media. Gene's expression was done by DDct compare with GAPDH.

Conclusion: Due to the use of the total extract, the antioxidant effects of chamomile also affect and increase the expression of the anti-apoptotic gene BCL2. However, MTT assay with total chamomile extract at IC50 dose shows lethal effects on ovarian cells.

Keywords: Keywords: Ovarian cancer, A2780 cell line, Chamomile extract, MTT, Real-Time PCR, BAX, p21, BCL2, p53.

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Study based on proliferation and programmed cell death of effect of total chamomile extract on lung cancer

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Page | 349

Introduction: Lung cancer has been diagnosed as one of the most common invasive malignancies and causes more than 1 million deaths worldwide. According to statistics, of all lung cancer patients, 85% have non-small-cell lung cancer (NSCLC) and 80% of lung cancer-related deaths are caused by NSCLC. This study aimed to investigate the anticancer effect of chamomile hydro-alcoholic extract on the A549 Non-small cell lung cancer line and also to study the expression of BAX, BCL2, and p53 genes that these genes are involved in the process of programmed cell death.
Methods and Results: For this purpose, the cell culture method has first been used the purpose of which is to study the growth of cells and their nutritional needs in vivo and in vitro. Then the cells were treated with chamomile hydro-alcoholic extract and the MTT assay was performed using IC50 (50% drug kill). MTT test data showed a dose of 13.19 μg / ml as IC50 for total chamomile extract on lung cancer cell line A549. In the next step, using this dose, cell treatment was performed, and after RNA extraction treatment was performed using the corresponding kit protocol the amount of RNA extracted was measured by Nanodrop and subsequently verified by electrophoresis technique. It is also using a Real-Time PCR assay was performed that shows the expression of genes by increasing fluorescent dyes.
Conclusions: Based on the results of this study, Real-time PCR data on the expression of target genes relative to the GAPDH gene expression ratio for chamomile extract was calculated. It can be concluded that treatment with soluble chamomile extract did not have any effect on the cell death-regulatedA549 cell line and did not induce apoptosis by the studied genes but even caused apoptosis.

Keywords: Keywords: Non-small cell lung cancer, A549 cell line, Chamomile hydroalcoholic extract, MTT, IC50, PCR, Real-time PCR, cDNA synthesis, Electrophoresis, BAX, BCL2, p53

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Study the Effects of Biochemical and Hematological Parameters on Human Erythrocyte Count by Using Multilayer perceptron.

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Page | 350

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Introduction: This study evaluates the significance of multilayer perceptron (MLP) as feedforward artificial neural networks (ANN) in biochemical studies.

Methods: Thirty-three biochemical and hematological parameters were assayed in 124 blood samples of participants who referred to Arak clinical laboratory. For designing MLPs, 22 parameters were considered as covariates in input layer to evaluate their importance on erythrocyte count as the dependent variable in output layer. Activation functions in hidden and output layers were hyperbolic tangent and identity, respectively. The standardized method was applied for rescaling of the variates and dependent variable.

Results: Our designed MLPs showed acceptable sum of squares error (0.07) and relative error (0.201) in testing step. Predicted by observed chart of erythrocyte count showed a positive linear correlation (y=0.56+0.86x, R2=0.956). The results of ANN analyses reveal the order of importance of hematological and biochemical parameters for erythrocyte count are MCV (0.155), HCT (0.150), MCH (0.108), Hb (0.064), cholesterol (0.052), iron (0.046), WBC (0.040) PLT (0.036), ESR (0.036), ALK (0.031), MCHC (0.0.30), BilT (0.029), HDL (0.027), Urea (0.026), Age (0.024), TIBC (0.023), TG (0.022), Gender (0.020), FBS (0.019), BilD (0.019), LDL (0.018), ALT (0.016) and AST (0.011).

Conclusion: MLPs are machine learning algorithms which allow approximate solutions for extremely complex problems in biological sciences. In this study we showed that MLPs make good classifier algorithms for evaluating the most important parameters on erythrocyte count of human blood samples.

Keywords: Artificial Neural Networks, Biochemical Parameters, Erythrocyte, Hematological Parameters, Multilayer perceptron

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Study of the effect of luteolin in chamomile plant on induction of apoptosis by molecular methods in skin melanoma cancer

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Page | 351

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Introduction: Melanoma is the most serious type of skin cancer in cells (melanocytes) produced by melanin - a pigment that gives your skin dyed. The risk of melanoma appears to be increasing in people under 40, especially women. This study aimed to investigate the lethality and toxicity of the active ingredient luteolin in chamomile on melanoma skin cancer cell line (A-375) and also to study the expression of P21, P16, Braf genes as target genes and GAPDH as The reference gene is after luteolin treatment.

Methods and Results: In this way, after treating the cell line with different concentrations of luteolin using the MTT method, the IC50 level of luteolin was determined (0.324 µg / ml). In the next step, RNA was extracted from the cells treated with a 50% lethal dose, and its quality and quantity were measured by nanodrop and electrophoresis methods. Then cDNA is extracted from RNA and controlled; Primer design and PCR steps were performed. Real-time PCR performed the expression of the desired genes. Real-time PCR data related to the expression of target genes relative to the GAPDH reference gene was calculated by the ΔΔCT method and the gene expression ratio for luteolin was calculated. The results showed that treatment of the A-375 cell line with a lethal dose of 50% luteolin could increase the expression of Braf and P21 genes and decrease the expression of the P16 gene.

Conclusions: According to the results obtained in changes in gene expression due to luteolin treatment, it was found that P21 and P16 genes, which are responsible for regulating the cell cycle, increase and decrease expression, respectively, as well as BRAF gene, which is serine-threonine Kinase has also been shown to increase expression. Thus, luteolin may be involved in some of the genetic factors influencing melanoma cancer.

Keywords: Melanoma, Luteolin, Real-time PCR, MTT, GAPDH, BRaf, P21, P16

Age and sex-specific reference intervals for routine liver function tests in infants

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Introduction: Age and sex-specific reference intervals (RIs) for biochemical laboratory tests determined using healthy pediatric participants are necessarily recommended for correct clinical diagnostics and interpretation of laboratory test results and better health care delivery. So, we aimed to determine for the first time the age and sex-specific reference intervals for liver function tests in Iranian pediatrics ages birth to 30 months old.

Methods: A total of 344 healthy pediatrics (boys: 158 and girls: 186) between the ages of 3 days to 30 months (mean age: 12.91 ± 7.15 months) were recruited from January to March 2021. Serum levels of liver function tests such as ALT, AST, ALP, direct bilirubin, and total bilirubin were measured using an Alpha classic-AT plus auto-analyzer. We determined age- and sex-specific RIs with confidence intervals usinge

Results: Our results showed that one age partitioning was required for all studied biochemical factors. So that, age-specific differences were showed in infants ≤ 5 and 5 to 30 months old. The lower and upper limits of established RIs for ALT in infants ≤ 5 months old were lower than those in children 5-30 months old. Especially, in infants ≤ 5 months old the established RI for AST and direct bilirubin were wider than infants 5-30 months old. While both lower and upper reference limits for total bilirubin and ALP were higher in infants 5 months old or younger than it. Sex partitioning was not required for all of them.

Conclusion: In this cross-sectional study, age- and sex-specific RIs for 5 routine liver function tests were determined to limit critical gaps involved in RIs for a representative population of Iranian pediatrics. The new database may be used in all hospital laboratories of Iran and can be helpful in clinical interpretation of laboratory test results and diagnosis wide range of disease.

Keywords: Pediatric population, reference intervals, liver function.

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MKN-45 cells become substantially more sensitive to chemotherapy After receiving magnolol

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Page | 353

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Introduction: In several studies, combination therapy improved the lethal effect of chemotherapy on tumor cells. Magnolol, a natural hydroxylized biphenylyl chemical frequently used in the treatment of gastrointestinal disorders, has been shown to have anti-cancer properties. We investigated the synergistic effect of cisplatin and magnolol on viability and maintenance of MKN-45 colon cancer cells.

Methods: The MTT method was used to assess the toxicity of magnolol and cisplatin. The expression of the genes was investigated using the qPCR technique. The effects of magnolol and cisplatin on tumor cell migration were assessed using the scrubbing procedure.

Results: According to MTT tests, the combination of magnolol and cisplatin significantly reduced cell viability. MMP9 and Bcl2 gene expression were significantly reduced after magnolol and cisplatin treatment. However, the expression of Bax showed significantly increased levels. The capacity of MKN-45 cells to migrate was dramatically reduced after treatment with magnolol and cisplatin.

Conclusion: These data suggest that magnolol, in combination with cisplatin, may be used to overcome cisplatin resistance in gastric cancer cells.

Keywords: Keywords: Gastric cancer, MKN-45, Cisplatin, Magnolol

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Correlation of serum lipid profile levels (triglyceride, cholesterol, HDLC, and LDLC) with DHEAs in fertile women; a cross-sectional study

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Page | 354

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Introduction: Dehydroepiandrosterone (DHEA) and its sulfated derivative, DHEAs, are 19-carbon steroids derived from cholesterol. Considering the role of lipids in the synthesis of the DHEA on the one hand and the effect that DHEA has on the plasma lipid profile level on the other hand, as well as its sex-dependent effects on the lipid profile level, in this study, we investigated the relationship between lipid profile level and level DHEA in fertile women in different decades of fertility.

Methods: In a cross-sectional-analytical study in Imam Reza Hospital, Kermanshah (Iran), the clinical records of women (20 to 50 years old) from 2015 to 2019 were reviewed. Inclusion criteria included body mass index (BMI) ≥30 Kg/m2, no history of diabetes, no history of hormone replacement therapy, no history of lipid-lowering or cardiovascular drugs, and the existence of complete information about fasting lipid profile tests (triglycerides (TG), cholesterol (Chol), HDLC and LDLC) and DHEAs serum level. The correlation between lipid profiles and DHEAs and the relationship between them in different decades of female fertility were analyzed by SPSS statistical software.

Results: Considering the role of lipids in the synthesis of the DHEA on the one hand and the effect that DHEA has on the plasma lipid profile level on the other hand, as well as its sex-dependent effects on the lipid profile level, in this study, we investigated the relationship between lipid profile level and level DHEA in fertile women in different decades of fertility The correlation coefficient between cholesterol and DHEAs was statistically significant (p = 0.04). Mean levels of DHEAs and cholesterol were significantly different among age groups (p <0.05).

Conclusion: There is an inverse relationship between the level of circulating lipid profiles and DHEAs. There is an inverse and direct relationship between age and DHEAs, age and cholesterol levels, respectively.

Keywords: DHEAs, Fertile women, Triglyceride, Cholesterol, HDLC, LDLC

The association of maternal food quality score (FQS) with breast milk nutrient content and antioxidant content of infant urine: A cross-sectional study

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Page | 355

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Introduction: Breast milk (BM) is a complex fluid with a variable within women over time and between women in the population. The BM compositional differences are likely to be partly due to maternal dietary patterns. This study was aimed to evaluate food quality score (FQS) in lactating mothers and its association with quality indicators of BM.

Methods: This cross-sectional study was performed among 350 lactating women aged 20 to 35 years. Data on dietary intake was collected using a validated food frequency questionnaire (FFQ). The FQS was calculated by summing all the scores obtained from healthy and unhealthy food groups. Antioxidant activity of the BM and infant urine samples was assessed using the Ferric reducing antioxidant power (FRAP), 2, 2'-diphenyl-1-picrylhydrazyl (DPPH), thiobarbituric acid reactive substances (TBARS), and Ellman's assay. The total content of protein, calcium, and triglyceride (TG) was also measured using standard biochemical kits.

Results: Subjects with the highest FQS adherence were in the last tertile and those with the lowest FQS in the first tertile. BM from mothers with the last tertile contained significantly higher Total antioxidant capacity (TAC) values (calculated via DPPH) assays, thiol, calcium, and protein compared to those in the first tertile ($p \leq 0.05$). Infant urinary total antioxidant capacity (masured by DPPH and FRAP assay) were also significantly higher in the last tertile vs. the first tertile ($P \leq 0.05$).

Conclusion: Our findings indicated that providing proper nutritional guidelines during pregnancy and lactation can improve the quality of BM and infant oxidative stress markers.

Keywords: food quality score, breast milk, antioxidant activity, lactating mothers, infant urine

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Age-specific reference intervals for kidney function tests in the healthy Iranian children younger than 2 years old

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Introduction: Age and sex should be considered in determining reference intervals (RIs), especially in the early months of life when physiological changes occur continuously. Because data on important biomarkers in healthy neonates and neonates, especially in Iranian populations, are limited, we have determined age- and sex-specific RIs for 7 laboratory biochemical parameters in healthy Iranian neonates and pediatric. **Method:** In this cross-sectional study, 344 child participants (boys: 158 and girls: 186) were aged 3 days to 30 months (mean age: 12.91 7 7.15 months) who were selected from January to March 2021. Serum levels of 7 biomarkers such as creatinine, urea, uric acid, calcium, phosphate, vitamin D and hypersensitive C-reactive protein (hs-CRP) were measured using Alpha classic-AT plus autoanalyzer. According to specific exclusion criteria, we determined age- and sex-specific RIs with 90% confidence intervals (CI) using nonparametric rating method and CLSI Ep28-A3 guidelines. **Results:** There was no need for gender segregation for any of the biomarkers. Age classification was required for most parameters, except calcium, hs-CRP, and vitamin D. Serum concentrations of calcium, hs-CRP, and vitamin D were relatively constant throughout the age range. Serum urea and creatinine concentrations increased with age. Serum levels of phosphate and uric acid decreased with age. **Conclusion:** In this study, age- and sex-specific RIs for 7 routine biochemical markers were identified to address critical deficiencies in early RIs for improved laboratory and clinical analysis, followed by better disease management in the Iranian pediatric population. Age classifications indicate biochemical changes that occur during the growth and development of children. These new results could be valuable for hospital laboratories with similar populations.

Keywords: Reference intervals, biomarkers, pediatri

A-10-1252-1

The effect of growth inhibition of nanobodies prepared against Pseudomonas aeruginosa after loading on chitosan and Alginate in Vitro

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Introduction: Pseudomonas aeruginosa is one of the leading gram-negative, rod-shaped organisms. P. aeruginosa encodes numerous virulence factors that enable it to establish various human infections. Targeted drug delivery leads therapeutic agents in a site specific Therefore, natural polymers are widely used in drug delivery systems. Single-domain antibodies, also known as nanobodies, are small antigen-binding fragments that are derived from heavy chain only antibodies present in camelids. Nanobody are useful alternatives to conventional antibodies due to their small size, and high solubility and stability across.

Methods: In the present study, after immunization of camels with bacteria inactivated by chitosan or alginate used as adjuvant, nanobodies prepared against Pseudomonas aeruginosa were prepared three times with an interval of 14 days using CM-Sephadex C-50 ion exchange chromatography Were purified. After loading on chitosan and alginate nanoparticles to evaluate the growth inhibition of encapsulated nanobodies, experimental steps including positive control group and loaded samples were performed on 96 ELISA plates. Comparison of bacterial growth with control group were read at 630 and 490 wavelengths for 24 hours.

Results: The percentage of inhibition of bacterial growth at two wavelengths of 630 and 490 nm was observed in chitosan nanobodies used as adjuvant title, loaded on chitosan 85% and in alginate nanobodies used to the adjuvant title, loaded on chitosan 80% was observed. The percentage of inhibition of bacterial growth in chitosan nanobodies used as adjuvant title, loaded on alginate at 630wavelength, 20% and at 490, 35% wavelength were observed and in alginate nanobodies used as adjuvant title, loaded on alginate was observed at 25% at 630 nm and 40% at 490 nm.

Conclusion: Chitosan-loaded nanobodies had the best inhibitory growth of Pseudomonas aeruginosa compared to alginate-loaded nanobodies

Keywords: Drug delivery, Alginate, chitosan, Pseudomonas aeruginosa, Nanobody

Computational Selection of DNA Aptamer against CA125

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Introduction: Aptamers, single-stranded nucleic acids generated in vitro, can specifically bind to a target molecule. Many CA125 aptamers have been introduced in the past studies that have challenged researchers: "Which aptamer is the best one?". A high affinity and specific DNA aptamer was selected from CA125 aptamers in the literature through the Molecular docking (MD) strategy. The selected aptamer will be used as probes in an unmodified gold nanoparticles-based aptasensor to measure CA125 concentration in body fluids.

Methods: Twenty-six CA125 single-stranded DNA aptamers were isolated from the literature. Their secondary and tertiary structures were predicted by the Mfold server and RNA composer respectively. Output 3D ssRNA molecules were converted to ssDNA in the Molecular Operating Environment (MOE) v2019 software. Using ZDOCK and Patchdock server, the aptamer-target interactions were predicted. Finally, the interaction scores were compared to select the high affinity and specific DNA aptamer.

Results: The initial library consisted of 26 ssDNA and contained three different types of secondary structures including a simple hairpin loop (H-loop), internal loop (I-loop), and multi-branch loop (MB-loop). The aptamers were sorted according to their scores and compared with each other. In addition, the analysis of different aptamer-CA125 complexes demonstrated that simpler secondary structure, appropriate loop size (~12-20 bases), lower binding energy, lower DG, binding pocket, and type of interactions can be considered important factors in the selection of high-affinity aptamers.

Conclusion: in the present study, we successfully selected the best CA125 aptamer from previous studies with MD to use in biosensors. The computational methodologies facilitate the selection or improvement of desired aptamers by clarifying the interaction between ligand and receptor at the molecular level.

Keywords: Aptamer, Molecular docking, CA125, aptasensor.

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Molecular Dynamics Simulation Study of Doxorubicin Drug Interaction with Specific Aptamer AP-9R of Lung Cancer Stem Cells with Theranostic Potential

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Introduction: According to the statistics published in 2020, lung cancer is the second most common cancer after breast cancer that causes death. Lung cancer stem cells (CSC) with tumorigenic potential, self-renewal, and proliferation have special importance over other cancer cell types. Because of these features, therapeutic activities against these cells are difficult. Doxorubicin is an antitumor chemotherapy drug that affects the DNA target cells. Aptamers are short single-stranded oligonucleotide sequences that can bind to a wide range of specific targets, including small molecules, proteins, and cells with high affinity. This study evaluated the loading ability of doxorubicin on the CSC-specific aptamer, AP-9R sequence.

Methods: Mfold and RNAComposer web servers were used for determining the two-dimensional and three-dimensional structures of the AP-9R aptamer. Also, YASARA software was applied for converting the RNA sequence to the DNA strand. The molecular dynamics (MD) simulation of AP-9R in the presence of 10 doxorubicin molecules was done for 100 ns by GROMACS 2018.4 with the CHARMM27 force filed at 300 K.

Results: The RMSD analysis for the aptamer proved 100 ns as a suitable time for the MD simulation study. The interaction energy results revealed that doxorubicin molecules numbered 1, 4, 6 in the center and doxorubicin 8 in the left arm cavity of the strand possessed less energy values (lower than -300 kJ/mol). Ligand binding analysis demonstrated that hydrophobic interactions, hydrogen bonds, and π-stacking involved in doxorubicin loading, while hydrogen bonds were more effective. Also, doxorubicin 1, 4, 6, and 8 possessed the most interactions with the AP-9R.

Conclusion: In-silico analysis of the interaction between the AP-9R aptamer and doxorubicin highlighted that doxorubicin could intercalate in the center and arm-induced cavity of the AP-9R aptamer with high stability. Hence, the AP-9R aptamer is an attractive candidate for the drug delivery and therapeutic aims.

Keywords: Cancer stem cells, Lung cancer, MD simulation, Doxorubicin, Aptamer, Ligand binding

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The emerging role of N6-methyladenosine in Breast Cancer treatment

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Page | 360

Introduction: Breast cancer is common cancer diagnosed in women and is the leading cause of cancer mortality worldwide. Novel drugs have recently developed excellent therapeutic techniques for breast cancer prevention and control. As we know, Dysregulated gene expression is one of the characteristics of cancer. So, a new method was presented due to the transcriptome-wide mapping of N6 methyl adenosine (m6A). In breast cancer, m6A modification modulates RNA termination codons (UTR), influencing RNA transcription, processing, splicing, degradation, and translation.

Methods: We searched PubMed, NCBI, Scopus, and Google Scholar for published updated articles.

Result: in general, m6A modifiers consist of three essential components: methyl-transferases (Writers), which promote or inhibit effects on the growth of breast tumors, dimethyl-transferase (Erasers), which remove m6A modifications; and Readers, which detect m6A-modified sites and further control m6A modification. "Writers" such as methyltransferase-like (METTL) could decrease cell proliferation and promote apoptosis in breast cancer. A notable "Eraser" that mainly has a vital role in Breast Cancer treatment is AlkB homolog 5 (ALKBH5). Recent studies noted that ALKBH5 increases the pluripotency factor expression because of its vital role in the stability and proliferation of cancer stem cells by demethylating m6A and thereby inducing breast cancer cell proliferation. These results showed that the ALKBH5 gene knockdown could suppress breast cancer development and progression.

Conclusion: Our findings suggest that aberrant mRNA expression, rather than gene mutation or amplification of m6A enzymes, particularly METTL3, METTL14, and ALKBH5, might be a potential diagnostic and predictive method for Breast cancer diagnosis. The current work marks the beginning of a new era of epi-transcriptome research in m6A-based breast cancer function and modification.

Keywords: N6 methyl adenosine (m6A), Breast Cancer, ALKBH5, METTL

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Evaluation ANGPTL3 gene polymorphism in patients with angiographic coronary artery disease compared to healthy individuals

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Page | 361

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Introduction: The Angiopoietin-like 3 (ANGPTL3) gene have been reported to be associated with cardiovascular risk. This study design to compare the genetic variant (rs1748195) of ANGPTL3 gene and the presence of a coronary artery occlusion of >50% in Iranian nation.

Method: In this study, 184 patients underwent angiography and 317 healthy individuals were evaluated for polymorphism of rs1748195 the ANGPTL3 gene using Tetra-ARMs PCR. coronary patients who experience angiography were categorized into two group: 54 patients who had an angiography indication for the first time and coronary occlusion was <50% (Angio-), 134 patients who formerly underwent coronary stent implanting at least one month before with coronary occlusion of ≥50% that again have an angiography indication (Angio+). In addition, individuals with angio+ categorized in two groups: 1) non-in-stent restenosis (NISR); patient with a patent stent (N=92). 2) in-stent restenosis (ISR); in-stent stenosis >50% (N=42).

Result: The fundamental of characteristics of our study design population was categorized base on undergoing angiography or not. In the present study, we investigated that the CC genotype, and also the A allele corresponding to rs1748195 at the ANGPTL3 gene loci, was associated with negative angiogram and directly related to the risk of coronary occlusion >50%. In contrast, this result was not significant in genotypes of ANGPTL3 between Non ISR and ISR groups.

Conclusion: The outcomes of this study showed that rs1748195 polymorphism at the ANGPTL3 gene loci is associated with an elevated risk for the existence of a coronary occlusion of > 50%.

Keywords: Cardiovascular diseases (CVD), Angiopoietin-Like3 (ANGPTL3), Atherosclerosis, Angiography

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Construction of a eukaryotic expression vector encoding the human immunodeficiency virus Nef gene linked to the interferon-gamma gene

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Introduction: Human immunodeficiency virus (HIV) is a major public health concern. HIV-1 genome encodes numerous proteins such as Gag, Pol, Env, Nef, Vif, Vpu, Vpr, Tat and Rev. Among these proteins, Nef protein has a positive effect on viral infection and replication by promoting the survival of infected cells. It was known as an antigen candidate in vaccine design. Moreover, one of the most important vaccine components is adjuvant that can increase antigen-specific immune response. For instance, some cytokines such as interferon-gamma (IFN-γ) cytokine play a major role in enhancing the cellular immunity. Indeed, IFN-gamma makes a significant contribution to host defense against viral infections. In this study, a eukaryotic expression vector encoding the IFN-gamma-Nef fusion gene was prepared to use as a DNA vaccine construct in future.

Methods: First of all, the reference sequences of HIV-1 Nef and mouse IFN-gamma were obtained from https://www.ncbi.nlm.nih.gov. Then, IFN-gamma and Nef gene sequences were designed to clone in a eukaryotic vector using Snap Gene software. After synthesis of the IFN-gamma-Nef fusion gene in the pUC57 cloning vector, the fusion gene was subcloned into the pcDNA3.1 eukaryotic vector using XbaI/ HindIII restriction enzymes. Finally, the purity and concentration of the recombinant pcDNA-IFN-gamma-Nef were determined by NanoDrop spectrophotometry.

Results: The results of enzymatic digestion showed a clear band of ~ 1220 bp in agarose gel electrophoresis indicating the correct subcloning of IFN-gamma-Nef fusion gene in the pcDNA3.1 expression vector. The purity and concentration of the recombinant pcDNA-IFN-gamma-Nef were ~ 1.85 and ~ 375 ng/ μL, respectively.

Conclusion: The recombinant pcDNA-IFN-gamma-Nef will be used as a DNA vaccine construct in the next studies.

Keywords: HIV, Nef, Cytokine, IFN-gamma, Eukaryotic expression vector, DNA vaccine

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A-10-1311-1

Evaluation of the expression of vascular endothelial growth factor (VEGF) gene in patients with coronary artety disease

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Page | 363

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Introduction: Vascular endothelial growth factor (VEGF) is one of the genes associated with CAD.VEGF plays an important role in preventing myocardial ischemia by monitoring and improving the dilation of blocked arteries.

Methods: In this study, 20 people were studied, 10 of whom are healthy and 10 of whom have cardiovascular disease undergoing angiography defined as angio-positive group. The RNA in the samples was extracted, c-DNA was synthesized. Quantitative and qualitative gene expression was determined by Real Time PCR.

Results: The VEGF expression was significantly increased in the angio-positive group compared to the control group ($P < 0.05$). Statistical analysis showed no significant relationship between demographic factors and vascular stenosis ($P > 0.05$). Also, there was no significant relationship between biochemical factors and vascular stenosis ($P > 0.05$).

Conclusion: In conclusion, the present study suggests that there is a link between VEGF gene expression and CAD and angio-positive group.

Keywords: CAD, expression, VEGF, angiography

A-10-1158-3

High-throughput virtual screening to inhibit furin protease with potential therapeutic purposes

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Page | 364

Introduction: One of the critical players in proteolytic cleavage is the serine protease furin, which catalyzes the proteolysis reaction in the plethora of protein substrates at polybasic recognition motifs. Furin proteolytic cleavage is important in mammalian homeostasis due to its wide range happening in numerous lysis processes including cytokines, hormones, growth factors, and receptors. Thus, it isn't far from the expectation that aberrant furin roles are associated with a broad range of disorders like Alzheimer's disease and cancer. Besides, the function of furin is exploited by vast viral and bacterial pathogens, thereby enhancing their virulence and spread.

Methods: The atomic coordinates of the furin structure obtained from RCSB PDB-ID: 5JXG and subjected to structure refinement in 3Drefine online web tools. The natural supplements library of the 35032 was downloaded from NPASS (http://bidd.group/NPASS/index.php). Before docking experiments, the FAF-drugs4 web server applied to clean the library according to Lipinski's physicochemical properties and availability. Screening processes were followed according to EVINA values, active site residues blocking, ligand efficacy score, ADMET properties, and pharmacophore profiling. At last molecular dynamic simulation carried out for the apo-furin and furin/screened ligand complexes in GROMACS simulation package.

Results: FAF-drugs4 decreased the search space to 16430 compounds to be docked against furin. By screening in EVINA cut-off on -6.0 kJ.mol-1, the library counted down to 640 hit compounds. In active site blocking criteria, the library reached 51 leads. Ligand efficacy score, ADMET properties, pharmacophore profiling, and MD simulation ranked the leads to 2 compounds that acquired the passing score. Hitherto, 2 candidate compounds including Limonin and Silymarin were picked out for further validation in experimental tests.

Conclusion: The screened supplements in the current research are promising novel candidates for inactive furin proteolytic activity. Therefore, characterized supplements can be suggested for more experimental efforts as inhibitor compounds.

Keywords: Keywords: Furin, Docking, MD Simulation, Virtual screening, Limonin, Silymarin.

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Comparison of sperm PLCζ levels between varicocele and fertile men

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Introduction: Varicocele is one of the most common causes of male factor infertility and an intricate process including various physiological and cellular mechanisms. This study aimed to compare the expression of phospholipase C ζ (PLCζ), as a sperm oocyte-activating factor (SOAF), at both RNA and protein levels in varicocele and fertile men.

Methods: in this study, semen samples were collected from 30 men with grade II and III unilateral varicocele and 17 fertile men without varicocele. Sperm DNA fragmentation and relative expression of PLCζ at both the RNA and protein levels were assessed by sperm chromatin structure assay (SCSA), real-time PCR, and Western Blot assay, respectively.

Results: The results of this investigation showed that sperm DNA fragmentation was significantly higher for infertile men with varicocele than for fertile men ($P < 0.05$). Moreover, the expression levels of PLCζ mRNA and protein were significantly lower in infertile men with varicocele compared to fertile men ($P < 0.05$).

Conclusion: Testicular hyperthermia is one of the pathophysiological mechanisms suggested to describe impaired sperm production and function in varicocele status and may reduce gene expression in testes like PLCζ. Therefore, low expression of PLCζ, a sperm-specific factor responsible for initiating oocyte activation, can be considered one of the etiologies of reduced fertility related to varicocele. Thus, it is recommended that varicocele men use varicocelectomy surgery or artificial oocyte activation (AOA) techniques to improve the rate of fertilization.

Keywords: Sperm, PLCζ, DNA damage, Varicocele

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Generation of an immunogenic HIV-1 multiepitope peptide construct in Escherichia coli

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Introduction: Epitope-driven vaccines harboring immunogenic and conserved T-cell epitopes of multiple HIV-1 antigens have been proposed as potential vaccine candidates in recent years. Herein, a recombinant multiepitope peptide construct harboring T-cell epitopes of five main HIV-1 proteins was generated in Escherichia coli (E. coli) strain.

Methods: The designed multiepitope DNA construct encoding T-cell epitopes of HIV-1 Gag, Pol, Env, Nef and Rev proteins using various in silico analyses (i.e., Gag-Pol-Env-Nef-Rev construct) was cloned into pET-24a (+) vector and transformed into BL21 E. coli strain. Gene expression was performed under the optimized conditions (IPTG inducer: 1mM, post-induction time: 16 h, temperature: 37ºC), and confirmed by SDS-PAGE and also western blotting using anti-His antibody. The recombinant multiepitope peptide was purified by affinity chromatography (Ni-NTA column) under denaturing conditions (8M urea buffer, pH 4.5). The imidazole-SDS-Zn reverse staining was carried out for further purification of the recombinant multiepitope peptide. Its concentration was determined by NanoDrop spectrophotometry.

Results: The recombinant Gag-Pol-Env-Nef-Rev multiepitope peptide was confirmed as a clear band of ~35 kDa in SDS-PAGE and western blotting. This recombinant multiepitope peptide was successfully purified by affinity chromatography and reverse staining. Its concentration was about 0.6 mg/mL for culture of 100 mL.

Conclusion: The purified HIV-1 multiepitope peptide can be used to develop an effective vaccine candidate against HIV-1 infection in near Future.

Keywords: HIV-1 vaccine, protein expression and purification, E. coli system

Plant nanoparticles in combination therapy in breast cancer

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Introduction: Plant virus nanoparticles (VNPs) have been studied as immunological adjuvants to activate an anti-tumor immune response. The VNPs might be employed as a vaccine adjuvant in cancer immunotherapy and as a delivery vehicle for other reagents, either alone or with other immunotherapies.

Method: We performed a systematic literature review in PubMed, Medline, and Google Scholar using specialized terms. Due to the novelty of this strategy, few kinds of research have been done in this area. We set a time limit of 2020-2022 and a language restriction of English. Based on relevance, the search provided 53 results; seven articles were checked following the removal of duplicates.

Result: VNPs' immunostimulatory capabilities can help treat malignancies when used as an in-place vaccination. The VNPs produced by the cowpea mosaic virus (CPMV) reverse the immunosuppressive tumor microenvironment and boost innate immune cells' antigen-presenting abilities, resetting the cancer immunity cycle. Breast tumor cells overexpress CD47 on their surfaces to escape being removed by macrophages. AntiCD47 therapy target both the innate and adaptive immune systems as a new therapy. While targeting the CD47 axis is an appealing strategy, most immunotherapies are ineffective when used in isolation. So, there is a need to create combination treatments that activate many distinct pathways to synergize and extend anti-tumor immunity. CD47 Ab and CPMV therapy increase tumor cell phagocytosis by macrophages. **Conclusion:** Data suggests that while CD47 inhibition can improve macrophage phagocytosis and kill tumor cells in vitro, it is inadequate to elicit systemic anticancer effects in breast cancer, immunocompetent hosts. Compared to solo treatments in breast models, the combination of CD47 Ab and CPMV shows a synergistic ability to promote tumor cell death through macrophage activation. This research reveals a unique technique for promoting macrophage activity to destroy tumor cells.

Keywords: Plant virus nanoparticles, Combination therapy, Breast cancer

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Targeting Nsp14 from SARS-CoV-2 using high-throughput virtual screening of the natural compounds library

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Page | 368

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Introduction: The pandemic of COVID-19 originated from SARS-CoV-2 has now posed an unprecedented threat to public health with the urgent need to develop new therapeutic options. Among the SARS-CoV-2 encoded proteins, non-structural protein 14 (nsp14) is a bi-functional enzyme consisting of a 3'-5' exoribonuclease (ExoN) activity and a N7-methyltransferase (MTase) domain that are critical in viral replication. Nsp14 could be a potential drug target for intervention due to its pivotal role in the virus life cycle.

Methods: A library of 35000 natural supplements were downloaded from NPASS (http://bidd.group/NPASS/index.php). To remove any spatial clashes and refine the initial structure a 20 ns MD simulation was carried out for the structure coordinates of the Nsp14 complex extracted from PDB ID: 7N0B in GROMACS 5.1.4 molecular dynamic simulation package. Firstly, the FAF-drugs4 web server used to filter out the library based on the physicochemical properties and availability. Screening processes were planned according to EVINA values, active site residues blocking, ligand efficacy score, pharmacophore and ADMET properties, and comparison with standard FDA-approved nucleoside analog drugs as control.

Results: In filtration levels; by screening in EVINA criteria on -6.5 kJ.mol-1, search space decreased to 590 hit compounds. According to active site blocking the library reached 46 leads. Ligand efficacy score ranked the leads to 8 compounds that acquired the passing score with approximately the same docking energy and ligand efficacy. In ranking the selected compounds according to pharmacophore and ADMET properties, in addition to comparison with standard, finally, 4 compounds including Limonin, Indirubin, Artemisinin, and Caffeic acid were picked out.

Conclusion: The introduced ligands in this study are the promising novel candidate molecules, inhibiting Nsp14 active site interactions with its cognate RNA. Therefore, characterized supplements can be suggested for more experimental efforts to be performed for recognition of the discovered ligands as inhibitor compounds.

Keywords: Keywords: SARS-CoV-2, COVID-19, Nsp14, Docking, MD Simulation.

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Therapeutic effect of royal jelly on speed of spatial learning and memory, serum and brain total oxidant capacity in rat model of multiple sclerosis

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Multiple sclerosis (MS) is a chronic inflammatory disease of the central nervous system (CNS), It is characterized by loss of myelin Data indicate that oxidative stress plays a major role in the pathogenesis of MS. The antioxidative activity of royal jelly (RJ) has also been proven. The aim of present study was to investigate the effect of RJ on the serum and brain total antioxidant capacity activity and spatial learning and memory in a rat model of MS. Twenty-five adult male Sprague Daweley rats were used and allocated into five groups. Control; Sham (intrahyppocampal injection of 3µl normal saline); Positive control (MS induction without treatment); experimental 1 (MS induction + RJ 100mg/kg/day for 20 days); experimental 2 (MS induction + RJ 200mg/kg/day for 20 days). Induction of MS was done by 3 µl of 1% ethidium bromide. Total antioxidant capacity was measured by ELISA method. Learning and memory test was done by Morris water maze. Data were analyzed by one-way ANOVA and post-hoc test was Tuckey. The significant level was considered as $P<0.05$.

Results: Present data showed that swimming speed in Morris water maze test in working memory stage of learning and memory significantly decreased in positive control and at low dose of RJ as compared to control and sham groups; while swimming speed in Morris water maze test in working memory stage of learning and memory at high dose of RJ was significantly ($P<0.05$) higher than positive control. According to data total antioxidant capacity of brain and serum were significantly ($P<0.05$) decreased in positive control as compared to control, sham and RJ high dose groups. RJ improves the swimming speed in Morris water maze procedure for learning and memory in working memory stage. In addition, RJ improves total antioxidant capacity of brain and serum in MS rats.

Keywords: Royal Jelly, Total antioxidant capacity, Morris water maze, hippocampus, multiple sclerosis, rat

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Lipid profile changes in patients with COVID-19

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Introduction: To evaluate blood lipid profiles in patients with coronavirus disease 2019 (COVID-19), and to explore the association with disease severity.

Methods: This case-control study included patients with COVID-19, referred to two medical centers in Kermanshah, Iran (between July 2020 and December 2020), and healthy controls. Lipid profiles were evaluated in patients who were grouped according to severe (intensive care unit [ICU]), or less severe (outpatient), forms of COVID-19, and in healthy controls, and were compared among the three groups.

Results: A total of 132 participants were included, comprising ICU (n = 49), outpatient (n = 48) and control (n = 35) groups. Mean cholesterol levels were lower in the patient groups than in controls; high-density lipoprotein cholesterol (HDL-C) levels were higher in the ICU group versus outpatients, and low-density lipoprotein cholesterol (LDL-C) levels were lower in the ICU group versus outpatients. The frequency of diabetes and hypertension was higher in the ICU group than in the outpatient group. Furthermore, LDL-C level was associated with disease severity (odds ratio 0.966, 95% confidence interval 0.944, 0.989).

Conclusion: Lipid profiles differ between severe and less severe forms of COVID-19. LDL-C level may be a useful indicator of COVID-19 severity.

Keywords: COVID-19, Dyslipidemias, LDL-C, HDL-C, Odds ratio, SARS-CoV-2

Investigation of anti-cancer properties of the Zingerone in the inhibition of histone deacetylase

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Introduction: Cancer is one of the causes of mortality worldwide. Histone deacetylases inhibitors interfere with Histone deacetylases activity and regulates biological events, such as cell cycle, differentiation, and apoptosis in cancer cells. As a result, Histone deacetylases inhibitor-based therapies have gained much attention for cancer treatment. Zingerone (4-hydroxy-3-methoxyphenyl-2-butanone) is a nontoxic and inexpensive compound with varied pharmacological activities. Aims: In the current study, we investigated the effect of Zingerone as a histone deacetylase inhibitor in cancers.

Methods: To investigate the mode of interaction of the Zingerone with histone deacetylase active site, the chemical structure of Zingerone was designed and optimized by using HyperChem software. The protein X-ray crystal structure of Histone deacetylases was received from https://www.rcsb.org. A docking study was performed by AutoDock 4.2 software and Possible H-bonding interactions were assessed by using the Discovery StudioVisualizer program.

Results: Our inspections show that Zingerone plays as an inhibitor for histone deacetylase with interactions through H-bonding with His 180, Phe 208, and Gly 206 of Histone deacetylases protein.

Conclusion: Our docking study reveals that Zingerone occupied the same space as cocrystal (SAHA). These results can thus serve as a template for further studies in vitro and in vivo.
Keywords: anti-cancer, inhibition, histone deacetylase, Zingerone

Keywords: anti-cancer, inhibition, histone deacetylase, Zingerone

Evaluation of genetic variant rs10789117 of ANGPTL3 gene in individuals with cardiovascular disease undergoing angiography compared with the healthy individuals in an Iranian population

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Introduction: Variants at the ANGPTL3 locus have been reported to be associated with cardiovascular risk. The aim of this study was to determine the association between a single nucleotide polymorphism (SNP) of the ANGPTL3 gene and the presence of a coronary artery occlusion of >50% in the Iranian population.

Method: In this study, 184 patients underwent angiography and 317 healthy individuals were evaluated for rs10789117 polymorphism of the ANGPTL3 gene using Tetra-ARMs PCR. The patients who underwent angiography were categorized into two groups: 134 patients who previously experienced coronary stent implanting at least one month previously with coronary occlusion of ≥50% that again have an angiography indication (Angio+), 54 patients who had an angiography indication for the first time and coronary occlusion was <50% (Angio-). Also, the patients who previously experienced coronary stent were categorized into two groups as follow: 1) in-stent restenosis (ISR); in-stent stenosis >50% (N=42), 2) non-in-stent restenosis (NISR); patient with a patent stent (N=92).

Result: Based on the findings, the basic characteristics of our study population were the difference between individuals undergoing angiography and not. The CC genotype of rs10789117 at the ANGPTL3 gene locus was directly associated with a positive angiogram. Also, individuals with the C allele are more likely to be in the Angio- group compared to the healthy group. In contrast, there was not significant difference in genotypes of ANGPTL3 between non-ISR and ISR groups.

Conclusion: The results of this study indicate that the rs10789117 polymorphism at the ANGPTL3 gene locus is associated with an increased risk for the presence of a coronary occlusion of >50%.

Keywords: Atherosclerosis, Cardiovascular diseases (CVD), Angiopoietin-Like3 (ANGPTL3), Angiography

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Altered Triglyceride glucose index and fasted serum triglyceride high-density lipoprotein cholesterol ratio predict the incidence of cardiovascular disease in the Mashhad cohort study

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Introduction: The Triglyceride glucose (TyG) index and TG/HDL-C are two important risk markers to evaluate the insulin resistance and cardiovascular diseases. To assess the association between TG/HDL-C and TyG index and cardiovascular diseases.

Method: The MASHAD cohort study started in 2010 and has been continued until 2020. During 6 year follow up of 9704 participants, 235 events including 118 acute coronary syndrome (ACS), 83 chronic coronary syndrome (CCS), 27 MI and 27 cardiac deaths were confirmed. SPSS software (version 21, Chicago, IL, USA) was used for statistical analysis and figures were drawn by Graph Pad Prism 6 software.

Results: The prevalence of ACS and cardiac death were higher in the fourth quartile of serum TG/HDL-C (>4.43) and higher prevalence of ACS was considered in subjects classified in the fourth quartile of TyG index (>8.98). A high TyG index was associated with an increased risk of ACS and cardiac death [1.362 (95%CI (1.013-1.831)) and 2.3 (95%CI (1.247-4.241))] respectively; based on Cox regression analysis elevated TyG and TG/HDL-C increased the chance of CVD by [1.634 (95% CI 1.304-2.047) and 1.068 (95% CI 1.031-1.105)], respectively. **Conclusion:** Our results strongly showed that TyG index and TG/HDL-C are independent risk factors for incident CVD, suggesting that TyG index and TG/HDL-C may be as an important unique biomarker for predicting CVD outcomes and progression.

Keywords: Triglyceride glucose index, triglyceride high density lipoprotein cholesterol, cardiovascular disease, cohort, risk marker

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Evaluation of growth inhibition of Staphylococcus aureus by nanobodies loaded on chitosan and alginate

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Page | 374

Introduction: Using nature and natural resources to suit human needs is one of the applications of life sciences. One of these necessities is the fight against infections like Staphylococcus aureus, which causes a variety of disorders. Nanobodies are heavy-chain, non-light-chain antibodies found in camels (single-domain antibodies). Chitosan is a natural polymer that is cost-effective, and alginates are natural polymers that are cost-effective, biocompatible, biodegradable, and non-toxic when used as a carrier. This is done to prevent the reaction between the active substance and the environment and to prevent side effects. The goal of this study was to see how effective nanobodies coated on chitosan and alginate were at stopping Staphylococcus aureus from growing.

Methods: Camels were immunized with Staphylococcus aureus inactivated microbes along with chitosan and alginate as adjuvants. During the manufacturing process, nanobodies are coated with chitosan to prevent undesirable reactions between the active material and the environment. After loading confirmation, the growth inhibition of nanobodies against Staphylococcus aureus was evaluated using the microassay method using an ELISA reader. Comparison of bacterial growth with control group was plotted using Excel software after reading the light absorption intensity at 490 and 630 nm for 24 hours at two-hour intervals.

Results: For bacterial samples, the correct development of bacteria in the curve was displayed as sigmoid. Furthermore, the graph's linearity for bacterial samples containing nanobodies implies that bacterial growth is slowed. For samples containing chitosan-loaded nanobodies, a more linear graph appeared than for samples containing alginate-loaded nanobodies.

Conclusion: Chitosan-loaded nanobodies exhibited a stronger reaction than alginate-loaded nanobodies in preventing bacterial growth, according to the findings.

Keywords: Nanobodies, Staphylococcus aureus, Chitosan, Alginate, Growth inhibition

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Evaluation of neurobiochemical changes due to acute and chronic stress on hippocampal oxidative stress following global cerebral ischemia

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Introduction: In the present study, the effect of biochemical changes caused by acute and chronic stress, oxidative stress criteria and the effect of these factors on global stroke were investigated.

Methods: Rats were divided into six groups and each group was tested in the following order. The first group (control group) was rats that were not subjected to any stress and did not induce ischemia and only an incision was made under their neck and sutured. In the second group (group I), global stroke was induced in rats. In the third group (SSA group), rats suffered from acute stress and then sham surgery was performed. In the fourth group (SSC group), rats suffered from chronic stress after sham surgery. In the fifth group (ISA group), rats were subjected to acute stress and were subsequently induced by global stroke. In the sixth group (ISC group) rats were subjected to chronic stress and then induced global stroke. Superoxide dismutase (SOD) and malondialdehyde (MDA) were measured in cortical and hippocampal tissues, and serum cortisol levels were also measured.

Results: Acute and chronic stress followed by stroke increased the concentration. Malondialdehyde enters the hippocampal tissue. But there was no significant difference in cortex and thiol groups in cortex and hippocampus and plasma cortisol concentration were not significantly different.

Conclusion: The results of this study showed that acute and chronic stress with the effect of biochemical factors cause oxidative stress in the hippocampus and subsequently cause global stroke.

Keywords: Stress, oxidative stress, hippocampus, global stroke

A-10-1322-1

Investigating of the predictive effect of biochemical markers in myocardial infarction in the induced animal model

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Page | 376

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Introduction: Cardiovascular disease is the leading cause of morbidity and mortality worldwide. Research in this field is especially important in finding ways to prevent it. One way is to use the blood biochemical factors associated with these diseases. The use of animal models allows for extensive research and greatly enhances our knowledge, so in this study, we intend to investigate the predictive effect of biochemical markers in myocardial infarction in induced rats.

Method: In the present study, 20 Wistar rats in two groups of 10 (myocardial infarction and healthy) were studied. The rats were first anesthetized with ketamine and xylazine, and then their blood was collected through a capillary tube through the sinus membrane of the eye for analysis. Next, we dissolved the isoproterenol drug in injected distilled water and injected it subcutaneously into rats for two consecutive days. 24 hours after the last injection, measurements of troponin and CK-MB confirmed the stroke. Finally, biochemical factors were measured with special kits using an autoanalyzer.

Result: According to our findings in this study, the mean serum level of SGPT was significantly reduced in the group of rats with AMI. in contrast, the mean cholesterol in the control group was significantly lower than in the patient group. Also, serum levels of bilirubin direct, bilirubin total, uric acid, and creatinine showed a significant difference in statistical analysis between the two groups ($P<0.05$).

Conclusion: The results of the statistical analysis demonstrated that some biochemical factors such as cholesterol can be recognized as a predictor of AMI.

Keywords: Cardiovascular disease (CVD), Myocardial infarction (MI), Biochemical markers

A-10-1321-1

Investigating the rs6983267 Polymorphism of LncRNA CCAT2 Gene and Susceptibility to Recurrent Spontaneous Miscarriage in Azeri population of Iran

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Introduction: Abortion has been described as termination of pregnancy prior to 20 weeks from the last menstrual period. Recurrent spontaneous abortion as one of the most important complications of pregnancy in the world is classically defined as three or more consecutive miscarriages. LncRNA CCAT2 (long noncoding RNA Colon cancer-associated transcript 2) transcript has been recently showed to be correlated with susceptibility to multiple cancers, besides decreased susceptibility of recurrent miscarriage. This study aimed to evaluate the polymorphism of rs6983267 of this gene in the recurrent spontaneous miscarriage in Azeri population of Iran. **Methods:** Genomic DNA was extracted from peripheral blood of 186 women with recurrent spontaneous abortions and 200 controls having no fertility problem. Then, the genotype of rs6983267 of lncRNA CCAT2 gene was determined by TETRA-ARMS-PCR method. Statistical analysis was performed with SPSS Version 11.0 statistic software package and the strength of each association was evaluated via 95% confidence intervals (CIs) and odds ratios (ORs).

Results: The results showed that GT genotype of rs6983267 of LncRNA CCAT2 gene is significantly associated with susceptibility to recurrent miscarriage. (GT vs. GG/TT: adjusted OR = 1.776; 95% CI = 1.181–2.671; p = 0.006; GG vs. GT/TT: adjusted OR = 0.515; 95% CI = 0.326–0.815; p = 0.004). Due to the fact that the T allele is mutant, the results showed that the TT genotype with two undesirable alleles showed a lower risk of recurrent miscarriage than the GT and GG genotypes (adjusted OR = 0.930; 95% CI = 0.536–1.61; P=0.798).

Conclusion: In conclusion, the data obtained in this study indicated that while the GT genotype of rs6983267 of LncRNA CCAT2 gene is significantly associated with susceptibility to recurrent abortions, the G allele might contribute to a decreased risk of recurrent miscarriage among Iranian Azeri women.

Keywords: Recurrent spontaneous miscarriage, rs6983267 polymorphism, Long non-coding RNAs, CCAT2 gene

A-10-1323-1

Evaluation of the effect of chrysin nanocrystal on liver and kidney damage induced by high dose of chlorpyrifos

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Page | 378

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Introduction: Chrysin is one of the important natural flavonoids with antioxidant and anti-inflammatory activity. The aim of this study was to assess the protective effects of chrysin nanocrystal (CHN) on biochemical indexes in the liver and kidney damage of male Wistar rats exposed to high doses of chlorpyrifos (CPF).

Methods: We induced sub-acute toxicity in rats using CPF (30 mg/kg/day, orally) and administrated CH at 5,10 mg/kg/day for 15 days.

Results: In this study, CPF increased the liver enzyme activities, creatinine, and urea compared with the control group ($p < 0.05$), and co-treated CHN with CPF reduced them compared with the non-treated CPF group ($p < 0.05$). A significant reduction in the liver GSH concentration with a significant elevation in the concentrations of MDA of the CPF group was observed compared with the control group ($p < 0.05$). However, CHN could reverse them nearly to the control group ($p < 0.05$).

Conclusion: These results suggest that CH attenuates hepatic enzymes and histopathological alterations induced by CPF via modulating oxidative stress and inflammatory indices in rats.

Keywords: Keywords: chrysin, chrysin nanocrystal, chlorpyrifos, sub-acute, kidney, liver, rat

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Directed Evolution of Cholesterol Oxidase with Improved Thermostability Using Error-Prone PCR

Cholesterol oxidase is industrially important as it is frequently used as a biosensor in food and agriculture industries and measurement of cholesterol. Although, most natural enzymes show low thermostability, which limits their application. Here, we obtained an improved variant of Chromobacterium sp. DS1 cholesterol oxidase (ChOS) with enhanced thermostability by random mutant library applying two forms of error-prone PCR (serial dilution and single step). Wild-type ChOS indicated an optimal temperature and pH of 70ºC and pH 7.5, respectively. The best mutant ChOS-M acquired three amino acid substitutions (S112T, I240V and A500S) and enhanced thermostability (at 50°C for 5 hours) by 30%. The optimum temperature and pH in the mutant were not changed. In comparison to wild type, circular dichroism disclosed no significant secondary structural alterations in mutants. These findings show that error-prone PCR is an effective method for enhancing enzyme characteristics and offers a platform for the practical use of ChOS as a thermal-resistance enzyme in industrial fields and clinical diagnosis.

Keywords: error-prone PCR, thermostability, cholesterol oxidase

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Subcloning and protein expression of caspase-9 double mutant D315A/D330A in E. coli

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Introduction: Caspases are a family of cysteine proteases necessary for apoptosis and the inflammatory response. Many apoptotic responses are initiated by activation of the apical caspases like caspase-9. Cleavage of procaspase-9 is required to modify its structure. Cleavage of caspase-9 at two sites of aspartic acid 315 and 330 makes it active along the IBM motif exposed and can be possibly inhibited by IAP family proteins. Here, caspase-9 mutant D315A/D330A was subcloned from eukaryotic vector to prokaryotic vector, expressed in E. coli and purified, and then compared with the native caspase-9.

Methods: Reverse and forward primers were designed and synthesized for caspase-9. pcDNA harboring caspase-9 double mutant D315A/D330A was used as PCR temple. The PCR product was cleaned, double digested by restriction enzyme and then ligated into the pET-28a (+) vector. After validation by sequencing, it was transformed to the E. coli BL21, and its protein expression was investigated in various concentrations of inducers (IPTG and lactose), different temperatures, and time conditions. Expression analysis was monitored by SDS-PAGE.

Results: The expression vector, pET28a-Caspase9 mutant D315A/D330A, was transformed into E. coli BL21(DE3) strain. To optimize the expression level of caspase-9 mutant, 2xYT medium was used with the different conditions. According to SDS-PAGE analysis, caspase-9 mutant was successfully expressed under the optimized condition (0.3 mM IPTG, OD600= 0.8 at 30 °C for 3 h and a post-induction time at 22 °C overnight).

Conclusion: The pET28a-Caspase9 mutant D315A/D330A was successfully expressed in the E. coli BL21 in the optimized condition in a relatively good amount as soluble form and then purified. A significant difference in activity was detected between mutant and native proteins.

Keywords: Caspase-9, Mutant, D315/D330, E. coli.

17th National Congress of Biochemistry & 8th International Congress of Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

Page | 381

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Production of citric acid from the waste paper by Aspergillus niger

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Introduction: For nearly a century, Aspergillus niger has been the principal commercial source of citric acid in fermentation methods. Citric acid ($C_6H_8O_7.H_2O$), also known as 2-hydroxy-propane-1,2,3-tricarboxylic acid, is a weak organic acid which has widespread application in industry. In 2006, global citric acid production was 1.4 million tons, with demand and consumption increasing by 3.5–4.0 percent per year. Even though many synthetic routes employing various starting materials have been described, fermentation has remained unsurpassed by chemical methods for large-scale production, because the final product is worth less than the substrates. Therefore, many studies tried to introduce the new economically efficient carbon sources in citric acid production.

Method: In this study, A. niger was isolated and cultured on the wastes of used paper as a culture medium. For this purpose, paper waste extract was prepared by mixing 1 kg of paper waste pieces with 1 L of distilled water and then filtered. The A. niger was cultured at different temperatures (25, 35, and 45 °C) and pH (3.5, 5, and 7.5) for 1 week with shaking at 200 r.p.m. under ambient light. Then, the ultrasonic extraction was performed and the culture mediums were harvested by filtration of the mycelia. Citric acid was extracted using the calcium chloride method in different condition.

Results: The production of citric acid by A. niger in different pH and temperatures were compared with each other. The most content of acid citric production occurred in pH 5.0 and 25 °C which resulted to 109.5 g/l acid citric production. Neutralizing the acidic pH, which was happened during A. niger growth, caused more efficient production.

Conclusion: This study focuses on optimum condition to citric acid production, which maximizes the utilization of industrial waste and develops a more efficient and environmentally-friendly manufacturing process.

Keywords: Aspergillus niger - Citric acid - waste paper - environmentally friendly

A-10-1273-1

Evaluation of the association between hepatocellular carcinoma and hepatitis C virus by using Bioinformatics approach

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Introduction: Hepatocellular carcinoma (HCC) is one of the most common cancers throughout the world; one of the leading causes of HCC is the hepatitis C virus (HCV). The genetic association between HCC and HCV is assessed in this work.

Methods: Genes identification associated with HCC and HCV was performed based on text mining by using geneclip3 software in the existing literature. Functional enrichment analysis was performed using Enrichr software to examine targeted genes' gene ontology and biological pathways. Protein-protein interaction (PPI) networks were constructed using the STRING tool and visualized by Cytoscape and were subjected to cytoHubba plugin of Cytoscape. The top 7 genes (STAT3, TP53, JUN, EP300, PIK3CA, STAT1, and SRC) were chosen. Finally, the hub gene expression validation was performed in the UALCAN database.

Results: 2170 genes for hepatocellular and 469 genes for hepatitis C virus were extracted from studies at the GenCLip3 site, which is a total of 322 genes that are common between the two states. The PPI network was extracted from the STRING and Visualized with the Cytoscape. The 7 Hub genes (TP53, EP300, PIK3CA, STAT1, SRC, JUN, and STAT3) were identified using the Cytohubba plugin. The results of the UALCAN showed that TP53, EP300, PIK3CA, STAT1, and SRC genes were significantly increased in HCC patients compared to healthy controls. The JUN gene significantly decreased expression in people with HCC, and the STAT3 gene did not differ significantly between cancerous and healthy individuals.

Conclusion: Our results indicate vital genes and biological pathways involved in HCC and HCV concurrently.

Keywords: Hepatocellular carcinoma, hepatitis C virus, Hub genes

A-10-1334-1

Studying the combined effects of Thymoquinone and Cisplatin on induction of apoptosis and inhibition of growth in 5637 cell line of bladder cancer

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Page | 383

Introduction: Bladder cancer (BC) is the ninth common cancer worldwide with high mortality annually. About 90% of BC patients suffer from Transitional Cell Carcinoma (TCC). Despite advances in cancer prognosis, TCC still has high recurrence rates of 50–70%. Hence in search for novel chemotherapeutic approaches against BC this study has been conducted to verify the combination effect of cisplatin and thymoquinone on 5637 cells; a cell line of TCC bladder cancer.

Methods: 5637 cells, were treated with increasing concentrations of CDDP (3, 6, 9, 12 µM) and TQ (20, 40, 60, 80 µM) to determine their IC50. Then, cells were treated with combined sub-IC50 concentrations of them. Cell viability and cell cycle distribution changes were evaluated by Alamar blue assay and PI staining, respectively. Real-Time PCR was performed to study the expression of apoptosis related genes (Bcl-2, BAX, p53) upon coadministration of CDDP and TQ. Beta-actin transcripts were considered as the internal control.

Results: the cell viability of combinatorial treated cells was significantly decreased compared to CDDP or TQ treated cells. Furthermore, flowcytometric analaysis indicates accumulation of 5637 cells in the sub-G1 phase of the cell cycle upon combinational treatment of CDDP and TQ. RT-qPCR results exhibited that in combinatorial treated cells, the expression level of P53 and BAX was increased, while a reduction was occured in Bcl-2 expression level ($p \geq 0.05$).

Conclusion: present results showed that TQ significantly increased the toxicity of CDDP in 5637 cells. Therefore, the future possible clinical impact of our study could be combinatorial use of CDDP and TQ as a novel and more effective approach for TCC bladder cancer.

Keywords: bladder cancer, cisplatin, thymoquinone, Bcl-2, BAX, p53

17th National Congress of Biochemistry & 8th International Congress of Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

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Assessment of sperm function tests in high-fat and AGE models

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Introduction: The advanced glycation end product (AGE) is produced in food and our body. Accumulation of AGE in our body could significantly effect on health of individuals. AGE bind to RAGE (receptor of advanced glycation end product) that is associated with inflammation factors. AGE in hyperglycemia and diabetic individuals could induce stress oxidative pathway. Therefore, we aimed to compare the effect of high-fat diet and AGE diet on sperm function in diabetic model mice C57BL.

Methods: In this study, twenty C57bL male mice fed with high-fat (HF) diet and AGE diet were divided into control, 45% HF, 60% HF, 45% AGE and 60% AGE diet groups. After 28 weeks, all animals were sacrificed, and body weight was assessed. Insulin concentration as well as insulin resistance were assessed by ELISA kit and Homeostatic model (HOMA-IR). In addition, sperm DNA fragmentation, and lipid peroxidation were evaluated by acridine orange, BODIPY probe, respectively. Study variations were compared within groups by one-way analysis of variance (ANOVA). A p-value less than 0.05 was considered statistically significant.

Result: The level of insulin concentration and HOMA-IR in 45% HF, 60%HF, 45% AGE and 60%AGE significantly higher than in the control group (mean and SD in groups 1.3± 0.04, 0.8 ± 0.09, 1.59 ± 0.07, 3.90 ± 0.19, respectively) (P<0.05). Sperm DNA fragmentation in the 45% HF group was non significantly higher compared to the control group (P=0.07). In our study, sperm lipid peroxidation remarkably increased in 45% HF, 60%HF, 45% AGE and 60%AGE compared to the control group (P<0.05).

Conclusion: The result of the current study show that male mice fed with high fat and AGEs diets show increased level of insulin and HOMO-IR as well as increased sperm DNA fragmentation and lipid peroxidation. Therefore, diets contain high fat and AGE could decrease the quality of sperm functions.

Keywords: Advanced glycation end product, male infertility, DNA fragmentation, lipid peroxidation

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Anticancer activity of curcumin and Bilhar extract loaded on nanoliposomes against oral cancer cells OCC-02

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Page | 385

Introduction: In spite of promising advances made in the field of cancer treatment, cancer still is one of the leading causes of death worldwide. The emergence of drug-resistant cancers, and the side effects of current therapies, call attention to finding effective drugs. Curcumin is one of the natural drugs that has recently shown promising activity against cancer cells; however, its efficiency is limited by low stability, insufficient bioavailability, poor solubility, and poor permeability. This study aimed to develop a nanoliposomes-based system for the co-delivery of curcumin and Bilhar (Dorema aucheri) extract.

Methods: The nanocompounds were synthesized using the lipid thin-film hydration method and characterized by HPLC, TEM, and DLS. The cytotoxicity and apoptotic activity of these compounds against the Oral Cancer Cell line (OCC-02) was evaluated via MTT assay and flow cytometry, respectively. Furthermore, the expression Epidermal Growth Factor Receptor (EGFR) gene in the cells exposed to the compounds was assessed using real-time PCR.

Results: Based on the results, the drug/extract-loaded liposomes were at 91±10 nm in size with a loading efficiency of 93% All curcumin, extract, and curcumin-extract showed dose-dependent toxicity against cancer cells; yet, the extract (IC50: 62 µg/ml) and curcumin-extract (IC50: 48 µg/ml) activities were much more than curcumin (IC50: 234 µg/ml). Also, curcumin/extract-liposomes showed a dose and time-dependent cytotoxicity. The IC50 of liposomes-curcumin-extract decreased by 150 µg/ml after 72 h, indicating a sustainable drug release and activity. Likewise, this compound induced the most apoptosis (95%) in cancerous cells and inhibited the EGFR gene expression in the cells to 81±3%.

Conclusion: These findings demonstrated the effectiveness of the Bilhar extract on oral cancer cells. Also, it revealed that the extract's activity could be enhanced and sustainable when it was co-delivered with curcumin by nanoliposomes.

Keywords: cancer, EGFR, curcumin, nanoliposomes, Dorema aucheri

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Molecular mechanism and cytotoxicity of allicin and all-trans retinoic acid against CD44+ versus CD117+ melanoma cells

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Page | 386

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Introduction: All-trans retinoic acid (ATRA) a differentiating agent inhibits cancer cell growth during the cell cycle. Despite its potent antitumor properties, some melanoma cells are resistant to ATRA. Here, we hypothesized that allicin can sensitize malignant melanoma cells to ATRA treatment.

Methods: After isolating The CD44+ and CD117+ cells from A375 melanoma cells using the magnetic-activated cell sorting (MACS), the potential anticancer effects of ATRA, allicin and allicin/ATRA were examined using MTT assay. In addition, flow cytometry was used to detect cell cycle arrest. The efficacy of the treatments in controlling cancer cell proliferation was assessed by quantitative real-time polymerase chain reaction (RT-PCR).

Results: Here, we demonstrated that CD44+ melanoma cells were more resistant to allicin and ATRA than CD117+ cells. Importantly, we observed that allicin sensitized melanoma cells to ATRA-induced cell death. The combination treatment with allicin and ATRA significantly reduced the IC50 value obtained for ATRA alone in CD44+ melanoma cells. Allicin treatment resulted in significant increases in the percentage of cells at the G2/M and G0/G1 phases in the CD44+ and CD117+ cells, respectively. The combination treatment caused the inhibition of CD44+ and CD117+ cells at the S phases compared to ATRA alone. Allicin, ATRA, and allicin/ATRA increased the expression of cyclin D1 mRNA in both CD44+ and CD117+ cells. Allicin in combination with ATRA increased the mRNA level of RARβ in CD117+ cells. Allicin alone reduced MMP-9 expression in CD44+ and CD117+ cells. In contrast, ATRA and the combination treatment significantly increased MMP-9 expression in CD44+ cells.

Conclusion: Based on our results, allicin reinforces the ATRA-mediated inhibitory effects on CD44+ and CD117+ cells and may provide a new approach for the treatment of malignant melanoma.

Keywords: All-trans retinoic acid, Allicin, Melanoma, CD44, CD117

A-10-1335-1

N-arachidonoylethnolamide inhibit AGS gastric cancer cell growth under inflammatory condition by regulating histone acetylation via cannabinoid receptor 1 and vanilloid receptors type1

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Introduction: Histone acetylation has fundamental role in gastric cancer tumorigenesis and metastasis. Endocannabinoids a class of endogenous compounds that affect the normal functions of the gastrointestinal tract through cannabinoid receptors; cannabinoid receptor 1(CB1) and vanilloid receptors type1 (VNLR1), have recently been considered as therapeutic agents in cancers therapy. The present study was aimed to determine whether endocannabinoid anandamide (AEA) has a potential effect on the histone H3 acetylation in lipopolysaccharide stimulated AGS cancer cell line via cannabinoid receptor 1 (CB1) or vanilloid receptors type1 (VNLR1).

Methods: The IC50 of AEA was determined in AGS gastric cancer cells using MTT assay. AGS cells were treated with 10 μg/ml LPS for 4 h to induce inflammation LPS stimulated AGS cells were treated with 10 and 15 μM AEA for 24 h under inflammatory and non-inflammatory conditions in the presence or absence of CB1 (AM-251) and VNR1 receptors (AMG-9810) antagonists. Histone H3 acetylation was evaluated by western blot analysis.

Results: Treatment of AGS cells with AEA, in a dose-dependent manner, inhibited the growth of AGS cancer cells. The increased level of histone H3 acetylation in LPS-treated AGS cells was attenuate following AEA treatment. Effect of AEA on regulation of histone H3 acetylation in LPS stimulated AGS cells was mainly modulated by CB1.

Conclusion: Based on the inhibitory effects of AEA on AGS cancer cell growth and histon acetylation in inflammatory conditions, it is possible that some of the therapeutic effects of AEA may be related to its effect on epigenetic mechanisms in tumor cells.

Keywords: endocannabinoid, anandamide, gastric cancer, inflammation, histone acetylation, cannabinoid receptors

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Exosomes: a novel biomarker in the diagnosis of prostate cancer

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Statistics published by the International Agency for Research on Cancer show that prostate cancer is the second most common cancer in men in the world (with an incidence rate of 29.3 and a death rate of 7.6 per 100,000 people). Hence, early detection of the disease helps to treat and control the prevalence. Exosomes are considered cell vesicles, which are released from MVB cells. They are also involved in pathological processes such as cancer. Exosomes have the potential to transfer various compounds to cells due to their small size, ability to cross membranes, and protection against the breakdown of proteins and RNAs enclosed in them. Exosomes derived from prostate cancer cells contribute to cancer chemoresistance. Furthermore, exosomes can be detected and isolated from various body fluids for the diagnosis of prostate cancer. Noninvasive and simple diagnostic assays are required for prostate cancer diagnosis. This study aimed to investigate the role of exosomes in the early diagnosis of prostate cancer due to their presence in urine.

Keywords: Exosomes, prostate cancer, diagnosis

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Evaluation of expression of the gene encoding Carnitine transporter OCTN2 (SLC22A5) in human breast cancer

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Page | 389

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Introduction: Fatty acid oxidation (FAO), a major energy production pathway, converts fatty acid to Acetyl-CoA in the mitochondria and supports growth and survival in cancer cell. carnitine, as co-factor, is essential for carry fatty acid to into the mitochondria. OCTN2 (SLC22A5) is a carnitine transporter that accumulates carnitine into the cell. Therefore, OCTN2 is a critical regulator in fatty acid β-oxidation and cell proliferation. The objective of this study was to evaluate OCTN2 expression, and its correlation with clinicopathological variables in breast cancer. **Methods:** In this study, 55 pairs of fresh samples of BC and adjacent noncancerous tissue were used to analyze OCTN2, using quantitative real-time polymerase chain reaction and immunohistochemistry (IHC) staining. The expression of other clinicopathological variables was also examined using IHC technique.

Results: Our results show that the relative expression of OCTN2 messenger RNA was significantly higher in BC tissues compared with the adjacent normal tissue. This upregulation was negatively correlated with Ki-67 and Progesterone Receptor (PR), and positively correlated with the tumor size.

Conclusion: Our results indicated that the expression of OCTN2 may be considered as a prognostic indicator. However, further studies are needed to confirm the significance of these findings.

Keywords: OCTN2, breast cancer, Fatty acid oxidation

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Differential expression of chemerin and chemerin receptor; ChemR23/CMKLR1 during the differentiation of human Wharton's jelly-derived mesenchymal stem cells into insulin-producing cells

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Introduction: Chemerin is an adipokine that regulates insulin secretion in β-cells by activating ChemR23/CMKLR1 receptor. Limited data are available about the expression pattern of chemerin and Chem23 in beta cells derived from differentiation of stem cells. The aim of the present study was to determine the alternative expression of chemerin and its receptor during the differentiation of Wharton's jelly-derived mesenchymal stem cells (MSCs) into insulin-producing cells.

Methods: MSCs were isolated from the human umbilical cord and differentiated into insulin-producing cells using 2-mercaptoethanol, b-FGF, and nicotineamide using a 14-days differentiation protocol. On days 1, 6, and 12 of differentiation, the expression of the chemerin and ChemR23 were determined using quantitative real-time polymerase chain reaction (RT-PCR).

Results: Expression of Chemerin was down regulated in a time dependent manner during the insulin cell production with the lowest expression level at day 12 of differentiation. ChemR23 expression showed no alteration on day 6 of differentiation, while it was increased on day 12 of differentiation compared to control cells.

Conclusion: Differential expression of chemerin and ChemR23 during the maturation of insulin-producing cells suggests that chemerin pathway may has an essential role on production of insulin prudicing cells in invitro condition.

Keywords: Warton's jelly mesenchymal stem cells, Insulin producing cells, Differentiation, Chemerin, ChemR23

A decrease in hippocampal apoptotic markers following treadmill exercise is correlated with reversal of β2-adrenergic receptor downregulation in the hippocampus of aged male rats

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Introduction: Hippocampus is one of the most susceptible brain areas involved in pathological alterations related to aging. Exercise is thought to delay the aging process through improving the function of the multiple aging mechanisms. The aim of this study was to investigate the effects of treadmill exercise on β-adrenergic receptors (β1 and β2) and proteins involved in apoptosis in the hippocampus of aged male rats.

Methods: The rats were randomly divided into: (1) control (young rats); (2) aged rats; (3) aged rats with treadmill exercise for 4 weeks groups (n = 8 each). Apoptotic signaling was followed via Bax, Bcl2, and P53 expression. Adrenergic- and apoptotic-related proteins were measured using Western blotting.

Results: Results showed that the expression of β2-, but not β1-, adrenergic receptors was markedly downregulated in aging hippocampus. Furthermore, aging was associated with increased apoptotic signaling including P53 and Bax/Bcl2 ratio in the hippocampus. In contrast, treadmill exercise rescued the abnormal expression of β2-adrenergic receptors in the hippocampus of the aged rats accompanied by reduced aging-induced neuronal hippocampal apoptosis.

Conclusions: Overall, this study suggests that exercise exerts its beneficial effects in aging brain at least in part via increasing β2 adrenergic transmission, leading to suppression of apoptosis in the hippocampus. Since, hippocampal apoptosis is assumed to play an essential function in cognitive deficits, thus, pharmacological treatments reducing apoptosis via the use of selective β2-adrenergic receptor agonists might improve cognitive deficits in aging.

Keywords: Aging, Apoptosis, Hippocampus, β-adrenergic receptors, rat

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Investigating the formation of diabetes type 1 through bioinformatics analyses

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Introduction: Diabetes mellitus is divided into three categories: type 1, type 2, and various causes. Type 1 diabetes is an autoimmune disease characterized by a decrease in insulin and the destruction of insulin-secreting cells in the pancreas. The genetic factors such as expression and translation of some genes play a crucial role in developing of this autoimmune disease. The interaction of genes in the immune system, which attacks pancreatic beta cells, is particularly important in preventing this disease. Understanding the expression pathways of genes associated with diabetes type1 and their interactions can prevent the destruction of pancreatic beta cells. This study aimed to determine the effect of insulin on the function of the Cytotoxic T-Lymphocyte Associated Protein 4 (CTLA_4) gene and Major Histocompatibility Complex, Class II, DQ Beta 1 (HLA_DQB1) gene.

Methods: The GeneCards database was used to identify the encoded proteins. The Ensembl database was used to determine the expressed genes in different body parts, especially in adipose tissue, pancreas, duodenum, adrenal glands, and skin. The GeneMANIA database was used to investigate the interaction between genes and signaling identification.

Results: The results of gene evaluations showed that Insulin (INS) is expressed in different tissues, but its synthesized protein functions only in the pancreas, and this protein activates the HLA_DQB1 gene. With positive feedback, the HLA_DQB1 gene also activates the CTLA4 gene. The CTLA4 gene inhibits T lymphocytes; otherwise, the immune system attacks insulin-producing cells.

Conclusion: It is concluded that the expression of each gene, HLA_DQB1 or INS, and their positive feedback exacerbates diabetes type 1. Downregulation of CTLA_4 gene causes the immune system to attack the pancreas.

Keywords: Gene expression, Pancreas, insulin, HLA-DQB1, INS, CTLA-4

A-10-1324-1

Antibacterial activity of PCL/Gelatin nanofiber mats blended with Green synthesized silver nanoparticles

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Introduction: Today, wound dressings made from nanofibers have attracted the attention of many researchers. The use of silver nanoparticles as antibacterial agents in wound dressings has also been developed. In this study, silver nanoparticles were incorporated into nanofiber texture to create a mat with antibacterial properties that could be used as a wound dressing.

Methods: The silver nanoparticles used in this study were regenerated and fabricated using the green method. Also, PLA and Gelatin nanofibers were fabricated using the solution blow spinning method. Finally, all these structures were analyzed using characterization methods. The antibacterial properties of these textiles were evaluated using non-growth methods.

Results: After studies on silver nanoparticles, they had a diameter of about 20 nm. Gelatin nanofibers had a diameter of about 300 to 700 nm and PLA nanofibers had a diameter of about 200 to 600 nm. It was also found that fibers containing silver nanoparticles showed more antibacterial properties than fibers without silver nanoparticles. However, due to the hydrophilicity of gelatin and the fact that the secretions in the wound environment cause it to disappear, it must have a protective coating such as PLA next to it, which strengthens its structure.

Conclusion: Considering that gelatin and PLA are both biopolymers and show good biocompatibility and also the reduction of toxicity of silver nanoparticles due to their coating by plant metabolites in the green synthesis method has been proven, it can be expected with The use of these nanoparticles in the nanofiber structures of the aforementioned polymers, to create a suitable tissue for use in antibacterial wound dressings to replace traditional wound healing methods

Keywords: Gelatin, PLA, Green synthesis, Silver nanoparticles, Antibacterial

Evaluation of DNA Interaction Probability and Cytotoxicity of Phenyl-tetrazolyl-thio-alkyl-phthalimide Derivatives

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Introduction: In the research line to design cytotoxic compounds, three derivatives of phenyl-tetrazolyl-thio-alkyl-phthalimide, PTP(n=4,5,6), were considered. These structures possess rings of phenyl-tetrazole and phthalimide in two terminals of their structure which are linked through sulfur atoms attached to a flexible carbon linker including 4 to 6 atoms. Electron distribution between N atom and 2 carbonyl groups in phthalimide causes the structure to be more planar. Therefore, expected intercalation interaction and interaction with DNA grooves of these designed compounds and DNA are increased. General structure of phenyl-tetrazolyl-thio-alkyl-phthalimide derivatives, PTP(n=4,5,6).

Method: MTT-based cytotoxicity was evaluated against HepG2 and MCF7 as two cancer cell lines and HEK293 as the non-cancerous cell line, for PTP derivatives in serial concentrations, 5×10^{-3} to 5×10^{-9} mM compared to two control drugs, including Adriamycin (ADR) and Mitoxantrone (MXN). Meanwhile, the probability of interaction with three types of DNA extracted from each one of the cell lines, was evaluated for PTP derivatives as the possible mechanism of their cytotoxicity based on two spectroscopic methods, including ultraviolet absorption and fluorescence emission using the titration technique.

Result: Cytotoxicity potential of PTP derivatives against HepG2, MCF7, and HEK293 were obtained from 1- 25%, 0-32%, and 0-9%, respectively, which were comparable with positive controls in some cases. Cytotoxicity of two derivatives, PTP5 and PTP6, were obtained considerably selective against the studied cancer cell lines compared to the non-cancerous cell line.

Conclusion: The ultraviolet absorption studies with three types of DNA showed hypochromic for PTP4 and PTP5 derivatives and hyperchromic for PTP6 as the major behaviour illustrating stabilizing interaction through intercalation and non-stabilizing interactions through groove binding as the most possible interaction type, respectively. Fluorescence emission for PTP derivatives with three DNA sample showed decrement change except for PTP5 with DNA-HEK293. Hence, the obtained results confirmed probable non-covalent DNA interaction for the PTP derivatives.

Keywords: Keywords: absorption ،cytotoxicity ،DNA ،emission ،fluorescence ،MTT ،phthalimide ، phenyl-tetrazolyl ،titration ،ultraviolet

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Autophagy Flux Correlates with Upregulation of AKT-1 in RAS Mutated Colon Cancer Cells

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Introduction: The AKT/PKB (protein kinase B) kinase is the main regulator of autophagy in mammalian cells, which consists of three isoforms, including AKT-1, AKT-2, and AKT-3. Rat sarcoma viral oncogene homolog (RAS), known as the most frequently mutated oncogene in colorectal cancers, is one of the major activators of AKT signaling. However, the relationship between AKT isoforms expression and autophagy level in RAS-driven cancer cells has not been fully investigated.

Method: In this experimental in vitro study, RAS mutated colon cancer cell lines (HCT116, SW480, and LS180) and HT29 cells, which are the wild type of RAS, were cultured and real-time polymerase chain reaction (RT-PCR) was utilized to determine the mRNA level of AKT-1, AKT-2, and autophagy markers, including microtubule-associated protein 1 light chain-3B (LC3B) and p62/sequestosome-1 (p62). In addition, Western blotting was performed to assess the protein expression of p62 and LC3B lipidation.

Results: We found that RAS mutated colon cancer cells up-regulate basal autophagy. Moreover, highly expressed AKT-1 was observed in RAS mutated colon cancer cells. However, no significant differences were found in AKT-2 expression between RASdriven cells and HT29 cells.

Conclusion: Our obtained data suggested that RAS-driven colon cancer cells regulated the autophagy machinery, possibly, through the upregulation of AKT-1 isoform.

Keywords: Colorectal neoplasms, RAS Oncogenes, Autophagy, AKT/PKB kinase

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Characterization of trypsin-polyphenol interactions using spectroscopic methods

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Page | 396

Introduction: Caffeic acid and ellagic acid are two kinds of phenolic compounds that are widely found in most plant products. Several pieces of evidence suggested phenolic compounds have diverse biological effects on the mammalian cell systems, including protecting low-density lipoprotein (LDL), antithrombic effects, antiviral and anti-cancer properties. However, it is documented some phenolic compounds have negative effects on the protein structure and function. Therefore, it is necessary to understand the interactions between phenols and proteins. Trypsin is a protease from the S1 family that hydrolyzes the peptide and ester bonds between the carboxyl and amino acids of lysine, arginine, and ornithine. In this paper, the interaction between these phenolic compounds and trypsin is investigated.

Methods: The alteration in trypsin absorbance was investigated by UV–Vis spectroscopy and fluorescence spectrophotometry investigation was done with the RF-5301 Shimadzu spectrophotometer.

Results: UV-Vis spectroscopy results showed that trypsin absorption decreases with the addition of caffeic acid and ellagic acid. The emission spectrum of enzyme decreased by phenolic compounds demonstrates that adding these compounds may cause an apparent decrease in trypsin fluorescence intensity at the concentration-dependent absorption peaks.

Conclusion: The complex formation of the ground state between these two phenolic compounds and trypsin could change the maximum intensity, and it can lead to a lower trypsin molar extinction coefficient. Fluorescence spectroscopy showed trypsin statically quenched in the presence of caffeic acid and ellagic acid concentrations and indicate a decrease of hydrophobicity in the Trp residue and probably more exposition of its aromatic amino acid.

Keywords: Caffeic acid, Ellagic acid, Phenolic compound, UV-Vis spectroscopy

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Study of the interaction behavior between Disperse Blue 65 and Human Serum Albumin by spectroscopy methods

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Page | 397

Introduction: In the current study we investigate the interaction between Disperse Blue65 (DB65) as a synthetic textile dye and Human Serum Albumin (HSA). Human Serum Albumin (HSA) is one of the most common proteins in plasma. It has broad physiological and pharmacological functions, such as regulation of osmotic pressure, and mediates lipid metabolism. DB65 is a synthetic dye that can enter the human body by skin absorption of clothes containing dyes.

Methods: The effects of DB65 on the structure and function of HSA were performed using experimental methods such as ultraviolet–visible and fluorescence spectroscopy.

Results: The UV-Vis spectroscopy results showed that DB65 could bind to HSA and make the DB65-HSA complex. Based on the fluorescence data, in the presence of DB65 a gradual increase in the emission spectra of HSA was seen.

Conclusion: Based on the obtained data, after joining DB65 to the reaction mixture, the amounts of absorbance intensity were increased. The hyperchromic impacts revealed that the protein microenvironment around the aromatic amino acids was changed. Fluorescence spectroscopy results showed that the interaction of DB65 with HSA caused an increase in the fluorescence emission peaks. The increased emission as a result of dye attachment was due to the Trp's shift to less hydrophilic positions, which caused a modification in the conformation and tertiary structure of HAS. In this study, we clarified the molecular interactions and binding affinity between DB165 and HAS.

Keywords: Keywords: Disperse Blue 65 (DB65) ‹textile dye ‹HSA ‹structure ‹spectroscopy methods

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Ferulic acid prevents cyclosporine-induced nephrotoxicity in rats through exerting anti-oxidant and anti-inflammatory effects via activation of Nrf2/HO-1 signaling and suppression of NF-κB/TNF-α axis

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Introduction: Cyclosporine is one of the main immunosuppressive agents used in the treatment of autoimmune diseases or transplantation. Despite the favorable effects, cyclosporine-mediated nephrotoxicity critically restricts the clinical use of the agent. Given this, herein, we aimed to evaluate whether ferulic acid could prevent cyclosporine-mediated nephrotoxicity in rats.

Methods: A total of 32 Wistar rats were chosen to be treated with cyclosporine, ferulic acid, and the combination of both agents for 21 days. To evaluate the nephron-protective mechanism of ferulic acid, the serum levels of biochemical parameters, as well as the tissue levels of several oxidative and anti-oxidative mediators, were examined. The expression and the tissue levels of nuclear factor (NF)-κB, tumor necrosis factor (TNF)-α, heme oxygenase (HO-1), and nuclear factor erythroid 2-related factor 2 (Nrf2) were evaluated using the qRT-PCR and ELISA, respectively.

Results: Our results showed while cyclosporine elevated the serum levels of renal-related markers in the rats, in the presence of ferulic acid, there was a significant reduction in the levels of urea, uric acid, creatinine, and sGOT. Moreover, we found that ferulic acid remarkably prevented cyclosporine-mediated nephrotoxicity by restoring the anti-oxidant system through activating the Nrf2/HO-1 axis. By halting the NF-κB-mediated upregulation of TNF-α, it also seems that ferulic acid prevented lymphocytes infiltration into kidney tissue and consequently suppressed inflammatory responses.

Conclusion: Overall, the results of the present study suggest that due to the anti-oxidant and anti-inflammatory properties of ferulic acid, this agent could be used alongside cyclosporine to reduce its adverse effects on kidney tissue.

Keywords: Cyclosporine, Nephrotoxicity, Ferulic acid

Quercetin exerts an ameliorative effect in the rat model of diclofenac-induced renal injury through mitigation of inflammatory response and modulation of oxidative stress

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Introduction: Diclofenac (DIC) is administrated to treat pain, inflammatory disorders, and dysmenorrhea but kidney problems are the main worries of the agent. The literature has revealed that quercetin (QR) has anti-inflammatory and antioxidant attributes. This study aims to highlight the possible nephroprotective effects of QR on DIC-exposed rats.

Methods: In this study, the animals after exposure to DIC (50 mg/kg, i.p) were administrated to QR (100 mg/kg, p.o). Then, the levels, as well as the activity of several oxidant and anti-oxidant mediators, were evaluated.

Results: Our results showed that DIC treatment was coupled with the elevation in the levels of malondialdehyde (MDA), nitric oxide (NO), and some pro-inflammatory factors such as TNF-α, NF-κB, and IL-1β, suggesting that probably this agent exert its toxicity in the kidney tissue through inducing both oxidative stress and inflammation. Interestingly, QR was successful in restoring the activity of antioxidant compounds such as GSH, GPx, SOD, and CAT in the kidney tissue of DIC-treated rats. Moreover, in the presence of QR, DIC was unable to increase the expression of pro-inflammatory cytokines, suggesting that perhaps QR might have anti-inflammatory properties. In agreement with this, the results of the histopathological evaluation also showed that while DIC increased the lymphocyte infiltration into the kidney tissue, QR reduced the number of lymphocytes in DIC-treated rats.

Conclusion: The results revealed that QR exerted a supportive effect against diclofenac-induced renal injury in male rats through modulation of oxidative stress and mitigation of inflammatory response.

Keywords: diclofenac, oxidative stress, renal injury, quercetin

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Protective Effect of Ellagic Acid on Induced Liver Injury

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Introduction: The application of one of the most important nonsteroidal anti-inflammatory drugs, diclofenac, has been restricted due to its hepatotoxicity. The hepatoprotective effects of ellagic acid against this agent were investigated.

Methods: Wistar rats were treated orally via gavage with diclofenac, either alone or in combination with silymarin (a complex mixture of polyphenolic molecules from Silybum marianum (L.) Gaertn., Asteraceae, as positive control, and ellagic acid. The serum levels as well as the activity of several liver-associated markers, and oxidative and antioxidant compounds were tested. The expression of pro-inflammatory mediators was also studied using the qRT-PCR analysis.

Results: Diclofenac was associated with the elevation in the serum levels of liver-related markers together with the increase in the serum and the hepatic levels of malondialdehyde and protein carbonyl. Moreover, this drug reduced the activity of the antioxidant system in the rats and increased the lymphocyte infiltration into the hepatocytes. **Conclusion:** Ellagic acid protected the hepatocytes from the toxic effects of diclofenac by enhancing the activity of the antioxidant enzymes such as catalase, superoxide dismutase, glutathione peroxidase, and glutathione. Through diminishing the expression of nuclear factor (NF)-κB and tumor necrosis factor (TNF)-α, ellagic acid was also capable of preventing the inflammatory effects on liver cells.

Keywords: diclofenac, oxidative stress, hepatotoxicity, ellagic acid

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Construction of Survivin-conjugated N-terminal fragment of firefly luciferase in pET28a

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Introduction: Apoptosis is a type of programmed cell death which exists naturally in normal cells. Some disrupts in this process cause various diseases including cancer and immune disorders. Inhibitor of apoptosis (IAPs) are a family of proteins that Inhibit caspases activity and suppress apoptosis. Survivin is a small protein from IAPS family that consists of 142-aa. Survivin has a "BIR domin" structure at "N-terminal" and a long "X-helix" at C–terminal. In this study, Survivin gene was linked to N-terminal fragment of firefly luciferase to construct the functional chimeric Survivin-luciferase.

Methods: Primers were designed for Survivin and then subjected to PCR. The PCR product was cleaned and inserted to pET-28a vector harboring N-terminal fragment of firefly luciferase (N-Luc) double-digested with Bamh1 and Hind3. After validation by sequencing, it was transformed to the E. coli BL21 and chimeric Survivin-NLuc protein expression examined in various conditions such as different concentrations of IPTG and/or lactose, different temperatures and times. Expression analysis was determined by SDS-PAGE.

Results: The expression vector, pET28a/Survivin-NLuc, was transformed into E. coli BL21(DE3) strain. To optimize the expression level of Survivin-NLuc, 2xYT medium were used with the different conditions. According to SDS-PAGE analysis, chimeric Survivin-NLuc protein was successfully expressed under the optimized condition, but the best conditions for expression have yet to be found. **Conclusion:** The pET28a/Survivin-NLuc was successfully constructed in pET-28a vector and expressed in the E. coli in a relatively good amount and then purified. Keywords: Survivin; NLuc-domain; Luciferase; E. coli; Cloning.

Keywords: Survivin, NLuc-domain, Luciferase, E. coli, Cloning.

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NOD2 rs5743278 Gene polymorphism and Susceptibility to Pulmonary Tuberculosis in Zahedan, Southeast Iran

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Introduction: Conferring to the World Health Organization (WHO), tuberculosis (TB) is in the top 10 reasons of death worldwide and approximately 10 million cases identified and diagnosed in 2019. Nucleotide-binding oligomerization domain 2 (NOD2) is one of the most studied pathogen recognition receptors (PRRs) that its role is due to the recognition of peptidoglycans in the bacterial cell walls. NOD2 gene polymorphisms might affect the gene expression and may attribute to the infection susceptibility.

Methods: This case-control study was conducted on 152 pulmonary tuberculosis (PTB) patients and 162 healthy participants to determine the possible association between NOD2 gene polymorphisms rs5743278 and susceptibility to PTB. These targeted polymorphisms were analyzed employing PCR-restriction fragment length polymorphism (PCR-RFLP).

Results: Our results showed that the NOD2 rs5743278 polymorphism under dominant/recessive model were related with the increased susceptibility to PTB (P <0.0001; OR =0.054).

Conclusion: we observed that the NOD2 rs5743278 polymorphism could be consider as a relative susceptibility factor to PTB in a sample of Iranian population. Keywords: Pulmonary tuberculosis, NOD2 Gene polymorphism, PCR-RFLP

Keywords: Pulmonary tuberculosis, NOD2 Gene polymorphism, PCR-RFLP

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The role of long non-coding RNAs in polycystic ovary syndrome

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Introduction: Polycystic ovary syndrome (PCOS) has been recognized as an endocrinopathy that influences 5–10% of reproductive-age women. The momentous characteristics of PCOS include chronic anovulation, polycystic ovaries, and hyperandrogenism. The genetic, endocrine, and environmental factors partake in the etiology and development of this syndrome. In recent years, studies have revealed the dysregulated expression of long non-coding RNAs (lncRNAs) in the serum, follicular fluid, and granulosa cells (GCs) of PCOS cases. Thus, the current review will summarize the impact of lncRNAs on PCOS pathophysiology.

Methods: Thirty-nine articles were reviewed by literature review from 2007 to 2020 including PubMed and Google scholar.

Results: Numerous lncRNAs such as PVT1, TUG1, HOTAIR, and HCP5 regulate the function of ovarian GCs in PCOS. Some of these lncRNAs in the role of a competing endogenous RNA sponge microRNAs, thereby effect on multiple signaling pathways, and modulate proliferation and/or apoptosis of GCs. In addition, the abnormal level of some lncRNA including CTBP1-AS, HCG2, and SRA can influence steroidogenesis in PCOS. There is evidence for the relationship between lncRNAs such as GAS5 and SRA and insulin resistance in PCOS.

Conclusion: The aberrant expression of lncRNAs may share in PCOS development through their impact on the proliferation and apoptosis of GCs, hyperandrogenism, and insulin resistance.

Keywords: Polycystic ovary syndrome, long non-coding RNA, Insulin resistance

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Evaluation of the frequency of the BOLA-DRB3.2 gene alleles that cause susceptibility or resistance to mastitis in Iranian Holstein cows

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Page | 404

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Introduction: Mastitis is the most common and economically problematic disease in the dairy cattle breeding industry worldwide. Doubling the Somatic Cell Count (SCC) can result in milk reduction by 0.5 kg. This among other hurdles calls for selective breeding of the cows with lower SCC. This is based on the fact that some gene clusters have a noticeable effect on mastitis. MHC is a cluster of genes that play an important role in immune responses. MHC has three different classes. In cows, MHC identifies as Bovine Leukocyte Antigen (BOLA). It is located on chromosome 23. The second exon of the BOLA-DRB3 gene is part of MHC class 2 in cows and it has a great polymorphism. According to the previous studies, MHC alleles have a crucial impact on resistance/susceptibility to diseases, breeding, and milk production.

Methods: In this study, we investigated the frequency of the BOLA-DRB3.2 gene alleles that cause susceptibility or resistance to mastitis. The polymorphism of the BOLA-DRB3.2 genes was evaluated by the PCR-SBT technique. In this regard, 67 blood samples were obtained from Holstein cows. After DNA extraction, the BOLA-DRB3.2 genes was multiplied by semi-nested PCR, and the products were sequenced.

Results: The results demonstrated that the most common alleles of BOLA-DRB3.2 were *0101, *1501, *1201, *0902, and *1101. Also, *0601, *0801, *1506, *1801, *1802, *20012, *1901, *2709, *3201, *3202, *3401, *3501, *6901 were among the rare ones. According to the results, the frequency of the alleles that cause susceptibility to mastitis was 37.32%. In contrast, the frequency of the alleles that can lead to mastitis resistance was 13.42%. This can explain the high number of mastitis cases in Holstein cows in Iran.

Conclusion: Molecular markers such as MHC alleles should be taken into consideration along with the phenotypic traits during the breeding process.

Keywords: MHC, Mastitis, DRB3.2, Allelic polymorphism, PCR-SBT, Holstein cows

A Dual Synergistic Effect of Titanium and Curcumin Co-Embedded on Extracellular Matrix Hydrogels of Decellularized Bone: Potential Application in Osteoblastic Differentiation of Adipose-Derived Mesenchymal Stem Cells

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Introduction: Bone tissue engineering (BTE) is a prospective method for providing effective scaffolds for the treatment of bone injuries. A novel hydrogel-based composite can be used as a functional biomimetic and biodegradable scaffold that amends osteoblastic differentiation of adipose-derived mesenchymal stem cells (ADMSCs). Curcumin (Cur) and titanium dioxide nanoparticles (nTiO2) improve the surface bioactivity, stability, and mechanical properties of ECM hydrogels.

Methods: In this study, nTiO2 and CUR coembedded extracellular matrix (ECM) hydrogel to fabricate Hy/Ti/Cur composite. In this way, the fresh bovine femur was demineralized and decellularized, then by digestion of these matrices, ECM hydrogel was obtained. Structural characterization including scanning electron microscopy (SEM), Fourier transform infrared (FTIR) spectroscopy, X-Ray diffraction (XRD), swelling behaviour, in vitro degradation, and compressive strength of these fabricated hydrogels were evaluated. Furthermore, cell viability and osteogenic differentiation of ADMSCs on these hydrogels were measured. Analyses of the outcomes were analyzed in GraphPad Prism Software (version 9.0.0 121).

Results: A synergistic effect of TiO2 and CUR causes strong capability in the Hy/Ti/Cur composite to stimulate bone differentiation markers such as Runt-related transcription factor 2 (RUNX-2) and osteocalcin (OCN) in the ADMSCs cultured in both normal and osteogenic medium. Moreover, the ALP activity and calcium deposition of ADMSCs cultured on engineered hydrogels were also increased. These experiments demonstrated that the new fabricated hydrogel composite is a safe and biocompatible material and has the potential to induce osteogenesis, which is recommended as an attractive scaffold in bone tissue engineering.

Conclusions: SEM micrographs of Hy/Ti/Cur composite showed that the cur and titanium were distributed and inserted in the hydrogel networks, indicating a mesh-like network structure that mimics natural tissues and can therefore be used as a biocompatible material in bone regeneration. Titanium as an effective combination in the hydrogel structure increased the scaffold' mechanical property.

Keywords: Decellularized bone matrix, Hydrogel, Titanium Dioxide, Curcumin, Adipose-derived mesenchymal stem cells, Osteoblastic differentiation

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Bioinformatics study on the role of CDK5 gene in Alzheimer's disease

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Introduction: Alzheimer's disease (AD) is a type of neurodegenerative disease which causes progressive memory loss and cognitive reduction. Deregulation in the Cyclin-dependent kinase 5 (Cdk5) gene has recently been associated with the abnormal metabolic activity of tau and β-amyloid precursor protein (APP), which play critical roles in the neurodegenerative processes that lead to Alzheimer's disease etiology. Cyclin-dependent kinase 5 regulatory subunit 1 (CDKR1) encrypts the cdk5's critical activator subunit, P35. Deregulation in the P35/cdk5 active complex is linked to several neurodegenerative diseases, including Alzheimer's disease. The aim of this study was to find the role of the CDK5 gene in the process of Alzheimer's disease.

Methods: to achieve this goal, the GSE36980 obtained from GEO datasets, was used to assess the status of CDK5 gene regulation between AD and non-AD; the miRdSNP database was studied to choose the potential microRNAs associated with Alzheimer's disease and collect data about the selected microRNA. The information about the CDK5 gene in the AD pathway was extracted from KEGG pathways.

Results: The results showed that two miRNAs, miR-103 and miR-107, located on the CDK5R1 3'UTR, are linked to Alzheimer's disease and may regulate the expression of the CDK5R1 gene and influence P35 levels. Furthermore, P35 can activate the P25, and the CDK5 gene and the CDK5/P25 complex increase the phosphorylation of tau protein. Followed by tau phosphorylation, paired helical filaments (PHFs), and neurofibrillary tangles (NFTs) form and eventually, neuronal cell apoptosis occurs.

Conclusion: Based on the studies, it is concluded that miR-103 and miR-107 can be suitable biomarkers for AD since their downregulation can lead to a rise in CDK5R1/P35 levels and amplify the activity of CDK5. Overexpression of the CDK5 gene causes abnormal phosphorylation of tau, APP, and neurofilaments (NF) in human AD brains.

Keywords: Gene regulation, AD, GEO datasets, CDK5/P25, APP, NF

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Effect of Nigella sativa on the glycemic index in Type 2 diabetes mellitus: a systematic review and meta-analysis of randomized controlled trials

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Page | 407

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Introduction: Type 2 diabetes mellitus is a group of metabolic disorders characterized by hyperglycemia (1). Supplementation with Nigella Sativa has been related to reduced concentrations of the glycemic index (2). Concerning clinical findings, the noticeable results have been controversial. In the present meta-analysis, a review investigates the effectiveness of N. Sativa, a popular herb, on the glycemic index in type 2 diabetes mellitus.

Method: The literature search was conducted covering PubMed, Scopus, and Cochrane up to February 2022 to obtain the relevant published intervention. Effect sizes of included studies were pooled using Comprehensive Meta-Analysis (CMA) V3 software (Biostat, NJ)(3).

Result: Seven trials were included in the meta-analysis of glycemic endpoints. The combined findings, using a random-effects model, showed that supplementation with N. Sativa significantly improved fasting blood sugar [-15.84 mg/dl, 95% CI: -191.19 to -8.49, p<0.001], and HbA1c [-0.51%, 95% CI: -2.12 to -0.28, p<0.001].

Conclusion: Current findings suggest N. Sativa supplementation is a suitable choice in managing the complications of type 2 diabetes mellitus, although future researches are necessary

Keywords: Nigella sativa, Type 2 Diabetes, Fasting blood glucose,

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The inhibitory effects of BMP4 and p21 siRNA complexes with Exosomes on Wnt signaling Pathway and sh-y5y neural stem cell differentiation

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Page | 408

Introduction: Exosomes are nano-carriers containing proteins and microRNAs which can be secreted from the majority of cells. Our main goal in this study was to investigate the efficiency of exosomes in effective delivering siRNAs targeting P21 and BMP4 in to SH-SY5Y cells.

Methods: Exosomes were isolated from SH-SY5Y cells' supernatant by using ultracentrifuge based protocols and they were loaded with test siRNAs using ExoFection kit. Afterwards, the effect of siRNAs targeting P21 and BMP-4 on the expression of genes, BMP-4, P21, NeuroD1 and Prox1 in SH-SY5Y cells were assessed by western blot and Real Time PCR.

Results: Exosomal markers (CD63 and CD9) were confirmed by Flow cytometry. Exosomes' size was estimated 49.23± 8.43nm by using DLS. Our data showed that exosomes' cytotoxicity in comparison to Lipofectamine were significantly low. Evaluation of gene expression showed significant increase in Neuro D1 and ProX1 expression level.

Conclusions: Our data showed that siRNAs targeting P21 and BMP-4 were efficiently delivered with low cytotoxicity via exosomes and exosomes played an important role as carrier in SH-SY5Y cell differentiation toward neurons.

Keywords: Exosome, Differentiation, western blot, Flow cytometry, SiRNA

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Evaluation of Long non-coding RNA- CASC2 in breast tumor tissues of Iranian Women

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Introduction: Breast cancer is the leading cause of cancer death for women worldwide. Identification of novel molecular markers that are involved in tumor development has allowed cancer diagnosis, targeted therapy and monitoring the response to cancer treatment. Long non-coding RNAs (lncRNAs) are involved in the regulation of various cellular processes, including chromosome transcription and remodeling. This study aimed to investigate the expression and significance of long noncoding RNA CASC2 [1] (lncRNA- CASC2) in breast cancer.

Methods: Breast cancer samples were obtained from Iran National Tumor bank. Total RNA was extracted from each sample and then treated with DNase. Q-PCR was used to detect the mRNA expression of lncRNA- CASC2 in breast cancer and adjacent normal tissues as respective controls.

Results: Analysis of Real Time-PCR data showed that CASC2 gene expression increased significantly in the breast tumor tissues compared to adjacent normal tissues ($P<0.05$). Examination of the relationship between CASC2 gene expression and various clinic pathological parameters of breast cancer tissues showed that increased CASC2 gene expression increased significantly in tumor size, different grades, different stages, estrogen levels, lymphatic invasion and vascular invasion of tumor tissue ($P <0.05$), High expression of CASC2 was shown in tumors with smaller size, lower grade, lower stage, positive estrogen level, tumor without lymphatic and vascular invasion. However, there was no significant relationship between CASC2 expression and progesterone levels, p53 and necrosis ($P > 0.05$).

Conclusions: Since the expression of lncRNA- CASC2 gene is increased in tumor breast tissues compared to normal tissues, this gene can be considered a suitable biomarker for breast cancer. Studies show that CASC2 gene expression is significantly different in tumor size, grade, stage, estrogen level and invasion of lymphatic and vascular tissues. [1] Cancer Susceptibility Candidate 2

Keywords: Breast Cancer, Long non-coding RNA, Gene expression, CASC2

Evaluation of the effect of iron oxide nanoparticles (Fe203) and cabbage extract on growth rate and histochemical changes of gastrointestinal tract, liver and muscle in larvae of Cichlid fish (Heros Severus)

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Introduction: Biochemical changes represent the stages of molecular development of the limbs. According to production of Iron oxide nanoparticles and useful application in biological systems, less studies on side effects of these material has been carried out in animals. These substances can be distributed in vivo in most tissue and following various biological effects. Consumption of cabbage (Brassica oleracea) due to vitamin C, E and antioxidants, probably plays important role in growth and development. The cichlid fishes (Cichlidae) are used as ornamental fish and biological model in the world.

Methods: Therefore, in this study the effects of iron oxide- nanoparticles Fe203(50,200mg/kg) and red cabbage powder(200mg/kg) in growth rate of 180 fish (Heros sevrus) with weighing 0.05± 0.01 and age of 10 dph were studied for 35 days in aquarium environment in 5 treatment groups compared with the control group were examined. Microscopic studies in the gastrointestinal tract by using PAS, alician blue staining and accumulation of iron in muscle and liver (with blue perls staining) were done.

Results: At the end of this study, staining intensity of the stomach and intestine in treatment 5 (biomar nutrition with red cabbage and iron nanoparticles 200 mg/kg) in gablet cells stronger reaction with pas and alician blue were observed than other treatments, that is probably due to the presence of neutral and acidic monopolysacharides mucosal compounds. These responses begun faster a week. Accumulation of iron nanoparticles in liver cells more than muscle cells were seen. In biometric study, treatment 5 had a higher growth rate than the others.

Conclusion: It seems that because of higher growth rate and histochemical activity of gastrointestinal tube with limited muscle accumulation, biomar diet with cabbage and iron oxide nanoparticles Fe203 (with appropriate concentrations), might be good suggestion for increasing production in fishery.

Keywords: Heros severus, Histochemistry, Iron oxide nanoparticle, Red cabbage (Brassica Oleracea).

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Histological changes of organs under the combined influence of iron oxide nanoparticles (Fe203) and alfalfa in larval stages of Cyprinus carpio kOi

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Introduction: Nowadays due to the increasing growth of production and consumption of nanoparticles, Problems arise such as such as their entry into high seas and aquatic toxicity. Iron oxide nanoparticles are among the most widely used in this field. Alfalfa (Medicago sativa) is a flowering plant that belong to the Fabaceae family that contain high amount of protein, calcium and vitamins which is exhibited significant antioxidant activity. Koi fish (Cyprinus carpio koi) is one of the Carp fish ponds that are breeding as aquarium and pond fish.

Methods: In this study the effects of concurrent Koi larvae feeding with alfalfa and exposure to 100 mg/L Fe_2O_3 nanoparticles for 2 weeks were investigated.

Results: In the present study, the groups were treated with Fe203 nanoparticles and alfalfa exhibited better growth in comparison with groups that treated with Fe203 nanoparticles. These effects could be probably due to antioxidant and growth enhancing properties of alfalfa. Moreover, the group treated with Fe203 nanoparticles showed less growth (average length and final weight) compared with control group. According to the results, the best growth was obtained with grout composed of 20% alfalfa leaves in the basic diet. In histology studies, the most histological changes including hemorrhage, hyperplasia, vacuolization, destruction of sinusoid, increase the number of Kupffer cells in the liver was observed in the group that treated with Fe203 nanoparticles. Besides vacuolization and hematopoietic tissue atrophy in kidneys, increased goblet cells, hyperplasia of the mucosa and submucosa and shortening of villi in the gut of this group were detected.

Conclusion: Therefore, it seems that biomar diet, if combined with alfalfa in appropriate concentrations, while reducing the toxic effect of iron nanoparticles is a good suggestion in increasing fishery productivity.

Keywords: Koi fish, alfalfa, histology, Fe203 nanoparticles

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The artificial peroxidase activity of magnetic iron oxide nanoplatform for tetracycline degradation

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Introduction: Antibiotics are an important part of treatment of bacterial infection origin, in humans and livestock, also treatment of agricultural products. In addition to human consumption, presence of residues of antibiotics in food and drinking water, that enter the human body indirectly and significant effects on public health. Side effects can include increased antibiotic resistance and allergies and liver damage. Therefore, the degradation of antibiotic residues is significant.

Methods: in most methods, ultraviolet light and ultrasonic are used to start the reaction. In this study, the nanoplatform used start the reaction without the need for any initiator. The nanoparticles were first synthesized by co-precipitation and then coated with cyclodextrin to increase the catalytic properties and then labeled with gadolinium ion to increase the magnetic properties. UV-Spectroscopy and GC-mass spectroscopy have been used to analyze degradation of this drug. And at the final step the nanoplatform expelled with external magnetic and use again for other degradation reactions.

Results: The characterization confirms the correct formation of these nanoparticles. The results show that tetracycline decomposes at different catalytic concentrations with the same percentage but at different times. As the concentration increases, the decomposition time decreases.

Conclusion: The results show that tetracycline decomposes at different catalytic concentrations with the same percentage but at different times. As the concentration increases, the decomposition time decreases.

Keywords: Keywords: Nano platform, tetracycline, enzyme mimicry

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Generation and differentiation of islet-like cells from umbilical cord-derived mesenchymal stem cells with a three-dimensional culture medium of optimised silk

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Page | 413

Introduction: Many studies have been done on the production of insulin-producing cells from stem cells, which is promising for thetreatment of type 1 diabetes. Due to these cases, in the present study, we aimed to produce the most compatible of insulin-producing cells with pancreatic islet cells using silk/gelatin nanofiber scaffolds from umbilical cord-derived mesenchymal stem cells (UCMSCs).

Methods: In this experimental study, UCMSCs were cultured in three groups: two-dimensional (2D), three-dimensional (3D), and control groups. After twenty days, differentiated cells were analyzed for expression of pancreatic gene markers by Q-PCR. Immunocytochemical staining was used to detect the presence of insulin and glucagon in the cells, and the presence of insulin protein was determined by western blotting. Also, the response rate of differentiated cells to different concentrations of glucose was measured by the ELISA method.

Results: Q-PCR analysis of differentiated cells in the 3D group showed high expression of gene markers specific for beta cells including insulin, glucagon, pdx-1, and glut-2. The presence of insulin and glucagon protein in 2D and 3D groups was confirmed by immunocytochemical staining and the presence of insulin protein was confirmed by western blotting. ELISA results showed insulin secretion in response to different concentrations of glucose in both groups, which was higher in the 3D group. Finally, by electron microscopy, the morphology of islet like-cells in the 2D and 3D groups was compared with each other.

Conclusion: Our results showed the differentiation of umbilical cord-derived mesenchymal stem cells towards insulin-producing cells in both 3D and 2D culture groups. Also, in the comparison between the 3D and 2D groups, the differentiation in the 3D culture medium was more optimal, so the use of silk/gelatin 3D culture medium could be a promising new approach to the production of insulin-producing cells in the treatment of type 1 diabetes.

Keywords: Umbilical cord-derived mesenchymal stem cells, differentiation, insulin-producing cells, silk/gelatin scaffold

17th National Congress of Biochemistry & 8th International Congress of Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

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Kolaviron: New hope for Alzheimer disease treatment?

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Page | 414

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Introduction: Alzheimer disease (AD) is the most common cause of dementia in the elderly. The number of patients is predicted that will reach 131.5 million worldwide by 2050. Okadaic acid (OA) is a toxic compound that causes conditions like Alzheimer disease. Kolaviron (KV) is a biflavonoid from Garcinia kola that has anti-inflammatory properties. KV has effect on many disease conditions such as cancer, hepatotoxicity, obesity, malaria and renal toxicity. So we decided to evaluate the effect of KV on hippocampal inflammation caused by OA.

Methods: 40 male Wistar rats (220 - 250g) were randomly divided into 5 groups including: sham, sham + KV (100 mg/kg), OA (200 ng/kg), OA + KV (50mg/kg) and OA+ KV (100mg/kg). KV was administered intraperitoneally and OA was injected into the right brain ventricle. Hippocampal sections were used for the inflammatory factors assessment by ELISA method.

Results: TNF-α, in response to OA, increased significantly in both OA and OA + KV 50 mg/kg ($P < 0.001$ and $P < 0.05$, respectively) compared to sham group. KV significantly reduced TNF-α levels compared to OA group at both doses of 50 and 100 mg/kg ($P < 0.05$ and $P < 0.01$, respectively). OA increased the level of IL-6 in the two groups of OA and OA + KV 50 mg/kg compared to the sham group ($P < 0.001$ and $P < 0.01$, respectively). KV significantly reduced the level of IL-6 only at a dose of 100 mg/kg ($P < 0.05$). sham Sham+ KV100mg/kg OA OA+ KV50mg/kg OA+ KV100mg/kg TNF-α (pg/mg) 27.83±2.57 27.83±2.91 55.13±3.46*** 41.09±3.55*, # 38.25±3.19## IL-6 (pg/mg) 25.13±2.38 30.38±2.91 48.51±3.57*** 42.35±3.76** 35.23±3.17#

Conclusion: Kolaviron (100 mg/kg) because of its anti-inflammatory properties can compensate the effect of OA on inflammation by reduction of hippocampal TNF-α and IL-6 levels.

Keywords: Alzheimer's disease, Kolaviron, Okadaic acid, Inflammation

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Synthesis and characterization of tungsten trioxide-albumin nanocomposite as peroxidase-mimic

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Page | 415

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Introduction: Enzyme mimics, which are non-protein compounds such as metal complexes, metal nanomaterials, polymeric and supramolecular molecules, have been regarded as strong substitutes for natural enzymes in recent decades. In this regard, nanostructured materials have gained considerable attention among researchers due to their unique properties, including electrical and thermal conductivity, catalytic activity, light absorption, and scattering, resulting in enhanced performance over their bulk counterparts.

Methods: In this work, tungsten trioxide-bovine serum albumin (WO3/BSA nanocomposite) was synthesized. Various characterization studies were performed using different methods, including field emission scanning electron microscope (FESEM), X-ray powder diffraction (XRD), and Fourier transform infrared (FTIR) techniques. The catalytic activity of prepared particles was investigated using colorimetric experiments, which were based on the oxidation of 3,3',5,5'-tetramethylbenzidine (TMB, as a peroxidase substrate) in the presence of H_2O_2 and a suitable catalyst.

Results: The obtained results indicated the peroxidase-mimic activity of BSA/WO3 NPs. The kinetic parameters were calculated and the results showed that the Km and Vmax values of the WO3/BSA nanocomposite were 0.015 mM and 0.313 µM. s-1 (in the presence of TMB as substrate) and 0.054 mM and 0.327 µM. s-1 (for H_2O_2 as substrate), respectively. The apparent Km value of the prepared nanoparticles with H_2O_2 and TMB as the substrates was lower than that of HRP, confirming the high affinity of the prepared particles toward substrates.

Conclusion: It can be considered that BSA molecules can protect nanoparticles, increase the stability of the particles, uniform the surface reactivity and let nanoparticles expose the same biocompatible surface, which results in increasing the catalytic activity of nanoparticles.

Keywords: Enzyme mimics, Tungsten trioxide, Bovine serum albumin, Peroxidase-mimic activity

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Effect of trehalose on SIRT1 and miR-132 expression in brain aging

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Introduction: Aging causes substantial molecular to morphological changes in the brain. Growing evidence has reported that the expression of Sirtuin1 (SIRT1) changes in aged brain cells. SIRT1 expression is regulated by microRNAs (miRNAs) such as miR-132. MiR-132 is a brain-specific miRNA which is implicated in neuronal homeostasis. Trehalose, a natural disaccharide, contributes to preventing neuronal damage through several mechanisms. However, little is known about the interactive effects of aging and trehalose on the expression of miR-132 and SIRT1 in the hippocampus which was studied in this investigation.

Methods: Male Wistar rats were divided into four groups. Two groups of aged (24 months) and young (4 months) rats were administered 2% trehalose solution for 30 days. Two other groups of aged and young rats received regular tap water. At the end of treatment, the level of SIRT1 mRNA and protein, as well as the expression level of miR-132 were measured in the hippocampus.

Results: Our data revealed that the expression level of miR-132 and SIRT1 was decreased in the hippocampus of normally aged animals in comparison with young rats. Moreover, trehalose treatment significantly increased the expression of miR-132 in the hippocampus of young and old rats. Our findings also showed that senescence-associated downregulation of SIRT1 in the hippocampus was reversed upon trehalose supplementation.

Conclusion: In conclusion, our data confirmed that trehalose improves healthy brain aging through the upregulation of miR-132 and SIRT1.

Keywords: Brain aging, SIRT1, MiR-132, Trehalose

A-10-1521-1

cervical cancer and expression of cadm1 gene
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Introduction: Cervical cancer is the second major cancers related to mortality between women. Hpv is the main and major cause that is involved in squamous cervical cancer majorly. hpv is a member of papillomaviridae family that is classified to high risk and low risk strain. high risk strains have a carcinogen trait. these viruses' activity mediated by epigenetic changes like acetylation, phosphorylation, methylation of histones and cpg areas of tumor suppressor genes and changes in long non coding rnas. cadm1 is a tumor suppresor gene that is a member of super immunogobolin family. it has a lot of function as follows in normal cell adhesion, proliferation, differention and plays an important role in the suppression of malignant tumor cell invasion and metastasis. it has been shown that the deactivation of tscl1 or cadm1 gene partly through promotor hypermethylation is associated with the occurance of wide variety of tumors like cervical cancer. these processes are done by hpv e6 and e7 proteins especially high risk types named 16 and 18 **Method:** this article is produced only from the most relevant ones published in high impact factor journals.

Results: the down regulation of cadm1 gene may result in the loss of the rb tumor suppressor pathway signalig which represents a relatively common events in cervical carcinogenesis. the frequency of cadm1 gene promotor hypermethylation increased with the degree of the disease and mostly are seen in high grade leisions and low expression of it is accompanied with poor income and widespreaded metastasis.

Conclusion: The lower the expression of this gene due to promoter hypermethylation in tissues, especially in cervical cancer, the higher the risk of metastasis and tissue rupture.

Keywords: cadm1 gene, human pailloma virus, cervical cancer, epigenetic changes, hypermethylation

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Neuroprotective effects of Aurone- and Arylidene oxindole- new synthetic derivatives, associated with oxidative stress

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Introduction: Oxidative stress plays a pivotal role in the development of neurodegenerative diseases such as MS and AD. Actually oxidative damage is a direct threat to cell survival. Dimethyl fumarate (DMF) is a novel oral therapeutic agent with anti-oxidant properties which exerts protective effects through activation of nuclear factor erythroid 2 (NFE2)-related factor 2 (Nrf2). The aim was to investigate the influence of new-synthetic derivatives of Aurone and arylidene oxindole on SH-Sy5y neurons under oxidative stress.

Method: In this study, SH-Sy5y cells were cultured and then the effect of new-synthetic derivatives of Aurone and arylidene oxindole on the viability of neuron cells under the oxidative stress induced by H2O2 was evaluated.

Results: Our results exhibited that some of derivatives acted similar to DMF and protect cells from oxidative stress induced H2O2 in cell culture.

Conclusion: Tested compounds probably follow the path used by DMF to suppress oxidative stress (through NRF2 signaling). This needs further investigation.

Keywords: oxidative stress, DMF, Aurone, Arylidene oxindole, SH-SY5Y.

The synergic effect of aspirin on apoAI-induced ABCA1 protein expression in human astrocytes

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Introduction: Neurons need a high amount of cholesterol for keeping their membrane-rich structures in a steady state. Astrocytes are responsible for the synthesis and distribution of cholesterol to neurons and ABCA1 is a key mediator of cholesterol efflux to generate HDL as a vehicle for cholesterol transport in the brain. Several studies imply the effect of aspirin on ABCA1 expression in peripheral cells such as macrophages. Here, we compared the effect of aspirin with apoA-I on ABCA1 protein expression and cholesterol efflux in human astrocytes.
Methods: Human astrocytes were cultured and treated with aspirin. RT-PCR and Western blot were performed to determine the effects of aspirin on the expression and protein levels of ABCA1. Also, cells were treated with apoA-I and aspirin to compare their effect on ABCA1 protein level. **Results:** RT-PCR and western blot data showed that aspirin is able to up-regulate ABCA1 expression and protein level up to 4.7-fold and 67% respectively.
Conclusion: The results are suggested a potential effect of aspirin on increasing ABCA1 expression in astrocytes as apoA-I dose. Therefore, aspirin may have the beneficial effect(s) on regulating the brain cholesterol balance and can be considered in some diseases, in particular in some neurological disorders related to cholesterol accumulation such as AD, via its ability to increase the HDL formation through the over-expression of ABCA1.

Keywords: Astrocytes, Brain cholesterol homeostasis, ABCA1, aspirin, Real-time PCR

A-10-1534-1

Effects of hyperthermia and chemo-radiation using Mega voltage radiation and drug-loaded magnetite nanoparticle on glioblastoma cancer cells

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Page | 420

Introduction: Recently, the development of new strategies in the treatment of cancer cells such as thermo-radiation-sensitizer have received a great deal of attention. In this work, Temozolomide-loaded magnetite nanoparticles (TMZ-MNP NPs) were proposed to enhance the cytotoxic effects of hyperthermia and radiotherapy.

Methods: Nanoparticles were synthesized and characterized for hydrodynamic diameter, zeta potential, and morphology. To evaluate the thermo-radio-sensitization effects of NPs, C6 cells were treated with nanoparticles for 24h and then exposed to 6-MV X-ray radiation. After radiotherapy, the cells were subjected to an alternating magnetic field (AMF) hyperthermia. Following the treatments, the therapeutic potential was assessed using the clonogenic assay, ROS generation measurement, flow cytometry assay, and qRT-PCR analysis.

Results: Colony formation assay proved that TMZ-MNP NPs enhanced the anti-proliferation effects of AMF by 1.94-fold compared to AMF alone (P<0.0001). Moreover, these NPs improved the radiation effects with a dose enhancement factor of 1.65. All results showed that the combination of carrier-based chemotherapy with hyperthermia and radiotherapy caused a higher anticancer efficacy than single- or two-modality treatments.

Conclusion: The nanoparticles advanced in this study can be proposed as the promising thermo-radio-sensitizer platform for the tri-modal synergistic cancer therapy.

Keywords: Radio-sensitizer, Thermo-sensitizer, Nanoparticle, Radiotherapy, Hyperthermia, Combination treatment

A-10-1534-2

Radiosnsitizing effects of metal-based hetero-nanoparticles on colorectal cancer cells

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Introduction: It is well known that conventional cancer treatment modalities are associated with their inherent shortcomings. Recently, the application of nanoparticles as radiosensitizers has become a field that has attracted a great deal of attention. In this study, we focused on the potential of magnetite copper hetero-nanoparticles to serve as a radiosensitizer agent to enhance the efficacy of radiation therapy.

Methods: nanoparticles were synthesized and characterized for hydrodynamic diameter, morphology, and X-ray diffraction. The toxicity of nanoparticles on colorectal cancer cells was evaluated using the MTT assay. The cytotoxic effects of different doses of radiation in the presence and absence of nanoparticles were investigated by the Nitric oxide (NO) assay, Glutathione Peroxidase (GPX) enzyme activity measurement, and colony formation assay.

Results: The results demonstrated that the intracellular Nitric oxide level significantly increased in the cells treated with the combination of nanoparticles and radiation. Whereas, the Glutathione peroxidase enzyme activity and the surviving fraction of cells in the combined treatment significantly decreased compared to the radiation alone. The sensitizing enhancement ratio (SER) of nanoparticles was 2.02.

Conclusion: Our study demonstrated that synthesized magnetite copper hetero-nanoparticles and ionizing radiation had synergetic effects on the colorectal cancer cells. So can be used as a promising radiosensitizer agent for the treatment of cancer cells.

Keywords: Colorectal cancer, Radiosensitizer, Ionizing radiation, Copper, Magnetite nanoparticles

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TEHRAN UNIVERSITY OF MEDICAL SCIENCES

Effect of atorvastatin in diet-induced NAFLD in rats

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Introduction: Nonalcoholic fatty liver disease (NAFLD) is considered the hepatic manifestation of metabolic syndrome and is the most common cause of liver dysfunction worldwide.

Methods: Twenty-four male rats were divided randomly into seven groups: 1) control, 2) HFFD (high fructose/fat diet) control that receive fructose, olive oil, and CCl4, and, 3) HFD + Atorvastatin that receive Atorvastatin 20 mg/kg. Interventions have done for 23 weeks and then biochemical measures were taken.

Results: Although the weight of the liver was not changed in the studied groups, fat around the liver was increased in HFFD compared to control. The treated group HFFD+ATO was able to reduce total cholesterol levels. The triglyceride level in HFFD was notably increased compared with the control group with a reduction observed in the HFD+ATO. There was no significant difference in HDL levels among groups. Compared with the control group, the ALT, AST, ASP and GGT levels in rats fed HFD were significantly increased. Atorvastatin led to a reduction in AST and GGT, not modulating ALT and ALP when compared to the HFD. Regarding renal function, there was no significant difference in urea and creatinine levels among the studied groups.

Conclusion: This study found some evidence that atorvastatin has effectiveness in the management of dyslipidemia and liver function being considered crucial for attenuating the progression of NAFLD.

Keywords: NAFLD, Atorvastatin, Rat, High fructose/fat diet

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The visceral adiposity index and lipid accumulation product as predictors of cardiovascular events in normal-weight subjects

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Page | 423

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Introduction: Visceral adipose tissue (VAT) has an important role in the incidence of cardiovascular disease (CVD) than obesity by itself. The visceral adiposity index (VAI) and lipid accumulation product (LAP) are surrogate indices for measuring VAT. We aimed to investigate the association of these markers with cardiovascular events among populations with different BMI category in Mashhad, northeast of Iran.

Method: The present study comprised a prospective cohort of 9685 men and women (35–65 years) who were recruited from MASHAD study. Demographic, laboratory evaluations, anthropometric and metabolic parameters were performed. Logistic and Cox regression analyses were used to determine the association and risk of cardiovascular events with VAT and LAP.

Results: The mean VAI and LAP in CVD patients were significantly higher than in healthy ones in all 3 groups. In terms of CVD event prediction, VAI and LAP had significant association with the incidence of CVD in the second (RR (95% CI): 2.132 (1.047-4.342) and 2.701 (1.397-5.222), respectively) and third tertiles (RR (95% CI): 2.541 (1.163-5.556) and 2.720 (1.159-6.386), respectively) in the normal group, but this association was only found in the third tertiles (RR (95% CI): 2.448 (1.205-4.971) and 2.376 (1.086-5.199), respectively) in the overweight group. We did not find this association for the obese group.

Conclusion: In this study, we found that there was a significant association between LAP and VAI and cardiovascular events in normal weight and over-weight groups; however, no significant relationship was found in the obese group.

Keywords: VAI, LAP, Normal weight, CVD

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An investigation of the SRY expression pattern in embryoid bodies and the effects of SRY overexpression on rosette neural stem cells.

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Page | 424

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Introduction: SRY is the first mammalian SOX gene (SRY-like HMG-box gene), and this transcription factor aids embryogenesis, epigenetic processes, and brain, heart, and kidney development, but its significance in their regulatory mechanisms remains unclear. Aberrant expression of SRY in non-gonadal cells may disrupt gene regulation, influencing tissue and cell pathophysiology. We used a male embryonic stem cell line (hESC-RH6) to explore SRY expression during spontaneous differentiation into embryoid bodies (EBs). SRY overexpression in rosette neural stem cells (R-NSCs) was also studied. **Methods:** hESC-RH6 and SRY over-expressing hESC (SRY-RH6) lines were induced to generate EBs and R-NSCs, respectively. Two groups of cells included collected EBs at six-time points, and the SRY-RH6 contained an inducible promoter overexpressing the SRY by the Doxycycline treatment. During EB formation, the expression patterns of specific markers for three germ layers were compared with SRY using qRT-PCR, and the expression of four groups of markers, including pluripotency genes, SOX members, and R-NSC markers, and bHLH genes, was analyzed in R-NSCs. **Results:** Downregulated pluripotent and upregulated differentiation markers indicated verification of spontaneous differentiation. SRY expression in hESC-RH6 was higher than EBs. After neural differentiation, qRT-PCR data was divided into two categories. The first examines the influence of SRY gain-of-function on day 0; the second compares R-NSCs on day 8 with hESC on day 0. Through doxycycline induction, the expression of pluripotency markers, SOXB genes, and PAX6 was reduced in the pluripotent state. Other SOX, bHLH, and rosette markers also increased expression. **Conclusion:** Similarities between SRY expression and pluripotent marker patterns in EB formation suggest the SRY gene's importance in early embryonic development. SRY gain-of-function may improve rosette survival by decreasing pluripotency markers and increasing neural differentiation markers. Since NSCs differentiate similarly in vitro and in vivo, these R-NSC-based models seem promising for further clinical application.

Keywords: SRY, Rosette Neural Stem Cell (R-NSC), Neural Differentiation, HESC, Gain-of-function, Embryoid Bodies (EBs).

Effects of Nesfatin-1 on cardiac function and oxidative stress in Isoproterenol induced heart failure rats

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Introduction: Nesfatin-1 is a novel hypothalamic peptide which is well-known for its involvement in the regulation of energy homeostasis. Also it has been found as a secretory agent in peripheral tissues and nervous system. Recent studies showed antioxidant and anti-apoptosis effects of this peptide on nerve tissue which can ameliorate ischaemic injuries. In this study we evaluated effects of Nesfatin-1 on heart failure rats through echocardiographic changes and oxidative stress markers. **Method:** 50 male Wistar rats were divided to 4 groups of control, Nesfatin-1 (Nesf-1), heart failure (HF) and heart failure+ Nesfatin-1 (HF+Nesf-1). Subcutaneous injection of 130mg/kg Isoproterenol was used in 2 doses to induce heart failure in both HF and HF+Nesf-1 groups. 28 days after induction, intraperitoneal injection of 10μg/Kg Nesfatin-1 started for 5 days in a row in HF+Nesf-1 group. 2 weeks after injection, rats serum lactate dehydrogenase (LDH) were examined and afterward echocardiography was done based on ejection fraction (EF %) and fraction of shortening (FS %) parameters. Then cardiac tissue was harvested for ELISA testing. Oxidative stress markers such as Superoxide dismutase (SOD), Glutathione (GSH) and Malondialdehyde (MDA) were assessed.

Results: Analysis of our data showed that echocardiographic parameters (EF and FS) worsened and oxidative stress increased by HF (P<0.01). Also treatment with Nesf-1 ameliorated cardiac function and level of antioxidant agents.

Conclusion: As discussed before, neuroprotective effects of Nesfatin-1 has been proven via different signaling pathway. In this study we focused on antioxidant and clinical effects of this peptide on heart failure models. It was concluded that Nesfatin-1 can alleviate oxidative stress signaling pathway by increasing antioxidant agents and decreasing oxidant markers in HF rats. Moreover, recovery of cardiac function was clinically approved by data obtained from echocardiographic assessments.

Keywords: Nesfatin-1, Heart failure model, Heart failure, Isoproterenol, Echocardiography, Oxidative stress

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Targeted delivery of simvastatin to restore dysfunctional HUVECs by mZD7349 peptide-conjugated PLGA nanoparticles directed against VCAM-1

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Page | 426

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Introduction: Impaired bioavailability of endothelial nitric oxide synthase (eNOS) is one of the main reasons of endothelial dysfunction. Improving bioavailability of eNOS by increasing its expression or activity using statins is an effective therapeutic strategy in restoring endothelial dysfunction.

Method: In this study, simvastatin (SIM) as a poorly water-soluble drug was loaded in poly (lactic-co-glycolic acid) (PLGA) nanoparticles (SIM-PLGA-NPs) made by electrospraying. NPs. NPs were then conjugated with mZD7349 peptide (mZD7349-SIM-PLGA-NPs) and directed against vascular cell adhesion molecule 1 (VCAM-1) expressed on activated endothelial cells. In vitro evaluation of the NPs for targeted delivery of SIM was performed on activated Human Umbilical Cord Vascular Endothelial Cells (HUVECs) by tumor necrosis factor alpha (TNF-α). Effect of mZD7349-SIM-PLGA-NPs and SIM-PLGA-NPs was compared on eNOS phosphorylation (ser-1177) by western blot. Results of western blot showed SIM post-treatment increased significantly phosphor-eNOS (Ser1177) expression but no total eNOS expression.

Results: The study showed that mZD7349-SIM-PLGA-NPs have particle size, zeta potential value, polydispersity index (PDI) and encapsulation efficacy % of 233±18nm, -9.6±1.1mV, 0.59±0.066 and 69±17.3%, respectively. Also phosphor-eNOS (Ser1177) expression in activated HUVECs treated with mZD7349-SIM-PLGA-NPs was significantly (p<0.05) better than treated cells with SIM-PLGA-NPs.

Conclusion: The results suggest that mZD7349-SIM-PLGA-NPs may be usable as an appropriate drug carrier for restoring endothelial dysfunction

Keywords: Endothelium, HUVECs, Phospho-eNOS (Ser1177), Poly (dl-lactic-co-glycolic acid) nanoparticles, Simvastatin, Vascular cell-adhesion molecule-1, mZD7349 peptide.

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Molecular detection of class I Integron and its gene cassette to antibiotics in E. coli

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Introduction: Integrons are one of the mobile genetic elements capable of carrying resistance genes to various antibiotics. Meanwhile, the role of class I integron is important in creating and transmitting antibiotic resistance. The purpose of this study is to isolate Escherichia coli strains, molecular investigation of class I integron and gene cassettes and determine antibiotic resistance and sensitivity.

Methods: This study was conducted on 150 Escherichia coli samples isolated from Khorramabad hospitals. After sampling and culture on specific media and DNA extraction, the presence of class I integron gene and aadB cassette was done by PCR method. Antibiotic sensitivity and resistance test was also done by disk diffusion method.

Results: After examining 150 strains, 86 samples were resistant to all antibiotics and 69 samples had multiple antibiotic resistance. The highest resistance was related to ticarcillin and cefepime antibiotics, the lowest resistance was related to gentamicin and amikacin antibiotics. Out of 150 samples of Escherichia coli, 51 samples had int1 gene and also out of 38 positive integron samples, 29 samples had aadB cassette.

Conclusion: In this study, according to the significant statistics of the presence of class I integron and the gene cassette inserted in it in Escherichia coli isolates and its relationship with the pattern of multiple drug resistance, it can be concluded that these elements can play an important role in creating and transmission of antibiotic resistance.

Keywords: Class I integron ‹Antibiotic resistance ‹Escherichia coli ‹Gene cassette

A-10-1561-2

Evaluation of natural and artificial RNA stabilities at different temperatures

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Introduction: Ribonucleic acid (RNA) is broadly uses in many molecular studies for cDNA synthesis, elucidation of gene splicing, probe preparations, etc. The genomic contents of many viruses are also consisting of RNA. When compared with DNA, RNA is more degradable and prone to hyolyses with enzymatic degradation like RNase which come from contaminated materials and regents. RNA can be obtained via natural RNA extraction from the organisms or to be artificially synthesized in test tube.

Methods: In this study, an artificial RNA from a part of the genome of severe acute respiratory synome coronavirus 2 (SARS-CoV-2) was synthesized in a test tube using T7 RNA polymerase. The natural yeast RNA extraction was performed using the culture media as control. The extracted RNAs from two origins were kept in -20oC, -40oC, -80oC for 6 months with regular examination interval of one month with three repeats. The RNA samples applied on 1.5% gel electrophoresis and the patterns of the intact or degraded bands were recorded.

Results: The results indicated that the pattern of stability of RNA in different temperatures are the same as expected. However, RNA samples which had come from synthetic sources were more stable and resistant to degradation when compared with the RNA samples naturally extracted at optimum condition which are more prone to degradation. These data show the existence of enzymatic hyolyses more occurred during the storage of natural extracted nucleic acids.

Conclusion: Here, we showed that even in the highest precautions for preventing the RNA extracted from natural sources, there are still remaining degradable enzymes available in final RNA product which reduces the stability of the RNA even in very low temperatures. We also showed that synthetic RNA would be a good resource of ribonucleic acid in molecular biology research.

Keywords: Ribonucleic acid (RNA), RNA stability, RNA degradation, RNA synthesis

SGLT2 inhibitors: current and future pharmacological therapies for HF

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Introduction: Overnutrition is the main culprit for metabolic synomes such as type 2 diabetes, obesity, and ischemic heart disease. Diet and exercise are beneficial in treating metabolic synome, but SGLT2 inhibitor therapy may contribute to its treatment by improving the cardiovascular and anti-hyperglycemic effects. The sodium-glucose cotransporter 2 is responsible for glucose reabsorption in the kidneys. Sodium-glucose cotransporter-2 inhibitors hinder glucose reabsorption in the kidneys, resulting in urinal excretion of glucose. SGLT2 inhibitors are an excellent choice for T2DM treatment where blood glucose levels are lowered without hampering insulin secretion.

Methods: PubMed databases were screened using the following search terms ("SGLT2 inhibitors") AND ("metabolic synomes").

Results: By causing glycosuria, these inhibitors significantly reduce HbA1c, fasting, and postprandial glucose levels. Gliflozins have become a popular treatment option for treating T2DM and may be used as an adjunct therapy for treating T1DM. Furthermore, gliflozins have demonstrated ancillary benefits, including decreasing blood pressure and body weight. Weight loss occurs due to increased glucagon: insulin ratio, causing increased lipid mobilization and reducing leptin. Heart failure is more common as people age and is linked to other conditions such as diabetes mellitus, hypertension, and obesity. In recent cardiovascular outcome trials, SGLT2 inhibitors are associated with a 30%–35% lower risk of hospitalization for heart failure. The use of dapagliflozin in patients with heart failure and reduced ejection fraction decreased the risk of deteriorating heart failure or death from cardiovascular causes by 26%, regardless of diabetes status. This indicates that these benefits are independent of the ug's glucose-lowering effect. In heart failure with preserved ejection fraction, empagliflozin decreases inflammatory and oxidative stress, thereby improving the NO-sGC-cGMP-cascade and PKGIα activity through reduced PKGIα oxidation. This ultimately reduces pathological cardiomyocytes stiffness.

Conclusion: Overall, SGLT2 inhibitors are potential candidates for the handling of T2DM, along with several other related benefits.

Keywords: SGLT2 inhibitors, Heart failure, Type 2 diabetes mellitus, Empagliflozin

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Melatonin ameliorates astrogliosis and microgliosis in a cuprizone-induced mouse model of multiple sclerosis

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Introduction: Several investigations have reported that melatonin is involved in the amelioration of the inflammatory process, improvement of myelin function and regeneration in the central nervous system (CNS). The aim of the current study was to evaluate the protective effect of melatonin in cuprizone (CPZ)-induced myelin damage in the corpus callosum (CC) and to explore the plausible underlying mechanisms of remyelination capacity and/or neuroprotection.

Methods: Adult male mice were fed with cuprizone for 6 weeks. Animals simultaneously received 100 nM/kg melatonin.

Results: Our data showed that cuprizone intoxication caused a significant oligodenocyte loss, demyelination and reactive gliosis in CC. Administration of melatonin prevented the demyelination in CC as determined by Luxol fast blue staining (and as well protected the only mature oligodenocytes) Furthermore, we found that the melatonin treatment significantly suppressed the cuprizone-induced microgliosis and astrocytosis. while the frequency of oligodenocytes (Olig2+) was significantly enhanced in the CC after melatonin administration. In addition, melatonin significantly modulated Musashi1, Hes1 and Notch1 mRNA expression in the CC of mice.

Conclusion: These results provide evidence that melatonin abolishes destructive cuprizone effects in the mouse corpus callosum by restoring oligodenocyte generation, remyelination as well as decreasing astrogliosis and microgliosis.

Keywords: Multiple sclerosis, Astrogliosis, Microgliosis, Demyelination, Cuprizone

A-10-1570-1

Serum calprotectin can indicate current and future severity of COVID-19

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Introduction: Predictive and prognostic biomarkers to guide 2019 novel coronavirus disease (COVID-19) are critically evolving. Dysregulated immune responses are the pivotal cause of disease severity, which is mediated by neutrophil activation. Thus, we evaluated the association of calprotectin, neutrophil secretory protein, with the severity and outcomes of COVID-19.

Methods: This two-center prospective study focused on PCR-proven COVID-19 patients (n = 76) with different clinical presentations and healthy subjects (n = 24). Serum calprotectin (SC) was compared with IL-6 and other laboratory parameters available in the clinic routine.

Results: Median levels of SC were significantly higher in COVID-19 patients in comparison to the healthy group (3760 vs. 2100 ng/mL, $p < 0.0001$). Elevated SC was significantly respective of disease severity (5700 ng/mL, $p < 0.0001$). Moreover, a significant negative correlation between SC and oxygenation status was found, indicating that SC was related to disease progression and respiratory worsening. It was found that SC was high in severe patients during hospitalization and significantly declined to normal after recovery. Although it remained significantly higher in patients with fatal outcomes. SC behaved as a better predictor of respiratory status or clinical severity, as it exhibited the largest area under the curve (ROC analysis), with the highest specificity and sensitivity when the predictive value of inflammatory biomarkers was compared. The binary logistic analysis also identified that the elevated SC was the most significant diagnostic and prognostic factor for COVID-19 ($p < 0.0001$).

Conclusions: calprotectin can be used as a reliable prognostic tool to predict the poor clinical outcomes of COVID-19 patients

Keywords: Calprotectin, COVID-19, IL-6, Inflammatory biomarkers, Outcome

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Determination of Optimum Conditions for Production of Recombinant Urate Oxidase Enzyme

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Page | 432

Introduction: Urate oxidase (EC 1.7.3.3) belongs to the family of oxidoreductases. Uric acid is an excretory substance in humans that is not metabolized, the high concentrations cause gout and hyperuricemia. Uricase is an enzyme with many medical applications. Urate oxidase is one of the most abundant antioxidant molecules in humans. Research shows that urate oxidase can protect cells from damage and increase the repair of damaged tissue. The positive correlation between longevity and urate oxidase levels among mammalian species suggests its potential role in delaying aging. Low uricase is associated with an increasing risk of Parkinson's disease and major depression.

Methods: In this research, , the pET-28a vector containing uricase gene (Aspergillus flavus) was first expressed in the BL21 strain of E.coli, and the enzyme was subsequently purified using Ni Sepharose column chromatography. SDS-PAGE was performed to ensure the purity of the enzyme. After confirming the expression, the concentration and activity of the purified enzyme were determined.

Results: According to laboratory findings, incubation at 30°C for 15 hours give the best conditions for the production of recombinant protein which has maximum activity and concentration. According to Bradford protein assay, the concentration of enzyme at the mentioned time and temperature is 0.9 mg/ml, which is the highest concentration, as depicted in the fig.1 . According to the findings, the highest activity level is related to the sample obtained from elution buffer No. 3.

Conclusion: The process performed so far indicated that it is possible to continue the activity of the enzyme successfully. Further studies on the temperature and structural stability of the enzyme will be performed. Finally, the enzyme will be stabilized by amino acid osmolytes.

Keywords: Urate oxidase, pet28a, SDS-PAGE, Ni-NTA

A-10-1513-2

Calorie restriction Increased Remyelination in a Cuprizone- intoxicated Demyelination Mouse Model of Multiple Sclerosis via Modulating Microglia polarization

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Page | 433

Introduction: Multiple sclerosis (MS) is a chronic immune-mediated demyelinating and debilitating neurological disease in the central nervous system. Increased inflammatory responses have been reported to play a critical role in the progression of MS disorder. MS hasn't definitive treatment, but it can be alleviated by changing life habits. Calorie restriction (CR) deliberate manipulation in daily diet is one of the helpful approaches to preventing metabolic and autoimmune-related disease such as MS. In this study, we attempt to investigated the remyelination potential of CR on cuprizone induced-demyelination, a model of multiple sclerosis.

Methods: To induce calorie restriction, 10% Carboxymethyl cellulose as a dietary cellulose fiber was mixed to the diet for 8 weeks. Mice were assigned randomly to 3 groups (n=10 per group). Control group: mice were fed a normal chow diet for 8 weeks. Cuprizone group: mice received a diet mixed with 0.2% cuprizone (w/w) to induce acute demyelination in C57/BL6 mice for8 weeks. Whereas Cuprizone and Calorie restriction group received a mixture of 10 % Carboxymethyl cellulose with normal diet was a second time mixed with 0.2% Cuprizone and was given to the animals for 8 weeks. Cuprizone is a copper chelator that impairs the oxidative phosphorylation in oligodenocytes. Demyelination and remyelination were studied by luxol fast blue staining. Microglia phenotypes were assessed by immunohistochemistry of Iba-1, iNOS and Arg-1, respectively. The expression of targeted genes was analyzed by real time-PCR.

Result: Luxol fast blue staining showed that myelin content was sharply increased in the corpus callosum of the CR regimen group. Moreover, the CR application significantly enhanced protein and gene expression of Sirt1, M2 microglial phenotype marker (Arg-1) and Akt1 gene expression, also caused decreasing in M1 microglial phenotype marker (iNOS), Akt2 and P53 gene expressions.

Conclusion: caloric restriction can counteract MS symptoms through alleviating inflammatory responses.

Keywords: Multiple sclerosis, Astrogliosis, Microgliosis, Demyelination, Cuprizone

A-10-1571-1

Development of enzyme-linked immunosorbent assay (ELISA) based on covalent immobilization of antibody on plate for measurement of digoxin

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Introduction: The aim of this study was designing an enzyme immunoassay based on modified ELISA with high sensitivity to detect digoxin.

Methods: The first step to develop was conjugation of digoxin to HRP (Horse Radish peroxidase) enzyme by sodium metaperiodate oxidation. Surface modification and thus assay modification was done by covalent immobilization of anti digoxin monoclonal antibody on a functional plate by 3-ATPES) 3-aminopropyltriethoxysilane.

Results: Developed ELISA had better sensitivity (0.026µg/ml) and lower variability in the measure repeated during a day, compared to conventional ELISA (0.051µg/ml). This assay detects the exact amount of digoxin. Sensitivity and specificity of a modified ELISA is higher than other methods. Measurement is performed within a few hours.

Conclusion: The availability of kits, being cheap, easy to learn, no hand washing etc, are the benefits of the ELISA and the selected method

Keywords: Digoxin, ELISA, Surface modification, covalent bonding

A-10-1576-1

Sensitivity of U937 leukemic cells to peganum harmala extract in vitro

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Introduction: Medicinal plants are presently used for cure of numerous diseases. Peganum harmala is a medicinal herb has been used for treatment of viral, bacterial and parasitic infections. The anti- proliferative, anti- inflammatory and anti-tumor effects of peganum harmala has also been revealed. Aims: In current study, cytotoxic effect of peganum harmala seed aqueous extract on U937 leukemic cells has been assessed in vitro.

Methods: U937 cells were cultured in RPMI with 10% FCS. Next the cells at logarithmic growth phase were incubated with different dosages of peganum harmala seed extract (0.1 – 2 mg/ml) for 24, 48 and 72 hours. The cytotoxicity of peganum harmala seed extract was evaluated by 3-[4, 5-dimethyl thiazol-2, 5-diphenyltetrazoliumbromide] (MTT) reduction test.

Results: Peganum harmala aqueous seed extract displayed a significant cytotoxic effect on U937 leukemic cells dose and time dependently in comparison with untreated control cells.

Conclusion: Our results presented that U937 leukemic cells were sensitive to peganum harmala aqueous seed extract in a dose and time dependent manner. Thus anti-tumoral effect of peganum harmala described by other investigators might be somewhat due to its cytotoxic features. Present therapeutic approaches in leukemia have not been very efficacious. Peganum harmala with cytotoxic effects could have potential implication in treatment of leukemic patients. Furthermore assessment of effective component (s) in the peganum harmala seed extract with cytotoxic activity and their mechanism of action could be appreciated in designing novel natural anti-proliferate/ cytotoxic remedies.

Keywords: Peganum harmala, Leukemia, Sensitivity

A-10-1573-1

Maternal & Cord Blood Signatures of Birth Weight: An Experience from Western India

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Page | 436

Introduction: Thyroid status of mother as well as neonate has profound impact on neonatal brain development. Hypothyroidism at birth is one of the preventable causes of mental retardation in chilen. Maternal thyroid disorders are known to have association with pregnancy complications. During pregnancy, production of thyroxine (T4) and triiodothyronine (T3) increases along with increase in the daily iodine requirement. Maternal hyper- and hypothyroidism have been associated with increased risk of adverse pregnancy outcomes. Gestational age at delivery and birth weight are important predictors of neonatal mortality and morbidity, and literature reports some of the complications associated with maternal thyroid disease may be secondary to preterm birth.

Methods: This study was performed at a medical college and tertiary care hospital. Eligible female participants were those who have enrolled in the hospital over a period of 5 months. The sample size was calculated on the basis of assuming two-sided type I error α =5 %, power (1-β) 95 % and correlation coefficient (ρ) 0.5, which provided the sample size required as 70. All statistical analyses performed using appropriate statistical software

Result: There is significant difference between the cord blood and maternal blood thyroid profile. Maternal TSH and thyroxin are more than that of cord blood counterparts while cord blood T3 levels found to be more than maternal T3. Lipid profile reports the significant difference between maternal and cord blood. Levels of lipid profile are more in the maternal serum as comapred to cord blood

Conclusion: Present study shows the effect of thyroid status of mother and fetus both has association with neonatal birth weight. More detailed analysis with sample collection per trimester is required to know more about the impact of various confounding factors on birth weight. Maternal TSH is better predictor than thyroxin of the neonatal birth weight.

Keywords: cord blood, birth weight, TSH, T3, T4

A-10-1508-1

MALAT1 lncRNA in patients with type 2 diabetes and its relationship with endoplasmic reticulum stress

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Introduction: Endoplasmic Reticulum (ER), which is the site of synthesis and processing of secretory and transmembrane proteins, plays an important role in cellular stress response. Loss of ER homeostasis caused by pathological stress conditions, leads to the activation of the ER stress pathway. Metastasis-associated lung adenocarcinoma transcript 1 (MALAT1), as a long non coding RNA (lncRNA), has been considered a critical regulator of gene expression and seems to be involved in the regulation of endoplasmic reticulum stress (ER stress). The present study intends to assess the expression of MALAT1 in patients with type 2 diabetes and its relationship with ER stress markers.

Methods: The study groups consisted of 57 patients with diabetes and 32 healthy individuals. The expression of MALAT1 lncRNA, as well as ATF4 and CHOP genes as the markers of ER stress were measured in peripheral blood mononuclear cells (PBMCs) by Real-time PCR. Plasma GRP78, advanced glycation end products (AGEs), and insulin were also determined by enzyme-linked immunosorbent assay (ELISA), and insulin resistance (IR) was determined by the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR)

Results: It was manifested that the expression of ATF4 and CHOP genes was increased among patients with diabetes. Although, high expression of MALAT1 was found in patient group compared to control group, this difference was not significant. The expression of ATF4, CHOP and GRP78 showed a strong correlation with glycemic control indices including FBS, HbA1c, HOMA-IR, and AGEs. Furthermore, there was a positive correlation between MALAT1 expression, and ER stress markers, including ATF4 and AGEs.

Conclusion: The results of the present study revealed enhancement of ER stress in patients with type 2 diabetes. MALAT1 showed a significant association with ER stress markers which requires further investigations to establish the connection between this lncRNA and ER stress in diabetes.

Keywords: MALAT1, Endoplasmic Reticulum stress, Type 2 Diabetes (T2D), CHOP, ATF4

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Uric acid to high density lipoprotein cholesterol ratio associated with critical care outcomes in COVID-19 patients

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Page | 438

Introduction: Loss of metabolic health such as metabolic synome condition is a key risk factor for the severity of severe coronavirus disease 2019 (COVID-19). Metabolic synome, in turn, has been found to be linked to high serum uric acid to HDL-cholesterol ratio (UHR). UHR is also a marker that increases in inflammatory oxidative stress conditions. However, the association between UHR values and the severity and mortality of COVID-19. We hypothesized whether the UHR could predict the severity and mortality of COVID-19.

Methods: The present study employed a cross-sectional design. A comprehensive electronic medical record including epidemiological, demographic, anthropometric, chronic medical histories, clinical, and laboratory data was created, from people admitted to SHMU hospitals due to a SARS-CoV-2 infection within February 20, 2020, and March 20, 2021. Only data from hospitalized and non-vaccinated cases with a COVID-19 diagnosis confirmed by real-time reverse transcriptase-polymerase chain reaction (RT-PCR) from oro- and nasopharyngeal swab specimens were included in our analysis. A total of 400 confirmed COVID-19 patients were included in the current research.

Results: Regression models were performed to evaluate the correlation between the UHR and severity and mortality of COVID-19. The UHR level was significantly higher in the severe patients ($P<0.05$). Also, the UHR level was significantly lower in survivor cases ($P<0.05$). Multivariate logistic regression analysis demonstrated that the UHR was predictor of the severity and mortality adjusted for age, sex and BMI (OR=7.4, OR=10.14 respectively).

Conclusion: In summary, the UHR index could be used as an early indicator of COVID-19 mortality. Furthermore, the study revealed that the UHR is a biochemical marker of COVID 19 severe prognosis.

Keywords: Uric acid to HDL-C ratio, severity, mortality, COVID-19

PERK inhibition in endoplasmic reticulum stress enhances cisplatin cytotoxicity in cisplatin-resistant A2780/cisR ovarian cancer cells

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Introduction: Various biochemical and pathological factors disrupt the stability of the internal environment of the endoplasmic reticulum and cause the accumulation of misfolded proteins in the lumen of the endoplasmic reticulum and finally lead to the launch of several mechanisms. The most important signaling pathways are endoplasmic reticulum stress or unfolded protein response. This signaling is caused by three endoplasmic reticulum transmembrane proteins, including PERK, IRE1α, and ATF6. The unfolded protein response and increasing resistance to anticancer ugs can be used as a pro-tumorigenic factor. The UPR signaling pathway can be used as an anticancer therapeutic strategy: Blocking the UPR signaling pathway activated following endoplasmic reticulum stress as a survival response. Raising stress endoplasmic reticulum above the threshold in cells on the UPR signaling pathway so that the cells are iven to death. Cisplatin inhibits DNA replication by adding an alkyl group to DNA and induces apoptosis caused by DNA damage. Resistance to chemotherapy ugs is one of the challenges in treating ovarian cancer. By using combined treatments, better treatment response can be observed in short treatment periods, and on the other hand, it also reduces the possibility of ug resistance.

Methods: After inducing endoplasmic reticulum stress with tunicamycin and confirming it with thioflavin dye in cancer cells and treating them with PERK inhibitor, cisplatin, and their combination, the gene expression level of PERK and PERK-dependent proteins in ug resistance with real-time PCR was evaluated. Cell viability was measured using MTT.

Results: After treating the cells with PERK inhibitor, cisplatin, and their combination, the expression level of the PERK and PERK-related gene decreased in cisplatin resistance, and cell viability decreased.

Conclusion: inhibition of PERK from the UPR pathway using GSK2606414 and their combination with cisplatin increases cisplatin toxicity in cisplatin-resistant cells.

Keywords: ER Stress, PERK, Cisplatin, ovarian cancer

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TEHRAN UNIVERSITY OF MEDICAL SCIENCES

Effect of incorporating modified nano-hyoxyapatite via Elaeagnus angustifolia extract in polycaprolactone nanofibers to odonto/osteogenic differentiation of dental pulp stem cells

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Introduction: Tooth tissue engineering is an innovative restorative method that studies substituting missing teeth with regenerated tooth or repairing damaged dental tissue. Scientific advancements in tissue engineering and stem cell technologies have demonstrated the practical application of dental stem cells, together with biodegradable scaffolds containing bioactive agents, for regulating the temporal and spatial arrangement of dental progenitor cell differentiation, activity, and proliferation. Plants are still discovering new uses in contemporary days, and combining biocompatible scaffolds with various plant extracts can beneficially enhance scaffold bioactivity. In this study, nanohyoxyapatite (nHA) was synthesized using Elaeagnus angustifolia (EA) extract and added onto polycaprolactone (PCL) nanofibers, with practical implications for odonto/osteogenic differentiation of dental pulp stem cells (DPSCs).

Methods: nHA and modified nHA via EA extract (nHA-EA) synthesized with the sol-gel technique. Then nHA and nHA-EA incorporated into PCL and blend nanofibers were prepared through the electrospinning method. The chemical properties and size of the fibers were assessed using Fourier transform infrared spectroscopy (FTIR) and Scanning electron microscopy (SEM). MTT assay was used to determine cell viability. The levels of osteogenic activity were evaluated using alkaline phosphatase (ALP) activity and Alizarin red S (ARS) staining.

Results: It was possible to create rod-like nHA and nHA-EA particles with lengths ranging from 62 to 146 nm and diameters ranging from 17 to 29 nm. The P/nHA-EA nanofibrous scaffolds prompted odonto/osteogenic achievement in the DPSCs, as confirmed by ARS assay and ALP activity.

Conclusion: As a result, the inclusion of nHA-EA in PCL scaffolds may have potential applications in dentin tissue engineering.

Keywords: Tooth tissue engineering, dental pulp stem cell, nanohyoxyapatite, Elaeagnus Angustifolia

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Comparison of biochemical and hematology markers reference intervals derived by direct and indirect procedures based on ICS cohort study

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Introduction: Reference intervals (RIs) are necessary to compare and interpret pathology results that are produced in clinical laboratories. Direct and indirect approaches have been developed to estimate RIs. We aimed to define specified RIs for routine biochemical markers using direct and indirect methods to determine differences between them in participants of the Isfahan cohort study (ICS).

Methods: Participants recruited the baseline database of ICS including 6500 adults aged 35 years and older in 2001. Participants were randomly selected from three provinces in central Iran. The Harris and Boyd method was used to define age/sex partitioning. Outliers were excluded based on Tukey's method. To calculate the central 95% for defining the lower and upper limits of each RI, the nonparametric rank method was performed, according to CLSI Ep28-A3 guidelines. To assess the potential clinical significance of the statistical findings, and statistically significant method differences for a given biomarker a bias ratio (BR) was calculated. From Fraser's theory of "allowable bias" in laboratory tests, the threshold or minimum bias limit is 0.375.

Results: Direct and indirect RIs for some biochemical factors (fasting serum glucose, LDL-C, and total cholesterol) remained stable, even before applying exclusion criteria for removing pathological samples. Direct RI for other biochemical factors including TG (UL-LL_indirect: 58-442 & UL-LL_direct: 65-368 mg/dL) and HDL-C (UL-LL_indirect:28-65 & UL-LL_direct 30-69 mg/dL) after including pathological samples showed significant differences when compared to the indirect method.

Conclusion: Data presented in the ICS clearly indicate that RIs derived from direct and indirect methods are similar, but not identical. So, for confirming these results as well as their clinical applicability of them and the importance of observed method differences further large-scale cohort studies are required.

Keywords: Reference Intervals, Direct, Indirect, Laboratory marker

Computational Analysis of Single Nucleotide Polymorphisms Associated with MicroRNA Affecting Hepatitis B Infection

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Introduction: MicroRNAs (miRNAs) have a pivotal role in Hepatitis B Virus (HBV) infection and its complications by targeting the cellular transcription factors required for HBV genes expression or by directly binding to HBV transcripts. Single Nucleotide Polymorphisms (SNPs) in miRNA genes affect their expression as well as the regulation of target genes, clinical course, diagnosis, and therapeutic interventions of HBV infection.

Methods: Computational assessment and cataloging of miRNA gene polymorphisms targeting mRNA transcripts straightly or indirectly through the regulation of hepatitis B infection by annotating the functional impact of SNPs on mRNA-miRNA and miRNA-RBS (miRNA binding sites) interaction were screened by applying various universally available datasets such as the miRNA SNP3.0 software.

Results: A total of 2987 SNPs were detected in 139 miRNAs affecting hepatitis B infection. Among them, 313 SNPs were predicted to have a significant role during the progression of hepatitis B infection. The computational analysis also revealed that 45 out of the 313 SNPs were located in the seed region and were more important than others. Has-miR-139-3p had the largest number of SNPs in the seed region (n=6). On the other hand, proteoglycans in cancer, adherens junction, lysine degradation, NF-kappa B signaling cascade, ECM-receptor binding, viral carcinogenesis, fatty acid metabolism, TGF-beta signaling pathway, p53 signaling pathway, immune evasion related pathways, and fatty acid biosynthesis were the most important pathways affected by these 139 miRNAs.

Conclusion: The results revealed 45 SNPs in the seed region of 25 miRNAs as the catalog in miRNA genes that regulated the hepatitis B infection. The results also showed the most important pathways regulated by these miRNAs that can be targeted for therapeutic purposes

Keywords: Hepatitis B, MicroRNA, Single Nucleotide Polymorphisms

A-10-1596-2

In silico analysis of Single Nucleotide Polymorphisms Associated with MicroRNA Regulating 5-fluorouracil resistance in colorectal cancer

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Introduction: The chemotherapeutic agent 5-fluorouracil (5-FU) is one of the most widely applied anticancer ugs for treating colorectal cancer (CRC) with a response rate of 50%. Because of the broad influence and reversible nature of microRNA (miRNA) on the regulation of genes expression, we believe that miRNAs may offer new insights into this resistance mechanism. Single nucleotide polymorphisms (SNPs) in miRNA genes may affect miRNA biogenesis, processing, function, and stability and provide additional complexity to 5-FU ug resistance in CRC.

Methods: In silico analysis and cataloguing of miRNA genes polymorphisms that target mRNA transcripts directly or indirectly through controlling of 5-FU chemoresistance in CRC was carried out using different publically available databases such as miRNA SNP3.0 database.

Results: We have detected 1255 SNPs in 85 miRNAs affecting 5-FU resistance which 167 of them affect 5-FU resistance in CRC. Among these 167 SNPs, 39 are located in the seed region and are more important than other SNPs.

Conclusion: It has identified that proteoglycan in cancer, adherents junction, ECM-receptor interaction, Hippo signaling pathway, TGF-beta signaling pathway, fatty acid biosynthesis, and fatty acid metabolism are the most important pathways targeted by these 85 predicted miRNAs.

Keywords: 5-fluorouracil resistance, colorectal cancer, Single Nucleotide Polymorphisms

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Expression of adenosine receptors in stem cells isolated from ovarian cancer cell lines (OVCA-3 and Caov-4)

Introduction: Ovarian cancer is one of the deadliest cancers in women. Cancer stem cells (CSCs) have been suggested as a major cause of cancer which show a significant increase in tumor tissues. Adenosine plays an important role in regulating of growth, proliferation, and death of normal and cancer cells through its receptors. Previous studies have exposed that targeting signaling pathways in CSCs is considered a promising strategy for cancer treatment. Therefore, in this study, we first examined adenosine receptors (A1, A2A, A2B, and A3) expression in stem cells isolated from ovarian cancer cell lines.

Methods: CSCs were isolated from ovarian cancer cell lines OVCA-3 and Caov-4 using mammosphere measurement. Real-time PCR was applied for the assessment of expression levels of adenosine receptors in ovarian stem cells.

Results: Our data revealed that the expression of adenosine receptors) A1, A2A, A2B, and A3) in stem cells isolated from OVCA-3 ovarian cancer cell line is higher than these cells. Moreover, we found that the expression of these receptors in Caov-4 cells were lower than stem cells isolated from Caov-4 cell line.

Conclusion: According to the importance of adenosine receptors in ovarian cancer stem cells, maybe they can be mentioned as a new strategy in the treatment of ovarian cancer that requires further and more detailed studies.

Keywords: Keywords: Adenosine receptor, Stem Cell, Ovarian Cancer

A-10-1619-1

Cloning, Expression and Purification of Filgrastim

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Introduction: Filgrastim is a recombinant human granulocyte colony-stimulating factor (rhG-CSF) and has been used as a therapeutic protein for neutropenia and chemotherapy treatment. The human granulocyte colony-stimulating factor is a hematopoietic growth factor that promotes the proliferation and differentiation of neutrophils from myeloid progenitor cells and decreases depression of white blood cell levels produced by cytotoxic agents.

Methods: Because the hormone tends to aggregate and forms inclusion bodies. Efficient production of hG-CSF using a prokaryote host is challenging. Many strategies are applied to improve protein solubility production in the cytoplasm. One of the strategies is to express the protein as a fusion protein, in this study, the SUMO-hGCSF gene was optimized based on the E. coli strain BL21 expression system and synthesized in a pUC-57 vector. Then it was subcloned into pET26b between NdeI and XhoI restriction sites. The constructed recombinant plasmid was transformed into E. coli strain BL21. The expression parameters were optimized.

Results: The highest expression level was obtained in 0.5 mM IPTG at 18°C for 12h after induction. The recombinant protein was expressed as a soluble protein. The expressed protein was first purified using NTA-Ni (2+) affinity chromatography and then its tag was cleavaged by protease. Commercially, filgrastim is produced using a recombinant strain of E. coli bacteria and in the form of inclusion bodies. Subsequently, it is necessary to spend time on solubilization and refolding to produce pure protein. This process is associated with low efficiency, as well as low reproducibility, and its protein production has little biological activity.

Conclusion: In summary, this study describes an efficient method for the soluble overexpression and purification of bioactive hGCSF in E. coli.

Keywords: Filgrastim, granulocyte colony-stimulating factor (rhG-CSF), SUMO

A-10-1467-2

Prognostic value of ANPEP expression in tumor progression: a meta-analysis

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Introduction: Alanyl membrane aminopeptidase (ANPEP) encodes a membrane-bound zinc-dependent protease termed aminopeptidase N (CD13), which belongs to a group of widely expressed ectopeptidases. The multifunctional APN is responsible for postsecretory processing. The APN is also involved in intracellular cell signaling and plays a major role in malignancies pathogenesis. The aim of the current study was o study the association between ANPEP gene expression and prognosis and clinical variables of cancer patients in a meta-analysis.

Methods: The electronic search was performed in PubMed, Scopus, Web of Science as well as Embase. Specific hazard ratios (HRs), data associated to tissue ANPEP expression and survival outcome for each study were prepared. Pooled odds ratios (OR) were applied to investigate the association of ANPEP expression and clinicopathological features in patients with cancer. Finally, 17 studies including 3001 patients with 9 different tumors were included in this meta-analysis.

Results: The pooled odds ratio showed a strong relationship between increased ANPEP expression and poor clinicopathological characteristics, such as tumor differentiation (OR=4.11, 95% confidence interval [CI]: 0.29 to 58.57), TNM stage (OR=4.21, 95% [CI]: 0.81 to 21.87), tumor size (OR=0.67, 95% CI: 0.18 to 2.61), T stage (OR=1.78, 95% CI: 0.34 to 9.23), gender (OR=4.14, 95% CI: 3.12 to 5.49) and clinical stage (OR=2.61, 95% CI: 1.15 to 5.93). Overexpression of ANPEP expression were predict of worsen overall survival in patients with different cancer (HR=1.5, 95% CI: 1.0 to 2.3; P<0.05).

Conclusion: Our results showed that ANPEP overexpression could predict unfavorable outcome in cancer patients.

Keywords: outcome, ANPEP, cancer, meta-analysis

The neuroprotective effects of gamma oryzanol on behavioral impairments and chronic neuroinflammation induced by lipopolysaccharide in male adult mice

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Introduction: Chronic neuroinflammation is responsible for multiple neurodegenerative diseases that can be caused by lipopolysaccharide (LPS), a potent stimulator and essential component of the gram-negative bacterial cell wall. Recently, natural compounds have received increasing attention as useful agents to alleviate neuroinflammation. Gamma oryzanol (ORY) is a phytochemical extraction from rice bran oil, exhibiting both antioxidant and anti-inflammatory properties. Based on this evidence, in the present study, we aimed to evaluate the neuroprotective effect of ORY against the detrimental effects of LPS, including behavioral impairments and neuroinflammation in the hippocampus of adult mice.

Methods: Adult male BALB/c mice (n=48, 12 mice per group) intraperitoneally (i.p.) received either LPS (0.75 mg/kg/day) or saline for a week. Meanwhile, animals were supplemented with ORY (100 mg/kg/day, gavage) or vehicle for 2 weeks (a week before injecting LPS and a week cotreated with LPS). After treatment, animals were subjected to behavioral assessments using a Morris water maze (MWM) and Y-maze. Then, qPCR analysis was carried out to measure the expression levels of several pro-inflammatory mediators in the hippocampus of adult mice. Furthermore, immunostaining was performed for the evaluation of astrocyte and microglial density on brain sections.

Result: Systemic LPS injections induced significant impairment in memory functions as well as increased hippocampal mRNA levels of IL-6, IL-1β, TNF-α, NF-κB, and GFAP. These findings were accompanied by the increased microglia and astrocyte density with degenerated neurons in the hippocampus of adult mice. Interestingly, ORY supplementation for two weeks could reverse the mentioned deficits induced by LPS.

Conclusion: In summary, our results demonstrate that LPS-induced neuroinflammation can be alleviated by ORY supplementation in adult mice. These findings support the idea that natural products can be beneficial against neurotoxicity.

Keywords: Hippocampus, Neuroinflammation, natural products

A-10-1569-1

In Silico Homology Modelling of Cell Surface Binding Protein of Monkeypox Virus

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Page | 448

Introduction: Human monkeypox is a zoonotic disease caused by monkeypox virus with noteworthy mortality and morbidity and characterized by smallpox like signs and symptoms. Several recent outbreaks and the need of dependable reconnaissance have raised the level of concern for this developing zoonosis. The cell surface binding protein binds to chonoitin sulfate on the cell0 surface to facilitate binding of the virion to the target cell and is found in the virion membrane and is important for monkeypox virus infection. Cell surface binding protein has been identified as one of the best immunogenic candidate proteins and allowed for preliminary investigation. Model of protein is important for further studies about design and discovery of anti monkeypox ugs.

Methods: For modeling of the protein structure, the sequence of target protein was retrieved from UniprotKB database (Accession number Q8V4Y0). The template select for the target sequence was conducted in PSI-BLAST against PDB database. The multiple sequence alignment of target sequence and selected templates was performed with Clustal Omega server. Then, structural model of the cell surface binding protein was constructed with Swiss-Model. Further, the modelled structure was validated using Procheck and ProSA, and structure with high confidence value was selected and used for analysis.

Results: The quality of final model was evaluated by various tests. ProSA Z-score (-8.61) suggests good quality for obtained model protein. Ramachanan plot indicated 92.4% of the residues in favored regions, 7.1% residues in allowed region and 1% residues in generously allowed region. Appraisal of three dimensional profile with Verify 3D showed good quality and reliability for model (98.71% of the residues had an averaged 3D-1D score≥0.2).

Conclusion: These findings indicate that modelled protein seems to be an appropriate model for further studies as cell surface binding protein structure to control the pathogenicity of monkeypox virus via ug design.

Keywords: Mokeypox, Homology Modeling, Cell Surface Binding Protein

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Molecular docking study of Flavonolignans as X-linked inhibitor of apoptosis protein (XIAP) inhibitors for the cancer treatment

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Introduction: X-linked inhibitor of apoptosis protein (XIAP) is a member of inhibitor of apoptosis protein (IAP) family responsible for neutralizing the caspases-3, caspases-7, and caspases-9. Overexpression of the protein decreased the apoptosis process in the cell and resulting development of cancer. There is an emergent need to search for possible medications and we investigated the potential of Flavonolignans against XIAP protein.

Methods: The molecular docking process was performed using Molecular Operation Environment (MOE) software to predict the mode of interaction between the best possible biological conformations of compounds in the active site of XIAP enzyme. The 2D structure of flavonolignans including silybin A, silybin B, isosilybin A, isosilybin B, silychristin, isosilychristin, and silydianin were prepared by Chem aw ultra 8.0 software and converted into PDB format by Hyper Chem7 using AM1 semiempirical method. The compounds were docked into the active site of XIAP (PDB ID: 5OQW) by MOE software. The best pose of compounds with the higher score was selected for ligand-target interaction analysis by the LigX module in MOE software.

Results: The docking results showed a high potency of isosilychristin and silydianin as XIAP inhibitors with binding energies of -14.81 and -14.21 kcal/mol, respectively. Docking studies shows that flavonolignans bind strongly with some of the amino acid residues in the active site of XIAP and these active compounds could form hyogen bonds and π-π stacking interactions with Glu314, Trp323, Leu292, Lys299, Asp309, Thr308, Met248, Trp310 and Val293.

Conclusion: The results of the study showed that two active compounds of flavonolignans have high binding affinity with XIAP and could be considered as promising compounds for the development of cancer potential inhibitors after further studies.

Keywords: Flavonolignans, Molecular Docking, XIAP Protein, Cancer

Development of functional membrane based on bacterial nanocellulose and Basil (Ocimum basilicum L) essential oil; preparation and characterization

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Introduction: Improvement in biopolymers studies has indicated their potential for variety of uses. In particular bacterial nanocellulose (BNC) gain much more attention due to its several properties.

Methods: The BNC membranes have been freeze-ied and then coated with different concentrations of basil essential oil (BEO) by spray method. The antimicrobial activity of different concentrations of BEO in the BNC membrane was evaluated against Pseudomonas aeruginosa and Listeria monocytogenes according to the disc diffusion method. The antioxidant activity of the BNC-BEO membranes was assessed by DPPH and ABTS methods. However, the conceivable interactions between BNC and BNC-BEO and morphological characteristics were investigated using a Fourier transform infrared (FTIR) spectroscopy and Field emission scanning electron microscopic (FESEM) analysis, respectively.

Result: The FESEM micrograph shows that pure BNC has a porous structure which after coating, the porous structure and orientation of the BNC fibrils were changed, and a homogeneous and smooth surface was observed. The spectroscopic results confirm that the BEO has been successfully incorporated into the BNC through hyogen bonding with the carboxylic acid groups of the BNC. The antimicrobial activity of BNC-BEO membranes demonstrated the antibacterial activity on both gram-positive and gram-negative bacteria. BNC-BEO membranes showed the antioxidant activity in a concentration-dependent manner.

Conclusion: By addition of BEO into the BNC, an antimicrobial and antioxidant membrane was developed for different applications including food packaging and wound healing.

Keywords: Bacterial nanocellulose, essential oil, antimicrobial, antioxidant

Evaluation of the Prognostic Significance of PD-1, PD-L1 and CD45RO in non-Metastatic Intestinal-type Gastric Adenocarcinoma

Introduction: Gastric cancer (GC) patients have a poor prognosis. Thus, it is imperative to identify new treatment strategies and complementary biomarkers. In this regard, we evaluated the expression pattern and prognostic significance of programmed death 1 (PD-1), programmed death-ligand 1 (PD-L1) and CD45RO+ tumor-infiltrating lymphocytes (TILs) in non-metastatic intestinal-type gastric adenocarcinoma (GAC).

Methods: Formalin-fixed paraffin-embedded (FFPE) samples and data of 70 GC patients were retrospectively collected. The immunohistochemistry was used for staining for the markers mentioned above. For PD-1 and PD-L1, positive staining was considered for tumor cells (TC) and TILs separately; CD45RO positive staining was only evaluated on TILs.

Results: In 24.3% of GCs, tumor cells expressed cytoplasmic PD-1, significantly associated with poorer survival with a hazard ratio (HR) of 2.798 (P= 0.012). Furthermore, patients with higher CD45RO+ TILs and PD-L1 on TCs had longer OS, but there were no statistically significant (HR: 1.676; 95% CI: 0.908-3.091; P= 0.099) and (HR: 1.917; 95% CI: 0.806-4.559; P= 0.141), respectively. A significant positive association was found between CD45ROhi TILs and both PD-1 (P value= 0.026) and PD-L1 (P value= 0.014) expression on TILs.

Conclusion: PD-1 overexpression on TCs but not on TILs was associated with shorter overall survival (OS). There are positive associations between CD45RO memory TILs and PD-1 and PD-L1 expression on TILs.

Keywords: PD-L1, PD-1, CD45RO, gastric cancer, Immunohistochemistry

Evaluation of the Prognostic Significance of clinicopathological factors in non-Metastatic Intestinal-type Gastric Adenocarcinoma

Introduction: Patients with gastric cancer (GC) have a poor prognosis. Therefore, novel prognostic biomarkers for GC detection in early stages are urgently needed. So, we evaluated the prognostic value of clinicopathologic markers in this study in non-metastatic intestinal-type gastric adenocarcinoma (GAC).

Methods: Data on the clinical pathology and follow-up of 70 gastric cancer patients who underwent gastrectomy from 2004 to 2017 were collected. To evaluate the prognostic significance of the markers, we performed univariate and multivariate Cox regressions. A p-value of less than 0.05 was considered significant.

Results: At the Univariate level, clinicopathological factors were significantly associated with overall survival (OS) are as follow: Tumor location with a hazard ratio (HR: 2.344; P= 0.009), Gastrectomy type (HR: 3.631; P= 0.004), LVI (HR: 1.945; P= 0.041), extracellular mucin (HR: 2.901; P= 0.002), T stage (HR: 3.382; P= 0.045), N stage (HR: 3.177; P= 0.005), TNM stage (HR: 3.730; P= 0.000). At the multivariate level, TNM-stage, tumor location, and extracellular mucin showed stronger prognostic values (P value= 0.00 and 0.003 and 0.011, respectively).

Conclusion: All histopathologic factors like tumor location, TNM stage, and extracellular mucin seem to be still the best prognostic factors for non-metastatic intestinal-type GAC.

Keywords: Histopathologic factors, gastric cancer, survival

A-10-1605-3

Evaluation of the Prognostic Significance of MMR status in non-Metastatic Intestinal-type Gastric Adenocarcinoma

Introduction: There is still a poor outlook for gastric cancer (GC). Consequently, novel prognostic biomarkers for GC patients are urgently needed. In this regard, we evaluated the expression pattern and prognostic significance of DNA mismatch repair (MMR) proteins (MLH1, MSH2, PMS2, and MSH6) in non-metastatic intestinal-type gastric adenocarcinoma (GAC).

Methods: Formalin-fixed paraffin-embedded (FFPE) samples and data of 70 GC patients were retrospectively collected. The immunohistochemistry was used for staining MLH1, PMS2, MSH2, and MSH6. Nuclear staining of tumor cells (TCs) was considered positive if 10% or more were stained. The MMR system is considered to be proficient (pMMR) if the expression of all proteins is more than 10% and deficient (dMMR) if the expression of one or more proteins was less than 10%. Survival analysis was performed to evaluate the prognostic significance of the MMR system of tumor cells.

Results: Survival analysis for MMR status indicated that GC with a proficient MMR signature had shorter overall survival (OS) than the deficient group; Although, it was not statistically significant with HR of 0.205 (95% CI: 0.28-1.497; P= 0.118).

Conclusion: Although statistically insignificant, dMMR related to higher survival in non-metastatic intestinal-type gastric adenocarcinoma. However, more study is needed to confirm this result.

Keywords: DNA mismatch repair system, gastric cancer, Immunohistochemistry

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Serum levels of sestrin-1 and sestrin-2 are associated with the presence and severity of coronary artery disease

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Page | 454

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Introduction: Sestrins family participate in diverse physiological and pathological processes mainly via regulating oxidative stress. We sought to investigate the correlation between the sestrin-1 and sestrin-2 levels and the severity of coronary stenosis.

Methods: A total of 88 patients including 39 non-CAD subjects, 31 stable and 18 unstable CAD patients who underwent coronary angiography were enrolled in this study. Fasting blood glucose (FBG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C), total cholesterol (TC) and triglycerides (TG) were determined by enzymatic methods and hs-CRP was determined by immunoturbidometric method. Plasma sestrin-1 and sestrin-2 levels were measured using commercially available ELISA kits.

Results: The three groups were not significantly different in terms of sex distribution, age, Body Mass Index (BMI), FBG, TG, and blood pressure. Serum levels of TC and LDL-C were significantly lower in the unstable-CAD group than in the stable-CAD group. The unstable CAD patients also had lower serum HDL-cholesterol levels than the stable CAD patients and non-CAD subjects. The levels of sestrin-1 were significantly lower in both unstable (17.8 ± 4.6 ng/ml) and stable (20.0 ± 4.3 ng/ml) groups compared to control group (22.9 ± 3.6 ng/ml), but did not differ between the patients with stable and unstable CAD. The levels of sestrin-2 were significantly lower in both unstable (3.32 ± 0.75 ng/ml) and stable (3.61 ± 0.84 ng/ml) groups compared to control group (4.21 ± 0.76 ng/ml), but no differences were seen between the patients with stable and unstable CAD. In the whole study subjects, serum sestrin-1 ($p < 0.001$) and sestrin-2 ($p < 0.001$) were negatively correlated with the coronary artery score.

Conclusion: This data suggests that there is a negative relationship between the levels of sestrin-1 and sestrin 2 with the severity of CAD.

Keywords: Coronary artery disease, sestrin-1, sestrin-2

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Assessment of the relationship between Red Blood Cell Distribution Width (RDW) and oxidative stress indexes in patients with coronary artery disease

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Page | 455

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Introduction: Red blood cell distribution width (RDW), a measure of the variability in size of erythrocytes, has been shown to be a strong predictor of adverse cardiovascular events. The biological mechanisms involved are not fully understood, but may include oxidative stress. We sought to investigate the relationship between RDW and markers of oxidative stress in patients with coronary artery disease (CAD).

Methods: The study group enrolled 108 consecutive patients (including 39 non-CAD subjects, 31 stable and 38 unstable CAD patients) who underwent coronary angiography for evaluation of chest pain. Fasting blood glucose, lipid parameters, hs-CRP and hematological indices were determined by routine laboratory methods. Lipid peroxide levels in plasma and the erythrocyte membrane were measured using a fluorimetric method. Total antioxidant status and glutathione (GSH) levels in plasma were determined using spectrophotometric methods.

Results: Lipid peroxidation levels [measured as thiobarbituric acid-reactive substances (TBARS)] were significantly higher in the erythrocyte membrane of stable CAD patients compared with non-CAD subjects. No significant difference was observed in the serum levels of TBARS among the three groups. The levels of TAC were significantly lower in both stable and unstable groups when compared to that of the control group, but did not differ between the patients with stable and unstable CAD. In addition, no significant difference was observed in the serum levels of GSH among three groups. Membrane TBARS was positively correlated with RDW in all groups. By multivariate analysis, membrane lipid peroxidation remained directly associated with of RDW.

Conclusion: Data from the present study showed an independent association between lipid peroxidation of erythrocyte membranes and RDW. These findings suggest that oxidative stress may be a potential underlying biological mechanism for increased RDW in CAD patients.

Keywords: Coronary artery disease, red cell distribution width, Oxidative stress

A-10-1110-2

Effect of L-serine on biochemical markers of renal function in STZ-induced diabetic mice

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Introduction: L-serine supplements enhance glucose homeostasis and mitochonial function. They also reduce neural death and occurrence of autoimmune diabetes in NOD mice. Therefore, L-serine has been suggested as a therapeutic option for diabetes. However, there are not sufficient studies regarding its effects on biochemical markers of renal function in diabetes. So, this study aimed to evaluate the effects of daily L-seine intake on biochemical markers of renal function in STZ-induced diabetic mice.

Methods: Eighteen C57BL/6 male mice (weight 20–25 g) were randomly divided into three groups. Two of the groups were induced with diabetes by a single intraperitoneal injection of freshly prepared streptozotocin. Following this, diabetes in the two groups was confirmed by measuring their blood sugar. A group of diabetic mice was treated with 300 mg/day of L-serine in water. After for 4 weeks levels of serum total protein, urea, creatinine and albumin were measured Finally, all the data were analyzed with the ANOVA test.

Results: The results showed that the level of total protein and urea had significantly decreased and increased in the diabetic group in comparison to the non-diabetic control, respectively. However, there was no significant difference between treated diabetic mice with L-serine and the diabetic control group in all markers.

Conclusion: It seems that L-serine does not have a considerable effect on biochemical markers of renal function in STZ-induced diabetic mice.

Keywords: L-serine ‹Total protein ‹Urea ‹Creatinine ‹Albumin ‹STZ-induced diabetic mice

A-10-1110-3

Effect of L-serine on blood glucose of STZ-induced diabetic mice

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Introduction: Recently, the protective role of L-serine in diabetes has been shown by some studies. L-serine supplements enhance glucose homeostasis and reduce the occurrence of autoimmune diabetes in NOD mice. Moreover, it was found that a high L-serine concentration is correlated to the improvement of insulin secretion and sensitivity. This study aimed to evaluate the effects of daily L-serine intake on the level of blood glucose of STZ-induced diabetic mice.

Methods: Eighteen C57BL/6 male mice (weight 20–25 g) were randomly divided into three groups. Two of the groups were induced with diabetes by a single intraperitoneal injection of freshly prepared streptozotocin. Following this, diabetes in the two groups was confirmed by measuring their blood sugar. After that, a group of diabetic mice was treated with 300 mg/day of L-serine in water for 4 weeks. Their blood glucose was monitored during this time regularly by a glucometer. Finally, the serum level of glucose was measured and all the data were analyzed with the ANOVA test.

Results: The level of blood glucose which had significantly raised in the diabetic group with no treatment, declined significantly in the group treated with L-seine.

Conclusion: The results of this study suggest the possible role of L-serine in glucose homeostasis in diabetes. However further investigation is needed in this field.

Keywords: L-serine, Blood glucose, Diabetes

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Quercetin loaded liposomes effectively induced apoptosis and deceased the EGFR expression in colorectal cancer cells

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Introduction: EGFR is one of the tyrosine kinase receptors increasingly expressed in colorectal cancer (CRC) cells and its inhibition is effective in cancer treatment. Quercetin is also a flavonoid with anti-cancer effects. However, its pharmaceutical applications are limited by low stability, insufficient bioavailability, poor solubility, and poor permeability. This study aimed to enhance the cytotoxicity of quercetin against SW48 colorectal cancer cells and evaluate its effect on the inhibition of EGFR gene expression.

Methods: the lipid thin-film hyation method was used to synthesize quercetin-loaded liposomes, and characterization was done via TEM and DLS, and HPLC analyses. Then, cytotoxicity of quercetin-loaded liposomes on the CRC SW48 cell line, as well as the apoptosis incidence, and the expression of the EGFR gene in these cells, was investigated by MTT, flow cytometry, and real-time PCR.

Results: The produced nanoparticles were spherical, uniform, and in size of 150±10 nm. HPLC analysis revealed a 98% loading capacity for quercetin. Although both free quercetin and loaded on liposomes showed considerable cytotoxicity against cancer cells, the activity of the combined form was much higher. So that 50 µg.L-1 of this compound reduced the viability of SW48 cells by more than 80% (IC50: 10.6 µg.L-1), while the viability of free quercetin-treated cells was 66% (IC50: 18.7 µg.L-1). The apoptosis induced in the cells treated with quercetin-loaded nanoliposomes was roughly double compared to free quercetin (54.8% versus 27.6%). However, the EGFR gene expression was significantly lower in cells treated with quercetin-loaded liposomes compared to the quercetin alone.

Conclusions: Quercetin in combination with nanoliposomes presents a superior ability to inhibit cell proliferation, induce apoptosis, and inhibit EGFR expression than free quercetin.

Keywords: Cancer, Quercetin, CRC, EGFR, Nanoliposomes, Cytotoxicity

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The Effects of Silibinin on Apoptosis, Angiogenesis, and Migration of Cancer Cells: Gene Expression and Signaling Pathways

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Introductions: Silibinin (SB) is considered the major bioactive component of the natural compound silymarin; an extract from the seeds of Silybum marianum that contains flavonolignans and flavonoids.SB possesses well-known health-promoting properties such as hepatoprotective, anti-inflammatory, and anti-cancer effects over the last 50 years. This review aims at a systematic summary of known information on the anti-cancer effects of silibinin against various carcinoma cells including breast cancer, skin cancer, colon cancer, gastric cancer, cervical cancer, prostate cancer, ovarian cancer, bladder cancer, and lung cancer. Furthermore, we investigated the ug-induced modulation of gene expression and signaling pathways responsible for tumor suppression, cell growth and apoptosis, autophagy, migration and invasion, cell cycle kinetics, and angiogenesis involved in these cancers, as well as the synergistic effects of SB and chemotherapy ugs.

Methods: For this systematic review, we identified 75 papers for the search terms silymarin, silibinin, anti-cancer effects, and cancerous gene expression and signaling pathways from electronic databases including PubMed, Embase, and the Web of Science. Among them, only original articles that met eligibility criteria and investigated gene expression and signaling pathways involved in cancer cells were selected for analysis. These publications were analyzed from both molecular and clinical points of view.

Results: According to recent research, silibinin can mediate the expression of genes involved in the mitochonial apoptosis pathway [Bcl-2/Bax, BNIP3, mtor]; ROS/receptor-mediated apoptosis [AIF, Caspase 3,8,9, PARP]; cell growth and survival [Notch-1, Akt, MAPK, Survivin, ERK1/2, Cyclins (D1, D3, A, and B1), CDKN1A, CDKN1B, p53, GADD45, AP-1, SMAD, and c-MYC]; transcription factors [NF-κB, HIF1α, STAT3] and angiogenesis and metastasis [VIM, MMP-2, MMP-9, KRT18, KRT19, ZEB1, COX-1, COX-2, VEGF, NOS, NOS3, INOS, HOXB3] in various cancer types.

Conclusion: Silibinin can inhibit the proliferation, migration, and angiogenesis of various cancer types by regulating the molecular mechanisms involved in carcinoma cells.

Keywords: silibinin, apoptosis, angiogenesis, migration, cancer cells

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Relation of adiponectin paraoxonase and hsCRP with obstructive sleep apnea severity

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Introduction: Obstructive sleep apnea (OSA) is a highly prevalent sleep disorder which has a close relation with obesity and adipose tissue distribution. Adiponectin and leptin as two important adipokine play a crucial role in whole body metabolism and pathophysiological conditions like insulin resistance, dyslipidemia and inflammation.

Methods: 70 polysomnography (PSG) confirmed OSA patients included in this cross-sectional study. apnea-hypopnea index (AHI) and average and minimal SpO2 as indicators of OSA determined by PSG and serum levels of adiponectin, leptin, hsCRP were measured using ELISA kits. Moreover, paraoxonase activity (PONase) were measured.

Results: AHI indicated an inverse correlation with adiponectin and PONase and positive relation with hsCRP. Adiponectin positively correlated with average and minimal SpO2 and inversely related with hsCRP. Finally, leptin just inversely correlated with PONase.

Conclusion: the relation of adiponectin, hsCRP and PONase with AHI as marker of disease severity showed a possible role of adiponectin oxidative stress and inflammation with pathogenesis of OSA.

Keywords: Adiponectin, oxidative stress, inflammation, obesity

A-10-1597-2

Expression of FNDC5, GLUT4 genes in skeletal muscle following consumption of garlic aqueous extract and resistance exercise in diabetic rats

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Introduction: Obesity and its metabolic diseases such as diabetes are considered as one of the problems of global societies. An important step in this direction is to find compounds or solutions which can convert white adipose tissue to brown adipose tissue.The aim of this study was to investigate the effect of garlic aqueous extract and four weeks of resistance training on the expression of FNDC5, GLUT4 genes in skeletal muscle of diabetic rats.

Methods: In this study 48 male Wistar rats weighing 180 to 250 g divided into six groups (n=8): healthy control (C), diabetic control (D), diabetic with garlic extract 50 mg/kg body weight (bw) (D+50), diabetic with garlic extract 200 mg/kg bw (D+200), diabetic resistance training (D+Ex), and diabetic resistance training with garlic extract 200 mg/kg bw (D+Ex+200). Mice became diabetic using streptozotocin. The resistance training program was performed in two stages, each of which lasted two weeks. Exercises were performed three days a week, every other day. Resistance training included climbing a one-meter ladder with weights attached to the mice tails.

Results: the expression of FNDC5 gene was increased in all intervention groups compared to group D, and the highest increase in the expression of FNDC5 gene was related to group D+Ex+200, but this increase in expression was not significant. Also, GLUT4 gene expression did not show any significant difference in the intervention groups compared to the diabetic control group.

Conclusion: the expression of skeletal muscle FNDC5 and GLUT4 genes increased insignificantly following the simultaneous use of garlic extract and resistance exercise, which are probably to be noticeable with prolonged treatment time. All of these changes in the direction of browning White adipose tissue and reduce the complications and treatment of diabetes.

Keywords: Garlic Extract, Resistance Training, FNDC5 Gene, GLUT4 Gene, Type 2 Diabetes

17th National Congress of Biochemistry & 8th International Congress of Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

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Isolation, Characterization and Genomic Analysis of vB_PaeP_TUMS_P121, A Polyvalent Lytic Bacteriophage against Pseudomonas aeruginosa

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Introduction: Pseudomonas aeruginosa is an opportunistic human pathogen that can cause life-threatening nosocomial infections. The alarming increase in antibiotic resistance has led to an urgent need for alternative therapeutic approaches, such as phage therapy, that has shown promising results in many studies. In this study, P121, a new lytic Pseudomonas phage, was isolated and characterized. Materials and

Methods: Untreated municipal and hospital wastewater samples were collected and screened. The host range determination was performed against standard strains and clinical isolates. The morphological characterization of the phage was made by transmission electronic microscopy (TEM). Then, the phage genomic DNA was extracted, sequenced and analyzed.

Results: Morphologic, genomic and phylogenetic analysis indicated that vB_PaeP_TUMS_P121 is a member of the genus Litunavirus, belonging to Schitoviridae family. Whole-genome sequencing showed that it has a genome of 73,001 bp that contained 91 predicted coding sequences. No genes involved in virulence or lysogeny pathway were found in the genome. It exhibited polyvalent properties and could infect some other bacterial pathogens in the Pseudomonadales order, including Acinetobacter baumannii and Pseudomonas syringae than Pseudomonas aeruginosa itself

Conclusions: The present study provides some basic information about Pseudomonas phage P121. Obtained data showed that P121 is potentially safe when it comes to therapeutic applications and it lays the groundwork for further research on treatment of P. aeruginosa infections.

Keywords: Pseudomonas aeruginosa, Multi-ug resistance, Phage therapy, Genome sequencing

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Specific cellular internalization and pH-responsive behavior of doxorubicin loaded PLGA-PEG nanoparticles targeted with anti EGFRvIII antibody

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Introduction: Antibody-conjugated nanoparticles have attracted much attention in the field of cancer treatment due to the enhancement of the tumor cell response to anticancer ugs as well as reducing the side effects of chemotherapeutic agents on healthy tissues. In this study, we loaded doxorubicin (DXR) in PLGA-PEG (D,L-lactic-co-glycolic acid)-(polyethylene glycol) biocompatible polymeric nanoparticles (NPs) and then conjugated with anti-EGFRvIII antibody. The resulting nanoparticles had remarkable sensitivity to pH decrease and were capable of targeting specific cells.

Methods: To this aim, PLGA-PEG-COOH was used for the synthesis of nanoparticles and stabilized by polyvinyl alcohol (PVA) according to the nanoprecipitation method. The carboxylic groups on the surface of PLGA-PEG NPs were activated by EDC/NHS and covalently conjugated to amino groups of the monoclonal antibody. The prepared NPs were characterized by Zetasizer and transmission electron microscopy (TEM). The resulting NPs were evaluated in terms of entrapment efficiency (EE), ug loading efficiency (DLE), ug-release profile, and cell internalization. Intrinsic cytotoxicity was assessed by the MTT, apoptosis (Annexin V-PI) and cell cycle assays.

Results: The in vitro ug release assessment of conjugated particles (MAb-DXR-PLGA NPs) showed a slow sustained DXR release in physiological pH (7.4) values, while the initial ug release was markedly higher (the 1.9 fold) in acidic pH (6.5) ranges. The selectivity for cellular internalization of MAb-DXR-PLGA NPs into U87MG vIII cells (overexpressing EGFRvIII) in comparison with U87MG cells (lacking EGFRvIII expression) was also confirmed. The MTT assay demonstrated that the cytotoxicity of MAb-DXR-PLGA NPs against U87MG vIII cells was more pronounced when compared with BSA-DXR-PLGA NPs. The results of the MTT assay were also confirmed by apoptosis and cell cycle assays.

Conclusion: Our findings suggest that the designed anti-EGFRvIII MAb-DXR-PLGA NPs could be considered as a proper option for targeted ug delivery systems due to pH sensitivity and specific cellular internalization.

Keywords: PLGA-PEG-COOH, Doxorubicin, EGFRvIII, Monoclonal antibody, Cell cycle, Apoptosis, pH responsive

A-10-1632-2

The Emerging role mir-128 in Development and Treatment of Glioblastoma

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Introduction: Glioblastoma is the most common type of brain tumor with high recurrence and fatality rates. There are several evidences that our lack of effective therapies is related to our increasing recognition that glioblastoma is a molecularly heterogeneous disorder. MicroRNAs are non-coding RNAs of proteins that are involved in regulating gene expression after transcription. Impaired regulation of gene expression could lead to malignancy. On the other hand, it can be said that improper expression of microRNAs can lead to cancer in two ways: first, through upregulating could suppressed tumor-inhibiting gene, and second, By down-regulation, it causes inability to mediate the tumor cell growth.

Methods: Keywords such as MicroRNA, Glioblastoma, etc have been searched in the Google Scholar database and after reviewing the articles, the results have been summarized.

Result: In glioblastoma the mir-128, which has antitumor properties, is reduced. Recently researchers have shown that upregulation of mir-128 expression, significantly decreased tumor proliferation and size. Additionally, Mir-128 modulates various oncogenes, including transcription factor E2F3a, and epidermal growth factor receptors EGFR and PDGFR. Consistently, one of the most identified targets of Mir-128 is Bmi-1 (B lymphoma Mo-MLV insertion region 1 homolog). The Bmi-1 Protein plays a pivotal role in suppressed aging and cell death. These proteins have no enzymatic activity and acts as a regulator of the PRC1 complex. In glioblastoma, Bmi-1 increases so if the amount of mir-128 increases and leads to a decrease in Bmi-1 levels, aging and apoptosis of tumor cells occur.

Conclusion: Since we are facing challenges in the treatment of glioblastoma, such as ug resistance and blood-brain barrier, etc. increasing mir_128 can be very helpful for suppressing the tumor of these patients.

Keywords: MicroRNA, Glioblastoma, Cell Death, Bmi-1

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A-10-1597-3

Expression of YBX2 gene in skeletal muscle and serum levels of ANGPTL8 following consumption of garlic aqueous extract and resistance exercise in diabetic rats

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Introduction: Activation of BAT increases glucose uptake, oxidation of fatty acids and improves diabetic conditions. Ybx2 (Y-box binding protein 2) has been identified as a regulator in brown adipose tissue (BAT) activation. The aim of this study was to investigate the effect of garlic aqueous extract and four weeks of resistance training on the expression of YBX2 gene in skeletal muscle and serum levels of ANGPTL8 in diabetic rats.

Methods :In this study 48 male Wistar rats weighing 180 to 250 g divided into six groups (n=8): healthy control (C), diabetic control (D), diabetic with garlic extract 50 mg/kg body weight (bw) (D+50), diabetic with garlic extract 200 mg/kg bw (D+200), diabetic resistance training (D+Ex), and diabetic resistance training with garlic extract 200 mg/kg bw (D+Ex+200). The resistance training program was performed in two stages, each of which lasted two weeks. Exercises were performed three days a week, every other day. Resistance training included climbing a one-meter ladder with weights attached to the mice tails.

Results: The concentration of ANGPTL8 in all intervention groups did not show a significant change compared to group D. a significant difference was seen only between the D+200 and D+Ex groups (P =. / 044). YBX2 gene expression in D+50, D+200 and D+Ex groups did not show a significant increase compared to D group, while YBX2 gene expression in D+Ex+200 group was shown a significant increase compared to D group (p=0.0247).

Conclusion: Simultaneous use of garlic extract and resistance exercise play an important role in increasing YBX2 gene expression. So far, the effect of garlic plant extract along with resistance exercise on YBX2 gene expression has not been investigated. It seems that the use of this protocol increases the expression of this gene and increases the activation of BAT, thus reducing the symptoms of diabetes.

Keywords: Garlic Extract, Resistance Training, YBX2 Gene, ANGPTL8, Type 2 Diabetes

A-10-1652-1

The effect of hyo-alcoholic extract of Eryngium Billardieri on kidney's oxidative stress parameters of type 2 diabetic male wistar rats

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Introduction: Eryngium billardieri which is belong to apiaceae family and its main habitat is Iran, has a long history of being used as an antidiabetic agent. in this experimental research we try to investigate the effect of hyoalcoholic extract of E.Billardieri (EEB) in diabetic rat's kidney function.

Methods: forty-two male Wistar rats (215 ± 15 g) were divided by accident into two groups : group 1(n=6): normoglycaemic control (NC) and group 2 (n=36) that had High Fat diet (HFD) and after two weeks were fasted overnight and received streptozotocin 30 mg/kg IP. Diabetes mellitus (fasting blood glucose ≥ 150 mg/dl) was confirmed 1week later. Then the rats were randomly grouped into six groups (n = 6): diabetic control (DC), diabetic + 100 mg/kg extract (EEB-L), diabetic + 300 mg/kg extract (EEB-M), diabetic+500 mg/kg extract (EEB-H), diabetic +2.5 mg/kg glibenclamid (Glib), diabetic + 200 mg/kg metformin(MET) . They were treated daily by gavage for 10 weeks. At the end of the experiment, biochemical assessment was performed by measuring total oxidant and total antioxidant statusvia measuring superoxide dismutase (SOD), catalase (CAT), and malondialdehyde (A) levels .

Results: the level of SOD ($P<0.005$) and CAT ($P<0.05$) significantly decreased in DC compared with NC, while A increased ($P < 0.01$). After administration of 70 days, a significant difference in the level of SOD and A of EEB-H comparing to DC ($P < 0.05$) was observed.

Conclusion: This study indicated that receiving hyo-alcoholic extract of E.Billardieri , especially high dose of 500 mg/kg could improve oxidative stress condition in diabetic rats as the same as or even better than metformin and glibenclamide.

Keywords: Diabetes mellitus, Eryngium Billardieri, Oxidative stress

A-10-1654-1

Evaluation of the expression of induced genes in response to dehyation stress of Camelina calli

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Introduction: Drought is one of the most important factors in reducing plant yield in arid and semi-arid regions in the world. The rate of yield reduction varies depending on the intensity of stress during the growing period and tolerance of the crop. Increasing air temperature during the growing season, especially in the summer months, increases the severity of dehydration stress in the plant (Kagale et al., 2014). Therefore, selecting cultivars that are more tolerant of dehydration will ensure higher yields.

Methods: To study gene expression, first callus samples were treated with liquid nitrogen and to study the effect of drought stress on gene expression, this sample was sent to Zagros Bioidea Company located in Razi University incubator. Gene expression was performed through microarray technology. The microarrays were designed using Imaxio, which is accelerated by agile technologies. These technologies have been approved for microarrays. For this purpose, 60 nucleotide probes were used to study the expression of genes.

Results and discussion: The results of DNA microarray experiments showed that many genes in drought stress conditions in Camelina plant significantly increased expression. There are seven different genes that have increased expression almost six times as much as the control. In the research of Wang et al., In a study on Arabidopsis taliana under drought stress conditions, they saw a significant increase in ABF4 factor (Hwang et al., 2019). CRK3 protein kinase plays an important role in controlling cell cycle progression in G2 / M phase transfer

Keywords: Gene expression, Drought stress, Camelina sativaL., Microarray

A-10-1213-1

Abemaciclib combined with Endocrine Therapy for the Adjuvant treatment of hormone receptor positive (HR+) HER2 negative breast cancer: A systematic review with statistical descriptions

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Introduction: In MONARCH2 (NCT02107703), abemaciclib plus fulvestrant after endocrine therapy (ET) demonstrated a high rate of progression-free survival (PFS) and superior efficacy for patients within hormone receptor-positive (HR+) HER2-negative metastatic breast cancer (MBC). In this systematic review, symptoms, global health-related quality of life (HRQoL), functioning, weight changes, and age-based improvement in Abemaciclib plus ET were statistically calculated and evaluated in detail.

Methods: A systematic review using the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guideline was conducted. Medline and PubMed databases were used to extract the required clinical studies. Eventually, results were reported as a risk ratio (RR) with a 95 percent confidence interval using the Cochrane–Mantel–Haenszel method for meta-analysis.

Results : A total of 5 studies that were examined careful scrutiny of the MONARCH 2 various dimensions were with the same society as the previous purpose, 669 patients were enrolled and randomly assigned to receive abemaciclib plus fulvestrant (n = 446; median age=59) or placebo plus fulvestrant (n = 223; median age=62). The estimated median difference in PFS in the abemaciclib + ET arm compared to the placebo + ET arm was 9.5 months. Furthermore, abemaciclib + ET with no significant difference independent of patient age and weight accelerated the healing process. Specifically, patients in the abemaciclib arm, compared with the control arm, experienced significantly delayed symptoms of pain, fatigue, nausea and vomiting, and physical and social functioning. While higher rates of adverse events were reported in older patients with other conventional treatments, they were manageable with dose adjustments and concomitant medication.

Conclusions: Treatment with abemaciclib plus fulvestrant has resulted in a statistically significant median PFS improvement for patients with HR-positive, HER2-negative MBC. Abemaciclib as an adjunct substantially delayed the receipt of subsequent chemotherapy, and it accelerated treatment.

Keywords: Abemaciclib, Breast Cancer, PFS

A-10-1618-1

The Emerging role of micro RNA 21 in the Gastric Cancer Diagnosis

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Introduction: Micro RNAs are small, non-coding RNA sequences (approximately 22 nucleotides) found in plants, animals, and some viruses which mediates RNA surveillance and epigenetic regulation. Posttranscriptional regulation of gene expression through microRNAs also plays a critical role in mediating different human tumors. Also, these could act as a tumor suppressor or oncogenes. In addition, these are associated with cancer progression and development. One of the first oncomiRs found in a variety of cancers was micro RNA21 (miR-21).

Methods: Search for keywords such as micro RNA, miR-21, and gastric cancer have been done in the Google Scholar and PubMed database. According to the English language criteria and the novelty (2018_2022) of the articles, the articles are selected and then studied and their abstracts are taken in the direction of the intended purpose.

Result: Recent studies have focused on the diagnostic and prognostic value of miR-21 as well as its role in the ug resistance of human malignancies. In summary, upregulation of miR-21 could attenuate the gastric tumor inhibitory proteins and enhances the oncogenic proteins expression. The miR-21 could promotes gastric cancer cell progression through oncogenic and anti-apoptotic signaling pathway.

Conclusion: In patients with gastric cancer, increased expression of miR-21 in the blood can be used as a non-invasive method in the early diagnosis of gastric cancer patients. The expression of this micro RNA in the serum could be considered as a diagnostic marker.

Keywords: microRNA, Malignancy, Gastric Cancer, miR-21

Transcriptome analysis confirmed CHGA gene and hsa-miR-137 as critical biomarkers in the CRC pathogenesis

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Introduction: Colorectal cancer (CRC) is one of the most prevalent cancers worldwide. The prognosis of this cancer is heavily dependent on early detection. This study aimed to identify the mRNA-miRNA network involved in CRC pathogenesis as diagnostic biomarkers using a systems biology approach.

Methods: We performed a transcriptome analysis using weighted gene co-expression network analysis (WGCNA) on online microarray datasets of coding (GSE81558) and non-coding (GSE108153) RNAs from CRC patients. To start with, we determined the differentially expressed genes/miRNA using limma packages. Afterward, the highly correlated genes and miRNAs were identified with specific WGCNA packages. Finally, common hub-genes and their specific miRNAs are coupled by Venn diagrams and TargetScan databases.

Results: Using the WGCNA algorithm and TargetScan database, we identified and validated upregulated hsa-miR-137 and downregulated Chromogranin A (CHGA) as a target gene of this miR among 32 hub-miRs and 14 hub-genes in CRC. Based on the Human Protein Atlas database, CHGA expression was downregulated in CRC tissues. Also, the CCLE database showed a high level of CHGA expression in primary (ECC4, SW1463, KM12, and TGBC18TKB) compared to metastatic (NCIH716, SNUC1, and SW626) cell lines.

Conclusion: In this study, the CHGA gene and its specific hsa-miR-137, were suggested as biomarkers prone to CRC diagnosis and prognosis in a systems biology approach. Further laboratory confirmation can validate the findings of this study.

Keywords: CRC, Biomarker, CHGA, hsa-miR-137, WGCNA

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Influences of the COVID-19 severity and gender on CCR2 and DPP9 expression

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Introduction: The pathophysiology of the severe types of COVID-19 highly depends on hyper-inflammatory reactions. CCR2 and DPP9 are two fundamental molecules that support the development of inflammation. This study aimed to assess the gene expression of CCR2 and DPP9 in COVID-19 patients different with disease severity.

Methods: Based on WHO, 470 patients (235 men and 235 women) were classified with RT-qPCR-confirmed COVID-19 test into moderate, severe, and critical groups. Also, one huned (50 men and 50 women) healthy subjects were selected as the control group. Peripheral blood mononuclear cells were collected and used for RNA extraction. Real-time PCR was used to evaluate the gene expression of DPP-9 and CCR-2. A p-value less than 0.05 considered as statistically significant differences.

Results: Compared to healthy controls, the COVID-19 patients in the severe stage revealed higher levels of CCR2 and DPP9. CCR2 and DDP9 expression levels signifiicantly varied between each COVID-19 form in both genders and between the moderate, severe, and critical forms. Compared to female patients in severe group, the male patients with severe COVID-19 exhibited higher levels of CCR2 and DPP-9. Compared to male patients, in the moderate and critical groups, female patients exhibited higher levels of CCR2 and DPP-9.

Conclusion: CCR2 and DPP9 are two fundamental molecules in the development of inflammation. We observed that COVID-19 patients with various disease forms had significantly higher levels of DPP-9 and CCR-2 expression. There were also considerable differences between male and female patients with different disease patterns. Therefore, it seems crucial to consider the disease severity and gender to manage COVID-19.

Keywords: COVID-19, CCR2, DPP9, Disease severity

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Effects of gender and disease severity on HLA-C methylation in COVID-19 patients

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Introduction: Viral infections and agents can exert epigenetic effects, such as methylation, on different genes. HLA-C is a critical player in immune defense and NK cell functions and is linked to many diseases, including viral infections. This study's focus was to investigate the HLA-C methylation in COVID-19 with different disease severity.

Methods: Based on WHO, 470 patients (235 men and 235 women) were classified with RT-qPCR-confirmed COVID-19 test into moderate, severe, and critical groups. Also, one huned (50 men and 50 women) healthy subjects were selected as the control group. Peripheral blood mononuclear cells were collected and used for DNA extraction. To determine the methylation status of the HLA-C, the methylation-specific PCR (MSP) were used. A p-value less than 0.05 considered as statistically significant differences. **Results:** HLA-C methylation has decreased in all COVID-19 stages in men and women. In different stges, HLA-C methylation was significantly more in men than in women as follows: moderate (men: %52.3, women: %41.0), severe (men: %64.86, women: %43.42), critical (men: %60.07, women: %42.33), and total patients (men: %56.97, women: %45.52). The severe group of just in men participants significantly showed the highest methylation levels among all groups .

Conclusion: HLA-C has a vital role in immune defense and NK cell functions and and strongly involved in immunity against viral infections. Our study founds that was significant HLA-C methylation decreasing in COVID-19 patients with different forms of the disease. Moreover, HLA-C methylation were higher in men than in women with different disease. Therefore, it seems crucial to consider the gender and disease severity for managing COVID-19.

Keywords: HLA-C, Methylation, Epigenetic, COVID-19, Disease severity

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Evaluation of the Effect of the Methotrexate on Expression Changes of CPEB2 gene in Acute lymphoblastic leukemia

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Introduction: and purpose: The aberrant proliferation and differentiation of a clonal population of lymphoid cells play a role in the pathogenesis of ALL. In cancer tissues, CPEB2 levels are elevated, which promotes this kind of cancer cell migration and proliferation. This work aimed to investigate the effects of methotrexate on the expression of the CPEB2 gene in an acute lymphoblastic leukemia cell line.

Methods: In the current research, two concentrations of Methotrexate were prepared: 1μM and 10μM at 72 hours. The Jurkat E6.1 cell line was purchased from Pasteur Institute and treated with prepared doses of the MTX 72 hours after cell passage. The expression changes of CPEB2 and GAPDH were studied using Real-Time PCR after RNA extraction and cDNA synthesis.

Results: The results of our research showed that after 72 hours of treatment with methotrexate at concentrations of 1 μM and 10 μM, the expression of CPEB2 reduced in comparison to the GAPDH housekeeping gene. The results showed a statistically significant increase in CPEB2 gene expression after 72 hours at a concentration of 1 M and10 M. At 72 hours, these changes comprised 1 μM (0.502) and 10 μM (0.701). (P <0.001)

Conclusion: The findings of the current investigation indicate that changes in CPEB2 expression following treatment with methotrexate at two concentrations were successful in lowering CPEB2 expression. Because the medicine could reduce gene expression in two concentrations in 72 hours, there is evidence that methotrexate has positive potential and effectiveness. (p-value 0.001).

Keywords: Methotrexate, CPEB2, GAPDH, Acute lymphoblastic leukemia

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Investigating changes in thyroid hormones in patients referred to Khorramabad Mehr Psychiatric Hospital in 2021-2022

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Page | 474

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Introduction: Usually, the thyroid regulates various body functions by releasing constant levels of thyroid hormones. Any thyroid functioning problem can lead to an imbalance in the thyroid level, which can affect the body in many ways. Thyroid imbalance can also lead to mood problems such as depression and anxiety. For a long time, researchers have known that people with thyroid diseases are more likely to suffer from depression and vice versa. Nevertheless, with the increase in the diagnosis of anxiety and depression, it seems necessary to re-examine this issue.

Methods: The results of thyroid tests of 500 patients referred to Mehr Khorramabad Psychiatric Hospital were included in this study.

Results: Subclinical hyperthyroidism (n=15/55; 27.27%), subclinical hypothyroidism (n=10/55; 18.18%), and secondary hypothyroidism (n=13/55; 23.64%) were the most common thyroid disorders based on laboratory results respectively. The highest prevalence of thyroid disorders was seen among patients with major depressive disorder (13.55; 23.64%), bipolar disease (13.55; 23.64%), schizophrenia (8; 14. 55%), and substance use disorders (6; 10.91%) respectively. **C onclusion**: In agreement with other studies, our results showed that thyroid hormone disorders could be effective in mental disorders, and both hypothyroidism and hyperthyroidism may play an essential role in the occurrence of these disorders. Not only are people with thyroid disorders more likely to develop depression, but evidence suggests that treating thyroid disorders can increase the effectiveness of antidepressants.

Keywords: Thyroid hormones, mental disorders, depression

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A-10-1126-2

Evaluation of the Effect of the Cytarabine on Expression Changes of CPEB2 gene in Acute lymphoblastic leukemia

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Page | 475

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Introduction: and purpose: The pathophysiology of ALL involves the abnormal proliferation and differentiation of a clonal population of lymphoid cells. Only 10% of adult ALL patients and 30% of pediatric ALL patients survive, indicating that ALL has a bad prognosis. In cancer tissues, CPEB2 levels are elevated, which promotes this type of cancer cell's migration and proliferation. The goal of this study was to see how Cytarabine affected the expression of the CPEB2 gene in a cell line that had been diagnosed with acute lymphoblastic leukemia.

Methods: Cytarabine was produced in two concentrations for the current study: 1 M and 5 M at 72 hours. A prepared dose of cytarabine was administered to the Jurkat E6.1 cell line, which was bought from the Pasteur Institute, 72 hours after cell passage. Following RNA extraction and cDNA synthesis, Real-Time PCR was used to examine the variations in CPEB2 and GAPDH expression. Finally, Excel was used to create the diagrams and Rest 2002 Software to analyze the data.

Results: The results of our research showed that, following a 72hour treatment with cytarabine at concentrations of 1 M and 5 M, the expression of CPEB2 reduced in comparison to the GAPDH housekeeping gene. According to the findings, changes in CPEB2 gene expression decreased after 72h at a concentration of 1µM and 5µM decrease were statistically significant These changes included 1µM (0.721) and 5µM (0.32) at 72h, respectively. ($P < 0.001$)

Conclusion: CPEB2 expression was shown to change after receiving cytarabine at two different concentrations, according to the findings of the current investigation. cytarabine's positive potential and efficacy were demonstrated by the fact that it was able to reduce gene expression in two different concentrations within 72 hours.

Keywords: Cytarabine, CPEB2, Acute lymphoblastic leukemia, GAPDH

1, 3, 8-trihyoxy-6, 12-eudesmanolide-4(15)-en extract from Artemisia kopetdaghensis induces cell death in breast cancer cell line MCF-7

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Page | 476

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Introduction: Breast cancer is the most common cancer in women and the leading cause of cancer death in women worldwide. The balance between cell proliferation and apoptosis plays an important role in the effectiveness of anti-cancer therapies, so the study of new therapies is very important. Artemisia kopetdaghensis is a plant that has been studied for its anti-cancer effects. The present study was performed to investigate the effects of sesquiterpene lactone compounds 1, 3, and 8-trihyoxy-6, 12-odesmanolide-4 (15) -N (THED) isolated from Artemisia kopetdaghensis on Induction of cell death were performed in MCF-7 breast cancer cell line.

Methods: The toxicity effect of THED was investigated in two breast cancer cell line MCF-7 using MTT method in different concentrations from 0.01 to 200 μM of THED. The results were analyzed with GraphPad Prism 8. The p-value ≤ 0.05 was considered as significant.

Results: THED decreased MCF-7 cancer cell proliferation dependently, so that cell viability at 0.01 μM was 97.6% for MCF-7, and in a concentration of 200 μM was observed for 29.2% for MCF-7(P-value <0.0001).

Conclusions: The results of this study showed that THED isolated from Artemisia kopetdaghensis induces cell death in MCF-7 breast cancer cells.

Keywords: Breast cancer, 1, 3 and 8 trihyoxy-6, 12-odesmanolide-4 (15) -N,Sesquiterpene lactone, cell death, MCF-7, Artemisia kopetdaghensis

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Evaluation and optimization of the anti- Vibrio aptamer using L-SPR and ELAA method

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Introduction: The identification and measurement of food pathogens and environmental samples require the use of accurate and high sensitivity and specificity methods. In addition, Vibrio cholera is a zoonotic bacteria and it can directly cause disease in humans. The purpose of this work is to evaluate the performance of DNA-based aptamer using Local Surface Plasmon Resonance (LSPR) and enzyme-linked aptamer assay (ELAA) to bind and identify Vibrio.

Methods: For this purpose, the sequence of aptamer (41bp) will be chosen to attach the surface protein of Vibrio (OmpU). Then, aptamer and biotin-labeled primers for amplification of specific sequence were synthesized. Finally, the performance of aptamer in order to detection of Vibrio was assessed by plasmonic effect of the surface of gold nanoparicles and also using streptavidin conjugated with horseradish peroxidase (SA-HRP) by ELAA method.

Results: The minimum amount of aptamer in the ELAA and the LSPR system to detect V. cholerae O1 with a diagnostic threshold limit of 107(CFU/ml) is 10 (ng) and 50 (ng), respectively. The binding of aptamer sequences to gold nanoparticles was confirmed by using the gel electrophoresis image, and the incubation time of 3 to 4 hours at 37 oC confirmed the binding of 70 to 80% of aptamers to gold nanoparticles. In conclusion, this aptasensor can be used for future investigations for the diagnosis of V. cholerae.

Conclusion: Our results showed that ELAA and LSPR colorimetric models had the same diagnostic power of bacteria 107 and 106 (CFU/ml) respectively. And the minimum optimal amount of aptamer in the ELAA model is five briars less than the LSPR model.

Keywords: Aptamer, Detection, Vibrio cholerae, ELAA, LSPR

A-10-1640-1

New pyrazole derivative induce apoptosis via ROS generation in the MCF-7 breast cancer cells

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Introduction: Breast cancer as the commonest malignancies worldwide, is a major reason for cancer death in women. Although chemotherapy is one of the most effective strategies for treating, but the ug resistance acts to be as a serious problem. Therefore, designing new ugs that could overcome this problem is necessary. Pyrazole derivatives propose their utilization to improve new antitumor agents. Here, we examined the effect of pyrazole derivatives on breast cancer cells. **Methods:** To evaluate the pyrazole derivatives cytotoxic effects on MCF-7 breast cancer cells growth compared with Paclitaxel, MTT assay was performed. The amount of apoptosis and cell cycle distribution were executed by Annexin-V-FITC and PI staining. Reactive oxygen species (ROS) generation and caspase-3 activity were measured in the presence of 3f.

Results: 3f as the most effective pyrazole derivative had the lowest IC50 on MCF-7 cells compared with Paclitaxel in 24 hours. The cells treated with 3f showed higher rates of apoptosis and accumulation in the sub-G1phase compared to the control groups. Also, the level of intracellular ROS and caspase-3 activity revealed a significant increase in MCF-7 cells treated with 3f compared with untreated cells.

Conclusion: The 3f as effective derivative of pyrazole could induce apoptosis in breast cancer cells by producing ROS and activating caspase-3. Therefore, it can be used as a promising cytotoxic agent for further research in breast cancer therapeutic strategies.

Keywords: Breast cancer, Pyrazole derivatives, Apoptosis, Reactive oxygen species.

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The study of serological and cytological changes and expression analysis of INSR1 gene in the mice with PCOS

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Introduction: Polycystic ovary synome leads to ovulation disorders in 10% of women. Symptoms of polycystic ovary synome are exacerbated by obesity. The onset of this disorder is associated with serological changes in the levels of hormones such as LH and FSH. Insulin resistance phenotype in addition to the morphological changes in the cells of the vaginal tissue are other features of PCOS, but few studies have been performed on the genes involved in metabolism. The aim of this study was evaluation of the cellular and serologic indexes in PCOS mice induced by estradiol valerate as well as the expression analysis of INSR1 (insulin receptor) gene as an important factor in diabetes. Understanding the possible mechanisms of action of this disease will help us to offer more successful treatment strategies and prevent adverse consequences such as diabetes and obesity.

Methods: In this study, three groups of 5 female Balb/c mice were treated with estradiol valerate for 60 days. Vaginal cells were examined by violet crystal staining. Serum levels of glucose using glucometer as well as LH and FSH were assessed using ELISA method. Finally, ovarian tissue was dissected and after RNA extraction and cDNA synthesis, the expression of INSR1 gene was investigated.

Results: Cytological changes including a sharp decrease in epithelial cells and an increase in the number of lymphocytes were observed in vaginal smear. Blood glucose levels and LH levels increased significantly while FSH levels decreased. Our study showed a decrease in INSR1 levels ($P \leq 0.05$, Sig. = 0.00, FC = 0.346), which was harmonic with an elevated blood sugar level.

Conclusion: PCOS has a variety of effects on the cellular structure, hormones and metabolism of the body. Our results present here INSR1 gene as a reliable marker in prediction of PCOS condition as complementary data.

Keywords: Polycystic ovaries, metabolism, diabetes, gene expression

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The polymorphism of miR-146a (rs2910164) and breast cancer risk: a meta-analysis of 17 studies

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Introduction: Single-nucleotide polymorphisms (SNPs) in genes responsible for coding microRNAs (miRNAs) are shown to be crucial in progression of breast cancer (BC). Objective: The purpose of this meta-analysis is to obtain more definitive and reliable results due to the ambiguity and inconsistency of the previous findings in this regard. This study aimed at clarifying the association of mir14a polymorphisms with breast cancer.

Methods: We searched PubMed, EMBASE, Web of Science and Google Scholar databases for papers published before August 10, 2019. Afterward, genotypes' distribution, genotyping methods and ethnicity groups were extracted and Overall analyses were conducted. A total number of seventeen researches on 7676 subjects and 7476 controls were found to meet our criteria in this meta-analysis.

Results: our observations confirmed the increased risk in breast cancer with rs 2910164 polymorphism in three genetic models: allele contrast fixed genetic model, Recessive fixed genetic model and CC vs. GG genetic model (P value 0.0109, 0.0404 and 0.0019 respectively).

Conclusion: the rs2910164 polymorphism is associated with increased breast cancer risk. We suggest that more multicenter studies with larger samples investigate this matter to further clarify the association and verify our findings.

Keywords: Mir 146a ‹rs2910164 ‹polymorphism ‹breast cancer ‹meta-analysis ‹Single-nucleotide polymorphisms

Hormone therapy in Breast Cancer

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Introduction: Breast cancer (BC), an abnormal growth in breast cells, has been recognized as the most critical cancer related-death cause among females. BC can metastasize over breast tissue and other organs, including lungs, brain, bones, and liver. One of the efficient strategies to cease or moderate the BC progression is Hormone therapy (HT), consisting of applying several medications that reduce the level of hormones or disrupt their biological activity.

Methods: The research was performed applying the keywords Breast Cancer, Hormone Therapy, and Treatment in various sources such as Science Direct, Google Scholar, Scopus, Springer, and Pubmed. The collected data was eventually analyzed and reviewed.

Result: HT declines the rate of BC cell growth or prevents it by interfering with the action of hormones involved in BC pathogenesis or restricting the capability of hormone-producing. Several ugs contribute to HT through the following pathways: 1. inhibition of the hormone binding to cancer cells, such as tamoxifen, which causes varied side effects, including blood clots, cataracts, and mood swings. 2. Suppressing the production of estrogen hormone by preventing anogens conversion to estrogens leads to estrogen reduction. These aromatase inhibitors such as letrozole, anastrozole, and exemestane also have several complexities, particularly hot flashes, sweating, and fatigue. 3. Blocking estrogen receptors by Folostrant results in complications such as bone pain and nausea.

Conclusion: In summary, HT is a promising treatment option for patients with recurrent gynecological malignancies. This method is classified as a "systemic" therapeutic since it imposes its effects on the entire body. Further studies should be conducted to clarify the new advantages and disadvantages of HT and the precise relationship between HT and tumorigenesis in cancer, including BC.

Keywords: Breast Cancer ،Hormone Therapy ،Treatment.

A-10-1671-1

Astaxanthin prevents Methotrexate-induced Nephrotoxicity through Nrf2/HO-1 pathway

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Introduction: Methotrexate is an antitumor ug and folic acid antagonist, and renal toxicity is one of its serious side effects. Astaxanthin is a natural carotenoid with strong antioxidant properties. In this study, we evaluate the antioxidant effects of astaxanthin on methotrexate-induced nephrotoxicity.

Methods: 42 Wistar rats were studied in 7 groups of 6. The control group did not receive any medication or antioxidants for 10 days. The olive oil group received 50 mg/kg of olive oil by gavage for 10 days. The astaxanthin group received astaxanthin (75 mg/kg) by gavage for 10 days. The methotrexate group received 10 mg/kg of methotrexate intraperitoneally on days 6, 8, and 10. MTX + AST groups (3 groups) received 25, 50, and 75 mg/kg of astaxanthin daily for 10 days and 10 mg/kg of methotrexate daily on days 6, 8, and 10, respectively. On day 11, their serum and kidney tissue were isolated for biochemical, histopathology evaluation, and examination of gene expression.

Results: Methotrexate decreases Nrf2 and HO-1 gene expression. Astaxanthin reduces the adverse effects of methotrexate by activating signaling and increasing the expression of Nrf2 and HO-1 genes.

Conclusion: Molecular data obtained confirm the antioxidant effect of astaxanthin which protects the kidney against methotrexate-induced nephrotoxicity.

Keywords: Astaxanthin, Nephrotoxicity, Methotrexate, Kidney, Nrf2/HO-1 pathway

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Influence of disease severity and gender on MX1 gene Methylation in COVID-19 patients

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Introduction: Epigenetic modifications during viral infection could occur in two aspect: the virus silences the expression of critical genes in the antiviral host cell while infected cells elicit an antiviral environmental response that induces and starts certain pathways for appropriate response to the virus. Since MX1 gene has vital immunomodulatory effects during viral infections, this study aimed to evaluate the methylation status of the MX1 gene promoter at different stages of COVID-19 patients.

Methods: 470 COVID-19 patients with a positive RT-qPCR test (235 women and 235 men) were recruited into the study. Patients were divided based on the WHO classification into three groups: Moderate, severe, and critical. Moreover, 100 healthy individuals (50 women and 50 men) were selected as the control group. Peripheral white blood cells were collected and to determine the methylation status of the MX1, the methylation-specific PCR (MSP) method and gel electrophoresis were used. P-value less than 0.05 considered as significant differences.

Results: There was a decrease in the methylation level of the MX1 gene promoter in moderate and severe groups. However, the MX1 gene promoter methylation increased in the critical group and it significantly was higher than the other groups. In addition, the level of methylation was significantly higher in men than in women.

Conclusion: Increased methylation of the MX1 gene in the critical group may indicate the role of SARS-CoV-2 in reducing the expression levels of this antiviral gene and thus promoting virus replication and disease progression. Also, different methylation levels in men and women could shows the importance of gender considering in COVID-19 management.

Keywords: COVID-19, MX1, Methylation, Disease severity

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Frequency of CYP1A1 gene T6235C polymorphism and null genotypes of GSTT1 and GSTM1 in patients with coronary artery disease

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Introduction: Given the significant physical, mental and economic problems of coronary artery disease (CAD), it is important that communities help reduce these costs. CYP1A1 enzyme can lead to coronary artery disease through various mechanisms. The enzyme glutathione S-transferase reduces free radicals in the body. Therefore, it is important to identify polymorphisms that affect the activity of these enzymes.

Methods: After collecting samples from 191 CAD patients and 191 controls which was identified by a cardiologist, PCR-RFLP method was used to diagnose T6235C polymorphism (rs4646903). Multiplex-PCR method was used to detect Null glutathione S transferase M1(GSTM1) and T1(GSTT1) genotypes. SPSS16 (SPSS Inc. Chicago Ill) was used for statistical analysis.

Results: frequency of heterozygous mutant rs4646903 genotype in patients was 36.6% and in control individuals was 20.9% (P value<0/001, OR=2/31, 95%CI=(1/46-3/66)). Frequency of homozygous genotype the polymorphism was 5.2% in patients and 2.1% in controls (P value=0/037, OR=3/31, 95%CI=(1/08-9/76))which was statistically significant. The frequency of null genotypes glutathione S transferase M1 and T1 genotypes in patients was 49.7% and 21.5%, and in controls was 37.7% and 16.8%, respectively. Only null genotype of glutathione S transferase M1 was associated with CAD (P value=0/018, OR=1/64, 95%CI=(1/09-2/46). Synergistic effect between null genotypes of GSTM1 and GSTT1 and heterozygous and mutant homozygous genotypes of T6235C polymorphism was not found in CAD developing (Pvalue > 0.05).

Conclusion: rs4646903 polymorphism of CYP1A1 gene and null genotype of GSTM1are involved in CAD susceptibility in the study population.

Keywords: CAD, CYP1A1, T6235C, GSTM1, GSTT1

A-10-1674-2

Superfoods vs. the COVID-19

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Introduction: In this paper, we strived for to describe the roles of some superfoods could combat against COVID-19.

Methods: In this paper, various databases, such as Google Scholar, Scopus, and Pub Med were Sought with the following keywords: superfood, White Button Mushroom (Agaricus bisporus), Pomegranate, Moringa oleifera, Honey, Spirulina, Egg, Ginger (Z. officinale) COVID19, SARS-CoV-2, and corona virus2. Also, papers with close to the field of our paper were searched.

Results: some compound such as protocatechuic acid, caffeic acid, Gallic acid, and p-coumaric acid in Agaricus bisporus, punicalagin, ellagitannin, punicalin, gallic and ellagic acid, Quercetin, Kaempferol, Rutin, Cafeic acid in Pomegranate, pterygospermin, kaempferol, quercetin, morphine, isoquercitrin, isoquercetin, apigenin-7-O-rutinoside, Mudanpioside and dihyoquercetin in Moringa oleifera, rutin, Luteolin and caffeic acid phenethyl, quercetin and naringin in Honey, sorbitol, C-phycocyanin (CPC), and adenosine derivatives, Prebiotics, phycocyanobilin, calcium Spirulan in Spirulina, ovalbumin, lysozyme, avidin, vitellogenin hyolysates, pleiotrophin and ovomucin in egg and geraniol, gingerol, , shogaol, zingiberenol, zingerone, paradol and zingiberene in Ginger could combat against COVID-19.

Conclusion: during illness and body recovery, there is a need for some nutrients in patients. Different vitamins, minerals and compounds with different properties such as antiviral, strengthening the immune system, and antibacterial are present in superfoods. They could be used in treating and preventing of COVID-19.

Keywords: Superfood, SARS-CoV-2, COVID-19, Corona virus2, Treatment

In Silico analysis on the identification of has-mir-3136 associated with ESM1 gene in gastric cancer

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Introduction: Gastric cancer (GC)is one of the most common malignancies of the digestive system, with few genetic markers for its early detection and prevention. This study aimed to identify the hub genes and uncover the molecular mechanisms through GC.

Methods: In this study, the expression profiles of associated genes were analyzed from GSE103236 obtained from the GEO datasets. The Differentially Expressed Genes (DEGs) were analyzed by the GEO2R tool. Adj. p-value < 0.01 and |log FC | >3 were considered as the cut-off criteria. Enrichment analysis was performed on KEGG pathways using the DAVID database to determine the functions of selected overlapping DEGs. STRING database was used to analyze the interaction between DEGs, and protein-protein interaction (PPI) network graph was obtained. The miRNASNP-v3 revealed the microRNAs (miRs) linked to ESM1 and the underlying signaling pathways playing significant roles in GC development. The miRWalk database was used for detecting the interaction between ESM1 gene and associated miRs.

Results: Based on the current research, 19 DEGs were identified. The KEGG and DAVID databases showed that Endothelial cell-specific molecule1 (ESM1) is essential in cancer initiation and progression, and Vascular endothelial growth factor (VEGF-A) is a specific inducer of ESM1 transcription. In addition, ESM1 can bind to proangiogenic molecules, exerting the effect of angiogenesis promotion. Studies revealed that ESM1 increased tumor cell survival rate via the Akt-dependent NF-kB/IkB pathway. The results also showed that has-mir-3136 could have a suppressive effect on the angiogenesis activity of the ESM1 gene by playing regulatory roles in the target gene expression by interfering with RNA-induced silencing complexes and interacting with the 3' untranslated regions of target mRNAs.

Conclusion: These findings imply that ESM1 could be a potential target in gene therapy for gastric cancer. Blocking ESM1 expression in GC cells repressore angiogenesis, which may provide a novel treatment approach.

Keywords: Bioinformatic analysis, biomarker, differentially expressed genes, KEGG pathway

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Evaluation of different doses of Tricyclazole on Triglyceride and Cholesterol in female Wistar rat

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Introduction: The increasing use of agricultural pesticides is associated with an increase in soil and water pollution. Among the commonly used pesticides in rice blast, pest control is Tricyclazole. These pesticides have the ability to be digested separately and can affect different body tissues, including the liver.

Methods: Twenty-four adult female Wistar rats weighing 200 ± 20 were distributed semi-randomly into 4 groups of six. Group Control, group A that received Tricyclazole (25 mg/kg b.w./day, PO); group B, were treated with Tricyclazole (37.5 mg/kg b.w./day, PO) and group C, were treated with Tricyclazole (50 mg/kg b.w./day, PO). The study period was 4 weeks. Blood samples were taken from all rats. serum samples were obtained from all groups and were used to measure Triglyceride and Cholesterol. Data obtained from the measurements were compared using the statistical analysis Duncan technique.

Results: A dose-dependent increase in levels of triglyceride and cholesterol has been shown ($p < 0.05$). triglyceride and cholesterol of the control group were at the minimum level. As the Tricyclazole dose rises, triglyceride and cholesterol levels get higher. Thus, the highest levels belonged to Tricyclazole (50 mg/kg) treated rats.

Conclusion: In this research, it can be manifested by elevated levels of Tricyclazole and Methyltiophanate can cause adverse effects on rats and nutrition health and it should be considered as a subsequence of this pesticide intake.

Keywords: Wistar Rat, Tricyclazole, Liver, Triglyceride, Cholesterol

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Evaluation of different doses of combination of Methyltiophanate + Tricyclazole on ALT, AST and ALP in female Wistar rat

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Introduction: With the existence of various plant diseases such as rice blasts and the fact that the health of agricultural products is essential, the use of pesticides is increasing. Among these pesticides is Tricyclazole. Recent studies indicate that the residue of these pesticides has the ability to be digested in living organisms, which can have harmful effects on different body tissues, including the liver.

Methods: This study is a case-control study that was performed on 24 female Wistar rats in the weight 200±20 g. Wistar rats were divided into 4 groups of 6 under the groups of treatment consisting of group A that received the combination of Tricyclazole (12.5 mg/kg b.w./day, PO) and Methyltiophanate (332 mg/kg b.w./day, PO); group B, were treated with the combination of Tricyclazole (18.75 mg/kg b.w./day, PO) and Methyltiophanate (498 mg/kg b.w./day, PO); group C, were treated with the combination of Tricyclazole (25 mg/kg b.w./day, PO) and Methyltiophanate (664 mg/kg b.w./day, PO) and the control one. The treatment groups (A, B, and C) were placed on gavage over 28 days. serum samples were obtained from all groups and used to measure the ALT, AST, and ALP.

Results: Biochemical evaluations demonstrated that there is a dose-dependent relationship between the elevated combination of Methyltiophanate + Tricyclazole and ALT, AST, and ALP values. In other words, by increasing the dose of this combination, mentioned factors rise ($p < 0.05$). In addition, the combination of Methyltiophanate (664 mg/kg) and Tricyclazole (25 mg/kg) causes the highest, whilst the lowest levels were linked to the control group($p < 0.05$).

Conclusion: According to mounting levels of ALT, AST, and ALP, it should be reckoned that this combination has negative impacts on human and animal health and toxicity effects on liver tissue.

Keywords: Methyltiophanate, Tricyclazole, liver, ALT, AST

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Identification of Potential Key Genes in hepatocellular carcinoma by Integrated Analysis of Gene Expression Profiles

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Introduction: The most frequent primary liver cancer is hepatocellular carcinoma (HCC), which also has a high mortality rate from cancer. Incidence and death are still increasing despite improvements in screening methods, preventative strategies, and new technology for both diagnosis and treatment. Regardless of the cause, cirrhosis continues to be the predominant risk factor for the development of HCC. inking alcohol continues to be a significant added danger. HCC is an aggressive malignancy that frequently manifests in an advanced stage when it develops in conjunction with cirrhosis. Potential biomarkers of HCC for the diagnosis at an early stage and prognosis have been found with the development of microarray and bioinformatics analysis in the screening of gene changes.

Methods: microarray dataset GSE30784 was downloaded from the gene expression omnibus (GEO). Then, differential expression genes (DEGs) were normalized and examined using the transcriptome analysis console (TAC). As DEGs between normal and HCC samples, the genes with adjusted p-value (F) 0.05 and |log2 FC|>2 were chosen. Protein-protein interaction (PPI) and visualization were built using string, Cytoscape, and Gephi, respectively.

Results: DEGs for 942 genes were obtained (412 upregulated, 530 downregulated). Five hub genes were identified by our analysis: MYC (v-myc avian myelocytomatosis viral oncogene homolog), ESR1(estrogen receptor 1), JUN (jun proto-oncogene), CD44(CD44 molecule), and GPT (glutamic-pyruvic transaminase). Additionally, the KEGG pathway analysis results showed that these genes were abundant in important pathways, such as ECM-receptor interaction, Bile secretion, and Tryptophan metabolism.

Conclusions: This knowledge, together with further details on the molecular processes underlying the onset and development of HCC, holds promise for use as biomarkers and prospective treatment targets. To validate the precise functional role and processes behind the three important genes MYC, ESR1, JUN, CD44, and GPT, more molecular biology tests, including q-RT PCR, colony-formation assay, and flow cytometry analysis, are necessary.

Keywords: GEO, hepatocellular carcinoma, bioinformatics, biomarker, Systems biology

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Histopathologic Evaluation of different doses of combination of Methyltiophanate + Tricyclazole on liver tissue in female Wistar rat

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Page | 490

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Introduction: One of the environmental health and animal life-threatening stuff is agricultural pesticides. In agriculture, the most common pesticide to fight against rice blast, which is one of the most important agricultural pests, is the combination of two pesticides, Tricyclazole and Methyltiophanate. Research has shown that these two pesticides separately have negative effects on different organs, including the liver.

Methods: Twenty-four female rats were divided into Four groups, group1, control group; group 2, rats that received the combination of Tricyclazole (12.5 mg/kg b.w./day, PO) and Methyltiophanate (332 mg/kg b.w./day, PO); group3, were treated with the combination of Tricyclazole (18.75 mg/kg b.w./day, PO) and Methyltiophanate (498 mg/kg b.w./day, PO); group4, were treated with the combination of Tricyclazole (25 mg/kg b.w./day, PO) and Methyltiophanate (664 mg/kg b.w./day, PO). At the end of the study, the tissue of the liver was obtained, and hepatic changes were examined.

Results: The examination of histopathologic lesions showed hyperemia, inflammatory cell infiltration, and vacuolar degeneration in all groups and it became more significant by elevating the dose of Methyltiophanate and Tricyclazole. There was significant edema in the combination of Methyltiophanate (664 mg/kg) and Tricyclazole (25 mg/kg).

Conclusion: Elevating levels of Tricyclazole and Methyltiophanate can cause destructive effects on liver tissue and it should be considered as a subsequence of this pesticide intake.

Keywords: Tricyclazole, Methyltiophanate, Liver, Histopathology

A-10-1560-1

The effect of (G4S)3 linker on the expression of the glargine and removal of SUMO tag

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Introduction: Diabetes is a group of metabolic diseases from defects in insulin secretion or action. Glargine is one of the insulin analogous. The difference between glargine and regular insulin is that in glargine A-chain is located in the amino acid 21 glycine instead of asparagine, in B- chain at the end of carboxyl there are two arginine residues. In this study, a construct was designed that contained a SUMO tag and a (G4S)3 linker to increase the expression of proglargine and cleavage of its SUMO tag by SUMO protease.

Methods: The construct was designed and synthesized, cloned into pET26b-(+) and then transformed into E. coli BL21(DE3). Various conditions were evaluated to determine the optimum expression condition. The inclusion bodies were dissolved in 8 M urea containing DTT (100mM). The unfolded protein was purified using Ni-NTA Sepharose column. The purified protein was refolded in various conditions. Finally, the SUMO tag was removed by SUMO protease.

Results: In all expression conditions the protein was expressed as inclusion bodies. The optimum expression was induced with 0.2mM IPTG at 37°C and 180 rpm for 6 h. The inclusion bodies were denatured in 8 M urea containing 100mM DTT. The denatured protein was then purified using Ni-Sepharose and eluted in 250 mM imidazole. The optimal refolding condition for the purified protein was obtained in 0.5 mg/ml protein, 10 mM glycine buffer pH 10.6, containing 0.5 M urea, and 0.2 mM DTT at 15°C for 20 h. Finally, separation of SUMO tag was done.

Conclusion: We observed that the presence of the GS linker lead to a high yield of expression. In addition, the SUMO protease cleavage efficiency was improved in comparison the construct without GS-linker. Results of this study can be used for glargine production.

Keywords: Proglargine,Linker,Diabetes,SUMO tag

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A-10-1676-1

Effects of Tricyclazole on Amylase and Lipase Levels in female Wistar rat

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Page | 492

Introduction: One of the most important factors that pollute soil and water is agricultural pesticides. Considering that Tricyclazole is a widely used pesticide to deal with rice blast disease, it is important to investigate its effects on Amylase and Lipase levels as indicators of body health.

Methods: This study is a case-control study that was performed on 24 female Wistar rats with a weight of 200±20 g. Wistar rats were divided into 4 groups of 6 under the groups of treatment consisting of group A, group B, group C, and the control one. The treatment groups (A, B, and C) were placed on gavage with 25, 37.5, and 50mg/kg body weight of Tricyclazole over 28 days. Serum samples were obtained from all groups and were used to measure Amylase and Lipase.

Results: Biochemical evaluations demonstrated that there is a dose-dependent relation between elevated Tricyclazole and amylase ($p<0.05$) but not a meaningful one with lipase values ($p>0.05$). In other words, by increasing the dose of Tricyclazole, the amylase value ops. In addition, the Tricyclazole dose (50 mg/kg/day) causes the lowest, whilst the highest levels were linked to the control group.

Conclusion: Through this research, it can be manifested by decreased levels of amylase, which can cause adverse effects on rats and pancreatic factors should be considered as subsequences of this pesticide intake so it's better to control the use of this pesticide in the future.

Keywords: Wistar rat, Tricyclazole, Pancreas, Amylase, Lipase

A-10-1676-2

Evaluation of different doses of Tricyclazole on Insulin and Glucose of female Wistar rat

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Introduction: One of the environmental health and animal life-threatening stuff is agricultural pesticides. In agriculture, the most common pesticide to fight against rice blast, which is one of the most important agricultural pests, is one of the most useful pesticides, Tricyclazole. Research has shown that Tricyclazole has negative effects on different organs, including the pancreas.
Methods: Twenty-four adult female Wistar rats weighing 200 ± 20 were distributed semi-randomly into 4 groups of six. Group Control, group A that received Tricyclazole (25 mg/kg b.w./day, PO); group B, were treated with Tricyclazole (37.5 mg/kg b.w./day, PO) and group C, were treated with Tricyclazole (50 mg/kg b.w./day, PO). The study period was 4 weeks. Serum samples were obtained from all groups and were used to measure insulin and glucose.
Results: There was a meaningful dose-dependent relationship between the increase in levels of Tricyclazole and insulin value ($p < 0.05$) but not a meaningful one with Glucose value ($p > 0.05$). The highest levels of insulin were observed in group C of Tricyclazole (50 mg/kg b.w). **Conclusion:** According to mounting levels of insulin and glucose, it ought to be reckoned that Tricyclazole has negative impacts on human and animal health and toxicity effects on pancreas tissue. It is recommended to use less of this pesticide in order to keep the environment much more safe for humans and animals.

Keywords: Wistar Rat, Tricyclazole, Pancreas, Insulin, Glucose

A-10-1201-1

The role of oncogenes genes in hepatocellular carcinoma

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Introduction: and aim: Because there are so many obstacles to preventing, diagnosing, and treating HCC, it continues to be one of the most fatal cancers in the world. The high degree of heterogeneity in HCC is due to a variety of induced factors, genetic make-up, and spatiotemporal molecular diversity. Cell division and viability are stimulated or improved by oncoproteins that oncogenes encode. This review abstract sought to determine the function of oncogene genes in hepatocellular cancer. Search

Methods: This study was conducted on the subject of the role of oncogenes genes in liver cancer, by collecting content from Science Direct, Springer, Google Scholar, and PubMed sites.

Result: The results of various studies have shown that oncogene genes play an important role in the occurrence of liver cancer in different signaling pathways, including these genes include Abelson murine leukemia viral oncogene homolog 1 (ABL1), Annexin A protein family, Focal adhesion kinase (FAK), Human forkhead box (FOX) family, Kinesin superfamily protein (KIF), Non-structural maintenance of chromosomes (SMC) condensinI complex (NCAP) family, Never-in-mitosis A (NIMA)-related kinase (NEK) family, Protein arginine methyltransferase (PRMT) family, Sirtuin (SIRT) family, Tripartite motif (TRIM) family, Ubiquitin-specific proteases (USPs) family.

Conclusion: Finally, a number of mechanisms important to cancer have been discovered, and there are now effective pharmacological treatments available, including those that target hormone receptors and signaling pathways. Cancer stem cells prevent growth. On the other hand, because of the complex function that oncogene proliferation plays in malignancy, one of the most crucial treatment approaches is the identification of oncogenes and their role in the development of different cancers. Keywords: Oncogenes, Hepatocellular Carcinoma, Cancer

Keywords: Oncogenes, Hepatocellular Carcinoma, Cancer

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A-10-1676-3

The study of different doses of Methyltiophanate on Amylase and Lipase in female Wistar rat

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Page | 495

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Introduction: The increasing use of agricultural pesticides is associated with an increase in soil and water pollution. Among the commonly used pesticides in rice blast, pest control is Methyltiophanate. This pesticide can be digested and can affect different body tissues, including the pancreas.

Methods: This study is a case-control study that was performed on 24 female Wistar rats in the weight 200 ± 20 g. Wistar rats were divided into 4 groups of 6 under the groups of treatment consisting of group A, group B, group C, and the control one. The treatment groups (A, B, and C) were placed on gavage with 664, 996, and 1328 mg/kg body weight of Methyltiophanate over 28 days. Serum samples were obtained from all groups and were used to measure Amylase and Lipase.

Results: Biochemical evaluations demonstrated that there is a dose-dependent relation between elevated Methyltiophanate and amylase ($p<0.05$) but not a meaningful one with lipase values($p>0.05$). In other words, by increasing the dose of Methyltiophanate, the amylase value ops. In addition, the Methyltiophanate dose (1328 mg/kg/day) causes the lowest, whilst the highest levels were linked to the control group.

Conclusion: Through this research, it can be manifested by decreased levels of amylase, which can cause adverse effects on rats and pancreatic factors. By using less amount of this pesticide we would have less pesticide pollution in the environment.

Keywords: Wistar rat, Methyltiophanate, Pancreas, Amylase, Lipase

A-10-1347-2

Nutritional Support in Chronic Heart Failure Patients

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Introduction: Chronic HF is an inexorable synome characterized by mitochonial dysfunction with a deficit in the production of myocardial adenosine triphosphate, and increased production of reactive oxygen species. Therefore, targeting mitochonial dysfunction can be a useful therapeutic strategy. All cells naturally manufacture CoQ10, an endogenous antioxidant that is crucial for both antioxidant defense and energy metabolism, but, its levels decrease with age and especially in HF patients.

Methods: PubMed databases were screened using the following search terms ("CoQ10") AND ("heart failure").

Results: There are two reasons for taking CoQ10 supplements in CHF. One is CoQ10's well-known function in mitochonial bioenergetics, and the other is its ability to act as an antioxidant. CoQ10 accepts electrons from complexes I and II and passes them on to complex III. Electrons are then forwarded downstream via cytochrome C to complex IV in the electron transport chain. As a result, a proton gradient is created across the mitochonial membrane, and ATP is made via oxidative phosphorylation. In 2014, the first large-scale prospective, randomized, placebo-controlled study was published on the effect of CoQ10 on HF. This study shows that 100 mg of CoQ10 three times daily can improve cardiac function and reduce NT-proBNP plasma levels. CoQ10 reduces the levels of biomarkers associated with fibrogenic activity (cathepsinS, galectin 3, growth differentiation factor-15, matrix metalloproteinase 1 and 9), suggesting the antifibrotic effects of this supplement and improving cardiac function.

Conclusion: In conclusion, in patients with ischemic cardiomyopathy and CHF in NYHA functional class II and III, oral supplementation with CoQ10 at doses that increase plasma CoQ10 levels four-fold is safe and induces significant improvements in endothelium-dependent relaxation, LV contractility, and functional capacity. Also, CoQ10 may have a role in reducing the risk of mortality in HF patients.

Keywords: Coenzyme Q10, Heart failure, Mitochonial dysfunction, Antioxidant

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Protective Role of Glutathione on Sperm Parameters in the Testis of Rats Intoxicated with Zinc Oxide Nanoparticles

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Introduction: Nanoscience has recently gained considerable attention in different areas. However, several studies have reported the detrimental influence of nanoparticles on human and environmental health. In this regard, zinc oxide nanoparticles (ZnO NPs) are applied in a variety of technologies and are also known as a toxic agent in the male reproductive tract. As such, we decided to explore the beneficial role of glutathione (GSH), as an important component of antioxidant defense system, on sperm parameters in rats following exposure to ZnO NPs.

Methods: In this study, 30 adults male Wistar rats were provided and then randomly assigned in to 5 groups of 6 rats including Control1(Water), Control2 (Olive oil), GSH (25 mg/kg), ZnO NPs (200 mg/kg) and ZnO+ GSH. Sperm characteristics including morphology, motility as well as viability were assessed. Furthermore, a light microscope was used to determine the sperm count.

Results: The findings found that sperm parameters including viability, normal morphology and motility were improved in the ZnO+ GSH-exposed rats as compared to the rats that only received ZnO NPs so that became close to the control. Furthermore, sperm count was meaningfully increased in rats co-treated with GSH and ZnO NPs relative to the ZnO NPs group ($P<0.05$).

Conclusion: Accordingly, GSH treatment could alleviate the sperm damages caused by ZnO NPs. Thus, the administration of GSH can be suggested as a treatment option for future research in NPs-induced toxicity. Keywords: Glutathione (GSH), Sperm parameters, Zinc oxide nanoparticles (ZnO NPs)

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Investigating the interaction between COMP gene as a biomarker and its associated miRNA in breast cancer through bioinformatics analysis

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Page | 498

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Introduction: Breast cancer (BC), an extremely aggressive malignant tumor, causes many deaths worldwide. In terms of its annual incidence (currently 17 million cases), it is expanding alarmingly. This study aimed to identify the differentially expressed genes in the carcinogenesis and progression of BC through bioinformatics study.

Methods: The GSE21422 was selected from GEO datasets to identify the differentially expressed genes (DEGs) between 9 tumor and 5 healthy samples in a breast cancer microarray experiment. Compared to noncancerous samples, the GEO2R analysis was performed on DEGs from BC samples. Adjusted P-value < 0.01 and log2FC (fold change) >2.5 were considered as statistical significances. DAVID database was used as a Gene Functional Classification Tool in order to determine the functional categories of genes. The analysis of the DEGs pathway was retrieved in the Kyoto Encyclopedia of Genes and Genomes (KEGG). The associated microRNA (miR) with Cartilage Oligomeric Matrix Protein (COMP) gene was found in the miRDB online database. The interaction between selected miR and associated genes was found through the miRWalk online database.

Results: A total of 14 DEGs were identified, and GO analysis revealed the role of COMP gene in the anti-apoptosis of breast cancer. The KEGG database showed that the COMP gene could play a role in PI3K-Akt signaling pathway in which inhibition or expression of this gene plays an important role in apoptosis of breast cancer. The results also showed that has-mir-3909 could have suppressive impact on the inhibitory activity of COMP gene through apoptosis.

Conclusion: Bioinformatics investigations showed that the COMP gene could act as a biomarker in breast cancer cells and has a role in the anti-apoptotic process. The has-mir-3909 can be used as a treatment strategy to lead these cells to apoptosis in treating such patients.

Keywords: has-mir-3909, Geo, anti-apoptotic, DEGs, treatment strategy

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Silencing of SiX-4 enhances the chemosensitivity of melanoma cells to Cisplatin

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Introduction: Melanoma is the most dangerous type of skin cancer. Its prevalence has been rapidly increased over the last three decades. SIX1, SIX2, SIX3, SIX4, SIX5, and SIX6 are members of the sine oculis homeobox (SIX) homolog family. Furthermore, patients with melanoma who are at high risk of relapse can be recognized with high accuracy, leading to a rethinking of conventional melanoma adjuvant therapy paradigms. Also, it is imperative to identify new melanoma biomarkers to improve the predictive value for melanoma prognosis, which could enhance our understanding of carcinogenesis and tumor progression. In this study, we investigated whether silencing of SIX4 in a melanoma cell line (A375 cells) in combination with Cisplatin can affect the apoptosis and suppression of cell cycle progression, migration of the melanoma cells. **Methods:** MTT test was applied to determine the IC50 of Cisplatin and the combined effect of SIX4 siRNA and Cisplatin on the viability of the A-375 cells. qRT-PCR was performed to determine the c-myc, BCL-2, BAX, MMP-9, CXCR4, and Rock genes expression. Furthermore, flow cytometry was applied to evaluate apoptosis, autophagy, and the cell cycle status in different groups. Finally, a wound healing assay was employed to evaluate the effect of this combination therapy on migratory capacity.

Results: SIX4 suppression increased the chemosensitivity of A-375 cells to Cisplatin and decreased its efficient dose. Also, the expression of SIX4 mRNA was reduced after using SIX4 siRNA and Cisplatin in A-375 cells. Furthermore, SIX4 suppression alongside Cisplatin reduced cell migration rate, arrested the cell cycle at the G1 phase, induced apoptosis by modulating the expression of apoptotic target genes, and also induced autophagy. **Conclusion:** SIX4 plays a significant role in the chemosensitivity and pathogenesis of melanoma. Therefore, SIX4 suppression, in combination with Cisplatin, may be a promising therapeutic approach in treating melanoma.

Keywords: Melanoma, siRNA, SIX4, Cisplatin, Chemo-sensitivity, Combination therapy.

Single Nucleotide Polymorphism associated with ERAP1 Gene in Ankylosing Spondylitis Disease

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Introduction: Human leukocyte antigen-B27 (HLA-B27) is the most well-known influential factor in the pathogenesis of ankylosing spondylitis (AS), a debilitating spondyloarthropathy associated with variants in different genes. HLA_B27 builds a destructive structure whose peak is seen in the function of the immune system. In addition to HLA_B27, polymorphism in the Endoplasmic reticulum aminopeptidase 1 (ERAP1) gene increases the risk of developing AS. This study aimed to evaluate the role of single nucleotide polymorphism (SNP) in ankylosing disease. **Methods:** The position of the ERAP1 gene was specified in the NCBI database. The mirdSNP database was used for searching SNPs associated with AS disease based on ERAP1 gene. The Ensembl and mirdSNP databases determined the position of considered polymorphisms in the regions of exons 11, 12, and 15 as well as in the 3'UTR regions of the ERAP1 gene. Since ERAP1 gene is associated with different genes and diseases, including cancers, and is expressed in most tissues, this gene's functional and pathological relationship with other genes were identified using DAVID database. The current study showed a significant association between rs30187 as a SNP and ERAP1 gene. The effect of T/AC allele polymorphism on 3'UTR of ERAP1 gene increased the risk of AS susceptibility.

Results: The studies revealed a dominant association between single nucleotide polymorphism rs30187 on ERAP1 gene and ankylosing spondylitis disease in European, East Asian, Chinese, Canadian, and Romanian communities. Although in some societies, for example, Iran, the dominant single nucleotide polymorphism was rs27044.

Conclusions: It is concluded that the effect of ERAP1 gene on HLA-B27 is very diverse at the population level because of the diversity and complexity of ERAP1 variants and the distinct effects of their co-occurring polymorphisms, leading to significant modulation of disease risk among HLA-B27 positive individuals. Keywords: HLA27; AS; Endoplasmic reticulum aminopeptidase; SNP

Keywords: HLA27, AS, Endoplasmic reticulum aminopeptidase, SNP

The serum level of interleukin-36 in patients with coronary artery disease

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Introduction: Atherosclerosis is a chronic inflammatory process maintained during all stages of the disease by several proinflammatory mediators, such as cytokines and chemokines. Interleukin (IL)-36 cytokines are pro-inflammatory and have an essential role in innate and adaptive immunity, but the role of IL-36 has not been determined in coronary artery disease (CAD). Therefore, this study aimed to measure the serum levels of IL-36 in patients with CAD.

Methods: A total of 168 subjects (84 CAD and 84 control subjects) were examined in this research. The total serum levels of IL-36 were measured using the Enzyme-Linked Immunosorbent Assay (ELISA).

 Results: The serum level of IL-36 was significantly higher in the CAD group compared to the controls. Furthermore, the serum levels of IL-36 significantly correlated with the CAD group's cardiac arterial stenosis (CS).

Conclusion: Higher serum levels of IL-36 may play a vital role in the pathogenesis of CAD, leading to an increased risk of clogged arteries.

Keywords: Coronary Artery Disease, IL-36, Inflammation

miRNA-mRNA regulatory network in salivary of pancreatic cancer patients

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Introduction: Pancreatic cancer (PC) is one of the most lethal malignancies, and the pathogenesis remains primarily obscure. As seen in other cancers, PC also emerges due to genetic alterations and turbulences of gene expression. MicroRNAs (miRNAs) are one of the regulatory-genetic factors that are known. miRNAs regulate the expression of specific genes through interaction with mRNA targets and are involved in cancers. Increasing evidence has recently uncovered the mRNA-miRNA network's role in many human cancers. We analyzed miRNA and mRNA expression data to construct the mRNA-miRNA regulatory network in the PC salivary samples. **Methods**: Four gene expression profiles GSE14245 & GSE53325 were downloaded from the Gene Expression Omnibus (GEO), and the differentially expressed genes (DEGs) and miRNAs (DEmirs) in PC salivary and normal salivary with a P-value < 0.05 and a |log fold change (FC)| > 1.0 in DEGs and a |log fold change (FC)| > 2.0 in DEmirs were first identified by GEO2R tools. Then we use the Toppgene database to select miRNAs related to mRNAs PC and reconstruct the miRNA-mRNA regulatory network with Cytoscape software and determined the highest degree. **Results**: A total of 295 DEGs were identified, including 199 upregulated and 96 downregulated DEGs and 75 DEmirs were identified, including 27 upregulated and 48 downregulated DEGs. Additionally, 6 hub miRNAs (miR-1275, miR-1246, miR-1290 were down-regulated and miR-190, miR-190b, and miR-4313 were upregulated), and 10 hub mRNA (ATF7IP, LARP4B, ZMIZ2 were up-regulated and SH3BP5, USP15, NPAS2 were down-regulated) were identified. **Conclusion**: We constructed a salivary miRNA-mRNA network that may show crucial functions in the PC, thus providing potential diagnostic biomarkers and therapeutic targets for PC.

Keywords: regulatory network, salivary, miRNA, pancreatic cancer

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Diphenylamine inhibition of carotenoid biosynthesis in the yeasts Xanthophyllomyces and Rhodothrola spp.

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Introduction: With more than one thousand distinct chemical structures, carotenoids are amongst wildly occurring pigments being naturally synthesized in a complex biochemical pathway. These compounds include a considerable portion from microbial sources such as some yeasts species which produce unique or rare carotenoids. Carotenoid are bioactive compounds with acts as natural antioxidant. Some of them including beta-carotene and astaxanthin are currently used in some industries. For biosynthesis of these compounds, several enzymes work together in a complex pathway to form specific carotenoids. Carotenoid biosynthesis can be inhibited by many compounds but the effect sites can be different. Diphenylamine is an inhibitor of phytoene desaturation leading to accumulation of phytoene and already introduced with different mode of action in organisms.

Methods: The yeasts including Xanthophyllomyces denorhous and two Rhodothrola sp. Including Rhodothrola glutinis and Rhodothrola mucilaginosa were cultured on yeast mold agar at optimum conditions with different concentrations of diphenylamine as carotenoid biosynthesis inhibitor. Initially, the maximum concentration of diphenylamine which permitted the growth of yeasts colonies were evaluated. Then, a range of concentrations of diphenylamine were examined for the maximum amount with colorful colonies. Finally, a correlation between yeast species from amounts of carotenoids, and carotenoids inhibitors point of view were determined.

Results: The results showed that the growth inhibition in presence of diphenylamine were almost the same for all yeasts but different concentrations of this carotenoid inhibitor were led to white hue of the colonies. The was a direct correlation between the amount of the carotenoids synthesized by the yeasts and the concentrations needed to for pale colonies to be appeared.

Conclusion: As diphenylamine is a phytoene desaturation inhibitor, adding this compound to the yeast culture led to accumulation of phytoene. The higher the amount of the carotenoid biosynthesis, the higher diphenylamine required for carotenoid inhibition.

Keywords: Carotenoid biosynthesis pathways, Carotenoid biosynthesis inhibitors, Microbial carotenoids, Yeasts, Diphenylamine

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Fluorescence Spectrometry Studies on the Interaction of SiO2 Nanoparticles with Bovine Liver Catalase

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Introduction: Due to the increasing use of silicon dioxide nanoparticles (SiO2 NPs) in medical biotechnology and probable side effects, oxidative stress and diseases resulting from its usage, this study was done for evaluation the toxic effects of different concentrations of SiO2 NPs on Bovine Liver Catalase (BLC). BLC is an important antioxidant that protects organisms by destroying reactive oxygen species. This research study aims to investigate the interaction between BLC and nanoparticles.

Methods: The structural change and interaction between SiO2 NPs and BLC are investigated under the physiological condition using fluorescence spectroscopy at 298 and 310 K. The quenching constants, binding constant as well as thermodynamic parameters are calculated and the interaction mechanism is also suggested.

Results: Fluorescence data represented the decreasing in intrinsic emission of enzyme with increase in SiO2 NPs concentrations, which indicates that changes have been done at three dimensional environments around the enzyme chromophore. Negative values of ΔG is obtained suggests that the interaction of the SiO2NPs with BLC is spontaneous. The negative thermodynamic parameters of enthalpy (ΔH) and entropy (ΔS), suggest that the binding reaction is mainly mediated by van der Waals forces and hyogen bonds. The binding constants and the number of binding sites at different temperatures are also calculated, and it is found that a single binding site exists.

Conclusion: The analysis of fluorescence data indicated the presence of static quenching mechanism in the binding. The negative values of ΔH and ΔS of SiO2NPs- BLC complexation indicate that the binding is mainly enthalpy stabilized and the entropy destabilized.

Keywords: Catalase, Spectrofluorimeter, SiO2 nanoparticle

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The anti-depressant effects of Crocin and Crocetin based on behavioral test and serum serotonin levels in the rat model of depression

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Page | 505

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Introduction: The therapeutic effect of saffron on depression has long been discussed. In this study, the effect of saffron carotenoids, Crocin and Crocetin, was investigated on improving behavioral symptoms in the rat model of depression and correlation between serum serotonin and behavioral tests.

Methods: Unpredictable chronic stress model (UCMS) Chronic stress was used to induce depression, which was confirmed using behavioral tests, including the sucrose preference test (SPT) and forced swimming test (FST). Then, rats in each group (control and UCMS) were randomly divided into 5 groups non-treated saline- treated (1 ml/kg/day), fluoxetine (10 mg/kg/day), crocin (30 mg/kg/day), crocetin (10 mg/kg/day) by daily intraperitoneal injection, up to 21 days. Serotonin levels were measured in their serum using serotonin ELISA kit (abcam; ab133053) according to the manufacturer's instructions.

Results: Before treatment, SPT and FST respectively showed, a significant ($p = 0.0010$) decrease in sucrose preference and significantly increase ($p <0.0001$) in immobility time in UCMS group in compared to control. Crocin and crocetin led to reduce immobility time in UCMS compere to nontreated and saline-treated groups. The results of serotonin measurements showed a significant reduction following UCMS induction. Serotonin in both UCMS groups treated with crocin ($p = 0.0134$) and crocetin ($p = 0.0454$) had a significant increase compared to the UCMS group received saline. In this study, positive correlations were observed between serotonin concentration and sucrose intake ($r = 0.3763$, $p = 0.0030$) in SPT.

Conclusion: Consistent with depression in humans, UCMS led to anhedonia, observed as a significant decreased sucrose preference. UCMS group showed significantly increase immobility time in FST. We observed crocin and crocetin improved depression-like behaviors such as increased consumption of sucrose solution in SPT and decrease in behaviors despair in FST. ELISA tests indicated the anti-depressant of crocin and crocetin.

Keywords: Crocin, Crocetin, Fluoxetine, FST, SPT, OFT, EPM

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Aptamer Based Nanosensors for Rapid detection of Uranyl Ions

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Page | 506

Introduction: In recent years, aptamers have been selected for rapid and on-site detection of heavy metal ions. The purpose of this research is to create a Nano-aptamer kit to have a great sensitivity and specificity for rapid detection of uranyl ions.

Methods: Aptamers are designed according SELEX process. The aptamers (Apt)were conjugated to silver nanoparticles (AgNP) and incubated at room temperature for certain times. Uranium samples were then added to the Apt-AgNP complex. After 30 minutes, CTAB salt was added to the reaction. The components of rapid kit were analyzed with UV-Vis spectrometer, FT-IR and agarose gel electrophoresis.

Results: This method causes the color of the reaction to change from light yellow to dark yellow due to a conformational change in aptamer in the presence of uranium and the CTAB-induced AgNP accumulation phenomenon, which can be controlled using the naked eye or visible spectroscopy. The results showed that the sensitivity and specificity of the designed kit is very high. Using this kit, uranium is detected at 10 mM and 100 mM with the naked eye and visible spectroscopy respectively.

Conclusion: This colorimetric assay only uses common reagents and assessed visually, and so has a great potential for rapid, on-site and real time detection of uranyl ions in environmental.

Keywords: Aptamer, Nanosensors, Rapid Test, Uranyl Ions

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A randomized double-blind, placebo-controlled trial on the effect of nigella sativa supplementation on cardiometabolic outcomes in patients with non-alcoholic fatty liver

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Introduction: and purpose: Non-alcoholic fatty liver disease (NAFLD) is one of the metabolic disturbances associated with liver cell inflammation. Nigella sativa (N.sativa) is a widely used medicinal plant known for its anti- inflammatory, antimicrobial, antioxidant, and hepato-protective properties. This study aimed to assess the ef-fect of supplementation of N. sativa oil on plasma levels of adiponectin, leptin, and blood pressure (BP) in patients diagnosed with NAFLD. Materials and

Methods: This randomized, double-blind, placebo-controlled clinical trial was conducted on 44 NAFLD patients. Participants were randomly assigned to two groups (n =22/group); the experimental group received 1000 mg of N. sativa oil per day, while the control group received a placebo for eight weeks. The primary outcome measures were serum levels of adiponectin, leptin, and systolic and diastolic blood pressure measured at the baseline and the end of the intervention. **Results:** After eight weeks of supplementation with N. sativa oil, no statistically significant differences were found in serum levels of adiponectin (p =0.40), leptin (p =0.89), systolic BP (p =0.13), and diastolic BP (p =0.09) between the two groups. Furthermore, after supplementation with N. sativa, no significant changes were observed in leptin (p =0.07), adiponectin (p =0.13), systolic BP (p =0.82), and diastolic BP (p =0.38) within the two groups.

Conclusion: These results indicate that administration of N. sativa oil 1000 mg/day for 8 weeks has no favorable effect on cardiometabolic measures in NAFLD patients. Further studies with higher dosage over a longer period are needed to investigate whether this effect is dose- and time-dependent.

Keywords: Nigella sativa, Non-alcoholic fatty liver disease, Cardiometabolic outcomes

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Designing an Aptamer-Based Colorimetric Mercury Assay

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Introduction: Mercury is one of the most highly toxic metals found in the environment that widely used global pollutants in industry. Occupational and environmental poisoning with mercury is a concern for public health worldwide and the ecosystem. Therefore, it is necessary to design a fast and cost-effective diagnostic method. Biosensors are highly desirable for easy and accurate detection of environmental pollutants. The purpose of this study is to design and fabricate a rapid and sensitive diagnostic kit for mercury.

Methods: In the first assay, we designed a mercury specific aptamer (HgApt) and was incubated it with GNPs (gold nanoparticles) at room temperature for 1 hour. Mercury samples were then added to the complex. The aptamer bined to the mercury and as a result, the solution of AuNPs undergoes aggregation. Nano- aptamer kits were characterised by X-ray diffraction (XRD) and spectrophotometry.

Results: In the presence of mercury, the gold nanoparticles were aggregated, owing to the formation of aptamer–mercury complex and the color turns from red to blue detected by colorimetric response of AuNPs aggregation. Detection limit of the aptasensor can reach 1mM only observed by naked eyes within 5 min. Other metal ions have no interferences

Conclusion: Aptasensor specially made for mercury has many excellent sensitivity and selectivity as a bioprobe for on-site and real time detection of mercury. Keywords: Aptasensor, Mercury, Rapid Test

Keywords: Keywords: Aptasensor, Mercury, Rapid Test

The role of tumor suppressor genes in hepatocellular carcinoma

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Introduction: One of the deadliest forms of cancer in the world is hepatocellular carcinoma. Indirectly or directly, tumor suppressor genes can stop cell division or cause cell death. The well-known tumor suppressor genes in HCC include tumor protein p53 (P53), phosphatase and tensin homolog (PTEN), axin 1 (AXIN 1), and retinoblastoma transcriptional corepressor 1 (RB1). When a tumor suppressor gene is turned off, either by accidentally deleting it or by mutation, the brake is relaxed, the cell may begin to grow and divide out of control, which could cause the cell to develop into a cancer cell. The purpose of this study was to determine TSG's function and significance in hepatocellular carcinoma. Search

Methods: This study was conducted by searching the keywords tumor suppressor gene and liver cancer from Valid scientific databases such as Science Direct, Springer, Google Scholar, and PubMed.

Result: The results of various studies have shown that tumor suppressor genes from different gene families play an important role in the occurrence of liver cancer, including these genes included, Suppressors related to the MEK/ERK pathway, Suppressors related to the PI3K/AKT pathway, Suppressors related to the transforming growth factor-beta(TGF-b) pathway, Tripartite motif (TRIM) family. Tumor suppressor proteins can move between particular cellular compartments, which is an effective way to transmit messages.

Conclusion: Numerous studies have shown that the "two-hit" model, which incorporates non-genetic/epigenetic events such as transcriptional regulation, proteasome degradation, or aberrant nucleocytoplasmic shuttling, demonstrates how a genetic and an epigenetic event leads to loss of TSG expression. Certain tumor suppressor proteins exhibit distinct localization patterns in normal and cancer cells, and it has been demonstrated that altered spatiotemporal dynamics of tumor suppressor protein signaling play a role in the development of cancer and the spread of malignancy.

Keywords: Tumor Suppressor, Cancers, Tumor Protein P53, PI3K/AKT

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Design of Aptasensor for Rapid Detection of lead ions based on Gold-nanoparticl

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Introduction: Lead is a major global heavy metal and pollutant with high toxicity that is obtained from various sources in the environment and has various applications. The use of lead has had detrimental effects on the world's ecosystem and public health for centuries. The aim of this research is to design a special nano-aptasensor for fast and high sensitivity detection of lead.
Methods: First, the special aptosensor for lead were designed and its 2-D structures were obtained using mFold and RNA structure tools. The PbApt (lead aptamer) was incubated with GNPs (Gold nanoparticles) for 21 at room temperature. The specificity and sensitivity of the rapid aptasensor was evaluated using optical colorimetry and spectrophotometry methods. Other characteristics of nano-aptasensor were determined using FT-IR, X- ray diffraction and agarose gel electrophoresis.
Results: The soluble color change from red to purple, which occurs in the presence of lead ions attached to PbApt, observed with the naked eye and by the spectrophotometry. The results showed that the designed kit detects lead ions with high specificity and sensitivity at low concentrations as low as 100 µM.
Conclusion: With this simple and specialized nano-aptasensor kit, lead ions can be detected with the naked eye, and due to its rapid detection, high sensitivity and cost - effectiveness, it can be used in community screening for lead contamination. Keywords: Aptasensor, Rapid Test, lead ions, Gold-nanoparticl

Keywords: Aptasensor, Rapid Test, lead ions, Gold-nanoparticl

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Evaluation of serum level of alpha 1-antitrypsin as an acute phase protein in patients with covid 19 by nephelometric method.

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Introduction: Alpha 1-antitrypsin (AAT) is a single chain glycoprotein containing 394 amino acids with 52 kDa molecular weight and a half-life of 3 to 5 days. This acute phase protein is mainly produced in liver and its gene located on chromosome 14 at position 14q32.1. Covid 19 virus can infect host cells by binding to the ACE2 receptor TMPRSS2 membrane protein. AAT as a serine protease inhibitor has been estimated that involving in this mechanism. Since this protein is acute phase proteins, its serum levels are expected to increase in patients with covid 19. **Methods:** Serum AAT in 31 hospitalized patients with covid 19 and positive PCR test and 31 healthy individuals measured by nephelometric method, which is based on the reaction between an antibody and an antigen. AAT forms a complex with a specific antibody, light is emitted from the source and the intensity of the light scattered by the antigen-antibody complexes is measured by a detector.

Results: Serum AAT in covid 19 patients exhibit a significant increasing (178.9±41.4) as compared to healthy controls (129.4±13.9). (P≤0.05).

Conclusion: The mean of AAT in covid 19 patients' serum was significantly higher than healthy controls. Accordingly it can be supposed that AAT as a protease inhibitor, should be measured in covid 19 patients and duo to its functional mechanism may be considered as covid 19 patients treatment.

Keywords: Alpha 1 antitrypsin ،Covid 19 ،Acute phase proteins

A-10-1695-1

The effect of methyl thiophanate and tricyclazole fungicides on the hematological parameters of blood plasma of Wistar rats

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Page | 512

Introduction: Tricyclazole (TC) and Thiophanate methyl (TM) fungicide combination are widely used in agriculture to eliminate rice blast disease. Thiophanate Methyl is a systemic fungicide that causes damage to red blood cell membranes and changes in the structural and functional integrity of proteins associated with plasma membranes. Also, tricyclazole, as a fungicide from the triazole family, leads to the production of free radicals and damage to the cell membrane. For this purpose, the present study examines the hematological changes caused by the combination of thiophanate methyl and tricyclazole in Wistar rats.

Methods: This study was conducted on 32 male Wistar rats weighing 200 ± 20 grams. Rats were randomly divided into four control groups and groups receiving combined poisons with doses of 25 mg/kg TC +664 mg/kg TM, 19 mg/kg TC +498 mg/kg TM and13mg/kg TC+332 mg/kg TM division and poison. It was administered orally for 28 days. At the end of the experiment, blood samples were collected in tubes containing EDTA, collected and various hematological parameters are evaluated.

Results: The obtained results indicated that the amount of hemoglobin, the average volume of red blood cells, hematocrit and the average hemoglobin per red blood cell in the groups receiving poison did not differ significantly compared to the control group ($P > 0.05$), but the number of platelets in the group receiving poison With the dose of 25 mg/kg TC +664 mg/kg TM and 19 mg/kg TC +498 mg/kg TM, it has increased significantly compared to other groups ($P < 0.05$).

Conclusion: According to the results obtained from this study, the combination of thiophanate methyl and tricyclazole in rats in high doses, the probability of thrombocytosis increases.

Keywords: Methyl thiophanate, Tricyclazole, Hematocrit, Thrombocytosis, Wistar rats

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Bioinformatic characterization of gene expression profile in esophageal squamous cell carcinoma

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Introduction: Esophageal cancer is one of the most lethal malignancies globally, with a major incidence rise in the Western countries over recent decades. 2 to 4 out of 5 cases are living in nonindustrialized regions, with the most significant incidence in Asia and Africa. Esophageal cancer is commonly diagnosed after its advanced stages, with the primary cause being the absence of early clinical signs. The Caucasian ethnicity, male sex, gastroesophageal reflux disease (GERD), smoking (or a history of smoking), and obesity are risk factors for this illness, according to research.

Methods: GSE161533, a microarray dataset, was acquired from the Gene Expression Omnibus (GEO) (GEO) (GEO). There are 28 tumor and 56 control samples in this collection. The transcriptome analysis console (TAC) was used to normalize and examine the differentially expressed genes (DEGs). DEGs between normal and tumor samples were chosen based on adjusted p-value (F) 0.05, and protein-protein interaction (PPI). visualization was conducted using String, Cytoscape, and Gephi, respectively.

Results: DEGs were discovered for 2280 genes (1036upregulated, 1244 downregulated). Our study found five hub genes (including HSP90AA1, JUN, IL1B, ACTA2, CDK1): Rheumatoid arthritis, Malaria, Toll-like receptor signaling pathway, IL-17 signaling pathway, and TNF signaling pathway. Furthermore, the findings of the KEGG pathway analysis indicated that these genes were overrepresented in key pathways for Thl and Th2 cell differentiation, T cell receptor signaling, and hematopoietic cell lineage.

Conclusions: In conclusion, the results of this research may contribute to the creation of novel targets for pharmaceutical discovery and cancer treatment.

Keywords: Systems biology, Bioinformatics, Gene network analysis, esophageal carcinoma

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Evaluation of methyle thiophanate and tricyclazole on white blood cells in wistar rats

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Introduction: Fungicides are one of the most important pollutants used to eradicate diseases. The combination of two fungicides, Methyl thiophanate (MT) and Tricyclazole (TC), is used to eliminate fungal diseases. Methyl thiophanate causes harmful changes in the cell membrane by disrupting the balance in the production of free radicals. Also; the fungicide tricyclazole causes biological damage by causing lipid peroxidation of the cell membrane. Xenobiotic agents cause tissue damage by activating the inflammatory response, so the immune system plays a key role in protecting organs against these agents. For this purpose, the present study examines the changes in the cells of the immune system caused by the consumption of methyl thiophanate and tricyclazole in Wistar rats.

Methods: This study was conducted on 32 male Wistar rats weighing 200 ± 20 grams. Mice were randomly divided into two control groups and a group receiving combined poisons with doses of 25 mg/kg TC +664 mg/kg TM, 19 mg/kg TC +498 mg/kg TM and 13mg/kg TC+332 mg/kg TM and the poison was administered orally for 28 days. At the end of the experiment, blood samples were collected in tubes containing EDTA and various hematological parameters are evaluated.

Result: The findings show a significant and dose-dependent increase in the number of white blood cells in the group receiving poison with a dose of 25 mg/kg TC +664 mg/kg TM compared to other groups (P<0.05). The highest amount of neutrophils and eosinophils was seen in the group receiving poison with a dose of 25 mg/kg TC +664 mg/kg TM, which had a significant difference compared to the control group (P<0.05) and the amount of lymphocytes decreased with increasing dose.

Conclusion: Based on the findings of this research, methyl thiophanate leads to leukocytosis, neutrophilia, eosinophilia and lymphopenia, therefore due to the side effects of these fungicides

Keywords: Methyl thiophanate, Tricyclazole, Immune system, Leucocytes, Wistar rats

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Evaluation of the protective effect of geraniol against bisphenol A-induced oxidative stress through the Keap-1 / Nrf2 signaling pathway in the liver of rats

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Introduction: Bisphenol A (BPA) which mostly is used as a monomer of polycarbonate plastics,has harmful effects on human health.Today,the use of this chemical agent in all aspects of human life such as food,clothing and medicine has increased amatically.Geraniol is a natural plant-derived antioxidant that has various medicinal properties including antioxidant,anti-inflammatory,antimicrobial and anti-tumor properties.In this study,the protective effect of geraniol against BPA-induced damage and expression of genes involved in oxidative stress pathways such as Keap1/Nrf2 and Ho-1 in liver tissue was investigated.

Methods: Forty male Wistar rats were divided into 5 groups:3groups were healthy animals that received physiological serum,olive oil and geraniol,the fourth group BPA and the fifth group BPA plus geraniol for 4 weeks.24hours after the last treatment,blood samples were taken from the heart and liver tissue was removed.Oxidative stress markers,antioxidant enzyme and biochemical factors were measured in serum and liver tissue.The expression of genes involved in the oxidative stress pathway such as Nrf2,HO-1 and Keap1 in liver tissue was measured by RT-PCR.

Results: BPA administration significantly decreased total antioxidant capacity (TAC), glutathione(GSH) and the activity of catalase(CAT), superoxide dismutase(SOD) and glutathione peroxidase(GPx) enzymes,and also significantly increased total oxidant status(TOS) and malondialdehyde(A) in serum and liver tissue. in addition, BPA administration significantly increased serum glucose, triglyceride and cholesterol levels, as well as increased serum aspartate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphatase (ALP).Geraniol administration significantly decreased serum triglyceride, TOS, A, ALT, AST and ALP and increased TAC and CAT enzyme activity in serum and liver tissue.BPA administration significantly decreased the expression of Nrf2,HO-1 and increased the expression of Keap1genes and geraniol treatment significantly increased the expression of Nrf2, HO-1, and decreased the expression of Keap1 genes but this reduction in Keap1 was not statistically significant

Conclusion: This study suggests that daily consumption of compounds containing geraniol, can have protective effects against the harmful effects of bisphenol A.

Keywords: Oxidative stress, Bisphenol A, Geraniol, Nrf2 gene, Keap1 geneh

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Chromatographic purification of Enterokinase from bovine duodenal extract

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Introduction: Mammalian Enterokinase (EC 3.4.21.9) is a duodenal digestive enzyme which has a two-subunit glycoprotein structure and contains a single disulfide bond. Enterokinase exhibits a remarkable specificity towards the $(Asp)_4$ -Lys sequence inside the protein structures. Hence, it is widely considered as a biotechnological tool in the digestion of fusion proteins and elimination of purification and reporter tags such as poly His, GST, and GFP. In the present study, we have developed a single-step chromatographic procedure for concentration of enterokinase from bovine duodenal extract.

Methods: 50 Bovine duodena were obtained from slaughter house immediately after death of animals and were frozen at -20. Samples were rinsed using 20 ml distilled water and duodenal extracts were pooled and filtered through paper. The filtrate was subjected to 45% ammonium sulphate precipitation. After centrifugation the supernatant was discarded and the pellet was dissolved in tris-buffered saline (TBS). The resulting solution was loaded on DEAE-Sepharose chromatography column. After a 5-CV wash using TBS, elution was performed using acetate or phosphate buffer with different pH values ranging from 3.5 to 7.5. fractions were collected and analyzed through BCA protein assay, SDS-PAGE and ELISA using anti-enterokinase polyclonal IgY and anti-chicken HRP conjugate.

Results: SDS-PAGE analysis showed a well-purified protein band for fraction collection of pH: 4 (figure 1) with apparent molecular size of 55 KDa which is equal to molecular size of light chain of bovine enterokinase. This collection was found to contain at least 0.5 mg protein per milliliter. ELISA analysis confirmed the presence of high amount of Bovine Enterokinase in mentioned fraction compared to pre-column sample. Figure 1. SDS-PAGE analysis of anion exchange chromatography.

Conclusion: Our designed simple procedure shows acceptable capacity in concentration of bovine enterokinase from duodenal extract. The process could be further optimized by including a gel filtration step.

Keywords: Enterokinase, bovine duodena, chromatography, enzyme purification

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A non-enzymatic diagnostic tool for pathogenic bacteria detection: An in-silico design

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Page | 517

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Introduction: An affordable, simple, and fast diagnostic technique has become a demanding hotspot during the past two decades. Nano-biosensing seems to be a good candidate providing both simplicity and precision, simultaneously. Therefore, DNA nanostructures have attracted significant attention due to their programmability and stability. Herein, an autonomous enzyme-free biosystem was designed for pathogenic bacteria detection specifically.

Methods: The target gene was selected through a literature survey and compared with the database to ensure the specificity of the method by NCBI's BLAST software. NUPACK was used to encode, design, and verify the hairpins used in the biosystem. The secondary structure predictions were confirmed by OligoAnalyzer, which was also utilized to design the hairpins.

Result: The results demonstrated that the selected target gene is specifically for designing the two components (i.e., hairpin one and hairpin two), in a reaction condition where the temperature was adjusted to 25℃, and 0.05M of the salt concentration. The target gene was used as a platform based on which the hairpins were designed by encoding the features of the sequences to the software. It was shown that the coding system and the corresponding adjustments yielded the best output for hairpin design. The resulted sequences were confirmed by the OligoAnalyzer™, showing that every single step in the designed biosystem was thermodynamically the most probable way of interaction between these structures.

Conclusion: The bioinformatic analysis of the designed DNA walker biosystem showed that this novel technique could detect the pathogenic genes without using sophisticated equipment (e.g., thermal cycler) at room temperature and needless of enzymes and proteins.

Keywords: DNA walker ‹biosensor ‹in-silico analysis ‹Klebsiella pneumoniae

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Mechanism of cell death induced by oxaliplatin in mouse bone marrow hematopoietic cells

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Page | 518

Introduction: Oxaliplatin is a platinum-based chemotherapeutic ug which is currently used in colorectal cancer treatment. One of the major side effects of oxaliplatin is myelosuppression. In our previous study, oxaliplatin has shown cytotoxicity effect on non-adherent mouse bone marrow hematopoietic cells in dose dependent manner.

Methods: Because of toxic effects of oxaliplatin on normal cells, in present study we have investigated mechanism of cell death in bone marrow hematopoietic cells after exposure to this ug. For this purpose, Hoechst 33252 and acridine orange/ethidium bromide fluorescent staining, PARP cleavage, DNA fragmentation, superoxide anion production and flow cytometry techniques were employed.

Results: morphological studies of cells treated with oxaliplatin, using fluorescent microscopy, display a typical apoptotic changes including reduction of cellular volume and, condensed and fragmented nuclei. PARP is a DNA binding nuclear enzyme that is cleaved to 85 kDa and 25 kDa fragments by caspases during apoptosis. Western Blot analysis showed that increasing the concentration of oxaliplatin, increases production of the 85 kDa fragment as a marker of PARP cleavage and apoptosis. In addition, diphenylamine reaction represents a remarkable increase in DNA fragmentation in the cells exposed to oxaliplatin suggesting induction of apoptosis in hematopoietic cells. The results of measuring the production of superoxide anion in treated cells, showed that increasing ug concentration stimulates the production of free radicals, which indicates the occurrence of apoptosis. Flow cytometry tests using an annexin V/PI detection kit, also confirm the effect of oxaliplatin in apoptosis induction in mouse bone marrow hematopoietic cells. **Conclusion:** oxaliplatin is a cytotoxic ug which induces cell death in bone marrow hematopoietic cells by apoptosis. Since platinum-based ugs are widely used for chemotherapeutic eradication of cancer, this result can be considered in design of new ugs with fewer side effects.

Keywords: chemotherapy, apoptosis, hematopoietic cells

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Nutrients target glioma cells by affecting molecular mechanisms, and signaling pathway

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Introduction: Glioma is the most common malignant brain cancer that has uncontrolled proliferation and is defined as an externally invasive tumor. Therefore, their recurrence rate is high and the prognosis is low. Despite significant advances in neuroimaging, neurosurgery, and radiation therapy, gliomas, in particular glioblastoma are highly resistant to treatments including radiotherapy, surgery, and temozolomide chemotherapy. The median survival of patients with malignant glioma is still less than two years, accordingly, the search for new treatment options has recently become an urgent need. Today, a number of nutrients have received attention due to their special role in inhibiting the process of angiogenesis, metastasis and promotion of apoptosis, and finally inhibiting tumor growth, including glioma. This review summarized the publications related to the biological roles of different nutrients in glioma.

Methods: PubMed and Web of Science databases were used to search publications related to nutraceuticals and glioma with the following keywords, nutraceuticals, molecular mechanism and glioma.

Results: Nutrients can disrupt cancer cells by affecting different pathways. One of the key targets of nutrients may be regulation of cell signaling pathways such as PI3K/Akt/mTORC1, JAK/STAT, and GSK-3 or exerting their effects through other mechanisms such as cytokine receptors and inflammatory pathways, reactive oxygen species, and miRNAs. The review refers to the results of recent studies and target molecules as well as signaling pathways affected by certain nutrients in glioma cells.

Conclusions: Herein, we clarified the functional roles of nutraceuticals in glioma. These studies indicated that clinical trials are imminent and that new approaches could benefit patients.

Keywords: Nutrients, signaling pathway, gliomas

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Investigating the Effect of Cyclophosphamide on Expression Changes of LncRNA TUG1 in Acute Lymphoblastic Leukemia

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Introduction: and purpose: Acute lymphoblastic leukemia (ALL) is a kind of blood cancer. 80 percent of ALL cases occur in chilen. ALL has a bimodal incidence pattern, with the first peak occurring in childhood and the second peak happening around the age of 50. TUG1 plays a role in tumor suppressors. The goal of this study was to see how the cyclophosphamide affected the expression of LncRNA TUG1 in the Jurkat E6.1 cell line.

Methods: In this research, appropriate doses of cyclophosphamide were prepared according to the IC50 of the ug which consists of 20 and 50 µM. The Jurkat E6.1 cell line was treated with cyclophosphamide 72 hours after cell passage. The expression changes of LncRNA TUG1 and GAPDH as the housekeeping gene were investigated using Real-Time PCR after RNA extraction and cDNA synthesis.

Results: The Results of the research showed that after 72 hours of treatment with cyclophosphamide at 50µM, the expression of LncRNA TUG1 increased significantly as compared to the control group. According to the findings, doses of 20 and 50 µM of cyclophosphamide over 72 hours were the optimal concentrations and time for this ug's effect. The expressions of LncRNA TUG1 were 0.158 and 2.82 at the specified concentrations and times.

Conclusion: According to the findings of the study of expression changes in LncRNA TUG1 as a Tumor suppressor gene after treatment with cyclophosphamide, in 50µM of the ug successfully increased. LncRNA TUG1 expression. Overall, cyclophosphamide had a positive effect on the LncRNA TUG1 and this increase in expressions was statistically significant (p-value 0.001). Keywords: Cyclophosphamide, cDNA, GAPDH, LncRNA TUG1

Keywords: Cyclophosphamide, cDNA, GAPDH, LncRNA TUG1

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Association between circulating visfatin and pre-eclampsia: a systematic review and meta-analysis

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Page | 521

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Introduction: Pre-eclampsia (PE) is a serious pregnancy status characterized by high blood pressure. However, visfatin is usually associated with PE. Observational studies evaluating the relationship between circulating visfatin and pre-eclampsia have reported inconsistent results. We conducted this systematic review and meta-analysis to summarize published data on the association between visfatin and pre-eclampsia

Methods: Electronic databases PubMed, ISI web of science, EMBASE, Scopus, and the Cochrane library were comprehensively searched for selection of eligible studies. A random-effects model and the generic inverse variance method were used for quantitative data synthesis. Sensitivity analyses and prespecified subgroups were conducted to evaluate potential heterogeneity.

Results: Thirteen studies comprising a total of 536 subjects were included in this meta-analysis. We observed that the pre-eclampsia risk is associated with a statistically significant elevation of visfatin level [S (1.33 µg/l) (95% CI 0.37, 2.2) p = .007]. No significant publication bias was observed in the meta-analysis. Subgroup and sensitivity analyses indicated that the pooled effects size was affected by systolic blood pressure, gestational age, body mass index, and pregnancy trimesters.

Conclusions: Our data revealed that the increase in visfatin level could be associated with the risk of pre-eclampsia. However, further studies on pre-eclampsia populations are warranted for the corroboration of our findings.

Keywords: Visfatin, pre-eclampsia, pregnancy, biomarker

A-10-1712-1

Molecular mechanism of high-intensity interval training (HIIT) intervention on metabolic disease managements

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Page | 522

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Introduction: Physical activity is highly advised as non-pharmacological intervention in metabolic disease management. Huge body of evidences showed effects of continuous endurance training (CET) and high-intensity interval training (HIIT) as different types of physical activity in management of metabolic synome. Our recent studies focused on molecular mechanisms of the effect of exercise training intervention in metabolic disease and compared CET and HIIT intervention.

Methods: Serum biochemical metabolic parameter determined in obese and regular exercise trained subjects in case-control study. To prove importance of sport intervention, 2 month exercise intervention trial performed in HFD feed animal model. Then effect of ET intervention at molecular level studied in HFD induced obese rats and confirmed by invitro study.

Results: The results indicated beneficial effect of exercise intervention and this finding confirmed in animal model via focusing on miRNA, macrophage polarization and adipokins such as CTRP12. High-intensity interval training (HIIT) alleviated NAFLD feature via miR-122 induction and miR-33 dependent autophagy induction, enhances heart function via miR-195 dependent cardiomyopathy reduction, miR-206 dependent HSP60 induction, improves diabetic cardiomyopathy via miR-1 dependent suppression of cardiomyocyte apoptosis, reversed high-fat diet-induced m1-macrophage polarization in rat adipose tissue via inhibition of notch signaling, ameliorate lipid profile imbalance by induction of CTRP12 in high-fat high-fructose diet-induced diabetic rats.

Conclusion: Therefor long life programmed physical activity recommended to manage metabolic disease.

Keywords: Metabolic disease, CET, HIIT, miRNA, adipokine and macrophage polarization

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The exosomes of TGFβ-pretreated Wharton jelly-derived mesenchymal stem cell improved liver fibrosis in the LX2 cell line

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Introduction: Pretreatment of mesenchymal stem cell () is considered as an important tool to improve the effects of s in the regeneration and repair of damaged tissues, including liver fibrosis. The purpose of this study is to investigate the effects of TGFβ1 pretreated of WJ-s in improving fibrotic markers in LX-2 cell line.

Methods: WJ- were pretreated with different concentrations of TGFβ1 (0.1, 0.5, 1, 5 and 10 ng/ml) and were co-cultured with activated Hepatic Stellate Cells (HSCs). Then, exosomes were extracted from TGFβ1 pretreated of WJ-s and they were treated with activated HSCs. Finally, Real-Time PCR and western blot were used to investigate fibrotic genes and protein levels.

Results: TGFβ1 treatment increased P-Smad2/3 phosphorylation, α-SMA and Collagen1α1 and decreased E-Cadherin gene expression and protein levels in LX-2 cells. Treatment with exosomes of TGFβ1 pretreated WJ- (low level of TGFβ1: 0.1ng/ml) caused a significant decrease in p-Smad2/3 phosphorylation levels in activated HSCs. E-Cadherin gene expression and protein levels increased and α-SMA and Collagen1α1 gene expression and protein levels were significantly decreased compared with exosomes of untreated WJ-s. These results were also observed in co-culture of TGFβ1 pretreated of WJ-s and activated HSCs.

Conclusion: Exosomes of TGFβ1 pretreated of WJ- can reduce TGFβ-Smad2/3 signaling and the expression of fibrotic markers in activated HSCs. However, these effects were significantly reduced by using exosomes from TGFβ1 pretreated of WJ- at a concentration of 0.1 ng/ml TGFβ1 in activated HSCs. Therefore, exosomes and paracrine factors derived from TGFβ1 pretreated of WJ- may be critical in ameliorating fibrosis and beneficial for patients with liver fibrosis.

Keywords: Liver fibrosis, TGFβ1, Pretreatment, WJ-s, LX-2 cell, exosomes, co-culture

Metformin affects macroscopic alterations in colon tissues of acetic acid-induced ulcerative colitis rat models

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Introduction: Ulcerative colitis, one of the subtypes of inflammatory bowel disease (IBD), which is characterized by aberrant immune responses in the colon leading to trigger the inflammatory cascades, is progressing all over the world, including in Iran. The aim of present study is to investigate the anti-inflammatory effects of metformin on the macroscopic changes in colon tissues of the colitis model induced by acetic acid.

Methods: Acute colitis was induced in Wistar rats by intra rectal administration of 2 ml of 3% acetic acid. The study included 5 groups of rats as follows: normal control group, negative control group, positive control group receiving 150 mg/Kg/ body weight of Mesalazine, first experimental group receiving 100 mg/Kg/ body weight of Metformin and second experimental group receiving 150 mg/Kg/ body weight of Metformin. Macroscopic parameters such as body weight loss, colon length changes, hematochezia and diarrhea severity were evaluated by researchers.

Results: The results of this study shows that metformin treatment significantly reduced body weight loss in comparison with negative control group. In addition metformin successfully reduced hematochezia and diarrhea compared to acetic acid group.

Conclusion: It is suggested that metformin treatment may has the potential to alleviate inflammation in the colon tissues of the colitis model induced by acetic acid.

Keywords: Ulcerative colitis, Metformin, Acetic acid model, colon

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Investigating the Effect of Complex1 (Methotrexate+ Cyclophosphamide), Complex2 (Cyclophosphamide+ Cytarabine), Complex3 (Cytarabine+ Mercaptopurine) on Expression Changes of LncRNA TUG1 in Acute Lymphoblastic Leukemia

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Introduction: and purpose: Acute lymphoblastic leukemia (ALL) is a kind of leukemia that affects lymphoid progenitor cells in the bone marrow and blood often in chilen. The goal of this study effect of the Complex1, Complex2, and Complex3, affected the expression of LncRNA TUG1 in the Jurkat E6.1 cell line.

Methods : In this research, appropriate doses of the Complex1 (1µM Methotrexate+ 20µM Cyclophosphamide), Complex2 (20µM Cyclophosphamide+ 1µM Cytarabine), Complex3 (1µM Cytarabine+ 5µM Mercaptopurine) were prepared according to the IC50 of the ug. The Jurkat E6.1 cell line was treated with prepared Complexes at 72h after cell passage. The expression changes of LncRNA TUG1 and GAPDH as the housekeeping gene were investigated using Real-Time PCR after RNA extraction and cDNA synthesis.

Results: The Results of the research showed that after 72h of treatment with Complex1 (1 µM Methotrexate+20 µM Cyclophosphamide), Complex2 (20µM Cyclophosphamide+ 1µM Cytarabine), Complex3 (1µM Cytarabine+ 5µM Mercaptopurine) the expression of LncRNA TUG1decreased significantly as compared to the control group. According to the findings, Complex1 (Methotrexate+ Cyclophosphamide), Complex2 (Cyclophosphamide+ Cytarabine), Complex3 (Cytarabine+ Mercaptopurine) over 72h were the optimal concentrations and time for this ug's effect. The expressions of LncRNA TUG1 were 1.25, 1.8, and 2.024 at the specified concentrations and times.

Conclusion: According to the findings of the study of expression changes in LncRNA TUG1 as a Tumor suppressor gene after treatment with Complexes, all three concentrations of the ug successfully increased LncRNA TUG1 expression. Overall, Complex1 (1µM Methotrexate+ 20µM Cyclophosphamide), Complex2 (20µM Cyclophosphamide+ 1µM Cytarabine), Complex3 (1µM Cytarabine+ 5µM Mercaptopurine) had a positive effect on expressions TUG1 at 72h, and this increase in expressions was statistically significant (p-value 0.001).

Keywords: cDNA, GAPDH, LncRNA TUG1, Methotrexate

A-10-1656-1

The effect of L-Carnitine against cyclophosphamid on expression and epigenetic changes of gene Lhx8, involved in mice Premature Ovarian Failure (POF)

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Introduction: Cancer treatments with chemotherapy ugs and infertility are related topics that have received significant attention from researchers in numerous fields. Cyclophosphamide (CP) as an anti-cancer ug is frequently used to treat various types of cancer and treatment with this ug can cause reproductive toxicity. A decreased number of ovarian follicles, impaired normal ovarian function, and subsequent premature ovarian failure (POF) are presented as side effects of Cyclophosphamide. The mechanisms involved in premature ovarian failure remain unclear and a better understanding of the biology of this problem may lead to finding a treatment for preserving the follicles against the adverse effects of chemotherapy.so, we investigated the effect of L-carnitine as a widely used antioxidant in possibly protecting the ovaries.

Methods: Six to week-old NMRI female mice were divided into three groups; Control, Cyclophosphamide (CP), and Cyclophosphamide / L-Carnitine (CP + L-CAR) group. After a 21-day period of ug injection, 24 hrs after the last injection ovaries were used to evaluate the expression of Sohlh1 and Lhx8 by Real-time PCR. Furthermore, alteration of Lhx8 promoter methylation was examined by Methylation-sensitive high resolution melting analysis (MS-HRM).

Results: Data showed the negative effect of cyclophosphamide by altering the expression of regulators genes of oogenesis including Sohlh1 and Lhx8. Also, an examination of the epigenetic status of the Lhx8 gene shows a change in promoter methylation of this gene following cyclophosphamide injection. Although L-carnitine is an effective antioxidant, in the present study, the use of L-carnitine failed to protect the ovaries from changes caused by cyclophosphamide injection.

Conclusion: These results identify that using cyclophosphamide can alter the expression of folliculogenesis genes through its effects on epigenetic changes and may cause premature ovarian failure. Our results show that L-carnitine consumption does not protect the ovaries against cyclophosphamide.

Keywords: Premature ovarian failure, Cyclophosphamide, L-Carnitine, Methylation, Follicular activation

A-10-1716-1

Investigation of the effect of culture medium on the Vero cell line growth and the expression of ACE2

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Introduction: SARS-CoV-2 is the causative agent of the COVID-19 pandemic. The Vero cell line is the most used cell line for SARS-CoV2 vaccine production. The virus binds to the ACE2 receptor on cell surface and enters the cell. Due to the high cost of FBS, reducing its concentration in the culture medium can be beneficial for the production of the Covid19 vaccine. For this reason, reduction of FBS in the Vero cell line medium was investigated and its effect on the growth and ACE2 expression was evaluated.

Methods: The cells were cultured in 10%, 5% and 1% FBS in high and low glucose DMEM medium. The viability and proliferation were tested using trypan blue and MTT assay. Primers for ACT-B (as a house keeping gene) and ACE2 receptor were designed. The quantity and quality of extraction was checked using nanoop and agarose gel. Gradient PCR was performed to set the annealing temperature for the real-time PCR. To compare the ACE2 expression in different amounts of FBS, RNA was extracted, cDNA was synthesized and finally, the expression of ACE2 was quantified using real-time PCR.

Results: As the FBS concentration decreased to 1%, the cell adherence and proliferation was reduced slightly. Trypan Blue showed that the cells were alive, however, MTT assay exhibited little changes in proliferation as FBS reached to 1%. The morphology of the cells were similar in all cases. Cell proliferation and morphology did not differ in the presence and absence of glucose. The expression of ACE2 was slightly changed in 1% FBS when compared to 10% FBS. **Conclusion:** In this project, reducing FBS revealed no changes in the morphology and only a slight variation in ACE2 expression. Therefore, this modified medium could make vaccine production process more economical, however, more investigation is required.

Keywords: Vero cell _FBS_ ACE2

A-10-1377-1

Investigation of the role of diethylnitrosamine in renal cancer

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Page | 528

Introduction: The most frequent form of cancer in adult kidneys, renal cell carcinoma (RCC), lacks early warning symptoms and frequently has metastasized by the time it is discovered. Different kinds of nitrosamine are known to be hazardous to both people and animals. The smallest doses of diethylnitrosamine or dimethylnitrosamine either parenterally or orally cause cancer and kidney impairment. Investigating the effect of diethylnitrosamine on kidney cancer was the study's main goal.

Methods: This research utilized scientific resources like Science Direct, Springer, Google Scholar, and PubMed to investigate the function of diethylnitrosamine in kidney cancer.

Result: In most organs and systems, nitrosamines have the possibility of causing tumors. Definitely one of the most important carcinogens is diethylnitrosamine (DENA). Nitrate reacts with amino acids to activate them, creating N-nitrosamines in the stomach's acidic environment. A recognized mechanism of carcinogenesis, such as DENA, is the induction of cell damage with increased cell proliferation and necrosis.

Conclusion: In general, hepatic cytochrome P450 enzymes (CYP450), specifically CYP2E1, are required for DENA's bio-activation, which results in DNA adducts and is initiated by an alkylation mechanism that causes genetically changed cells. Through subsequent oxidative stress and cellular processes, this bio-activation process is an important first step at the beginning of carcinogenesis. Additionally, nitrosamines have been linked to the emergence of esophageal squamous cell cancer (SCC), gastric adenocarcinoma, and renal cell carcinoma. According to the findings of numerous researches in the field of cancer, diethylnitrosamine substances are extremely carcinogenic and harm the kidneys even at modest dosages. Keywords: Diethylnitrosamine, Renal Cancer, Carcinogenesis

Keywords: Diethylnitrosamine, Renal Cancer, Carcinogenesis

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Meaningful expression of TSGA10 gene paralog, Cep135, in Testis tissues of osophila melanogaster

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Introduction: The TSGA10 gene encodes a protein found in mammalian spermatozoa which is associated with the ciliary structure of the sperm tail. The gene is highly conserved among mammalian species, and recent studies have identified the paralogue gene (Cep135) in osophila melanogaster encoding a centrosomal protein with 45% homology to TSGA10. Current study was aimed to primarily investigate the expression of Cep135 and TSGA10 genes in osophila melanogaster.

Methods: The banana medium was used to breed about 200 D. melanogaster off-springs. Following separation of testis tissue form flies bodies, RNA was extracted from testis tissue using protocol modified TRIzol based protocol and, cDNA was synthesized according to Thermo Scientific fisher cDNA kit instructions and then was amplified through RT-Real time PCR using specific primer pairs designed for TSGA10, Cep135, Cyp33, Act2A, and RPL32 genes.

Results: Based on the findings, the TSGA10 gene did not express in testis tissue of osophila melanogaster. Meanwhile, the expression of Cep135 gene could detect in mentioned tissue. Cep135 expression was significatnly different compared to reference studied genes.

Conclusion: Meaningfull different expression of Cep135 in testis tissue of osophila melanogaster indicating its critical role in spermatogenesis of insects, as well. Furhter studies are warranted to define other roles of Cep135 gene in osophila mimicking its paralog gene, TSGA10.

Keywords: TSGA10, osophila melanogaster, Cep135, gene expression

A-10-1405-1

Investigating the effects of new atorvastatin ug derivatives on liver enzymes of New Zealand male rabbits with hypercholesterolemia

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Page | 530

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Introduction: Increasing plasma cholesterol causes liver damage by inducing oxidative stress. Several studies have been conducted regarding the effect of atorvastatin on reducing lipids and atherosclerosis. The aim of the present study is to evaluate the effects of new derivatives of Atorvastatin on changes in liver function tests caused by hypercholesterolemia in New Zealand male rabbits.

Methods: In this study, 30 male New Zealand rabbits were divided into 6 groups including control, hypercholesterolemia caused by a diet rich in cholesterol, hypercholesterolemia + original ug atorvastatin (20 mg/kg daily, oral), hypercholesterolemia + new derivatives of atorvastatin (10 mg/kg kg per day, oral), hypercholesterolemia + new atorvastatin ug derivatives (20 mg/kg daily, oral) and hypercholesterolemia + new atorvastatin ug derivatives (40 mg/kg daily, oral) were divided. After 30 days, blood samples were collected for biochemical evaluation of liver enzymes. Data were evaluated using one-way analysis of variance with Duncan's test in SPSS software version 26.

Results: Hypercholesterolemia significantly increased liver enzymes (ALP, ALT, AST) in comparison with the control group. Administration of new derivatives of atorvastatin with a dose of 10 mg/kg daily significantly improved liver factors compared to the hypercholesterolemia group ($p < 0.05$).

Conclusion: According to the results of this study, the new derivatives of atorvastatin can be effective in improving liver function by reducing cholesterol and liver enzymes. This role is probably through the inhibition of HMG-CoA reductase enzyme, which inhibits cholesterol synthesis.

Keywords: Hypercholesterolemia, atorvastatin, liver enzymes

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Plasma levels of vascular endothelial growth factor in chilen with non-alcoholic fatty liver disease: a cross-sectional study

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Page | 531

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Introduction: Nonalcoholic fatty liver disease (NAFLD) is a health problem growing in line with the rising prevalence of obesity in chilen and adolescents, which leads to hepatocyte inflammation. The present study aimed to compare the plasma levels of vascular endothelial growth factor (VEGF) and soluble VEGF receptor-1 (sVEGFR-1) as inflammation markers in the overweight and obese chilen and adolescents with and without NAFLD.

Methods: This cross-sectional study was conducted on 70 overweight and obese chilen and adolescents (37 males and 33 females), who were selected from overweight and obese chilen admitted to a nutrition clinic in Mashhad, located in the northeast of Iran. The diagnosis of NAFLD was confirmed by Fibro Scan, ultrasound, and elevation of liver enzyme. In addition, plasma VEGF and sVEGFR1 were measured in each patient.

Results: Log-transformed VEGF levels had a significant, stepwise increase from grade zero to the first, second, and third grades ($P<0.001$). However, log-transformed sVEGFR1 showed a regular trend in various grades of NAFLD ($P=0.3$).The odds ratio (95% confidence interval [CI]) of VEGF across the NAFLD categories was estimated at 1.00, 0.99 (95% CI: 0.97-1.01), 1.02 (95% CI: 0.99-1.04), and 1.04 (95% CI: 1.02-1.06). The odds ratios remained relatively unchanged after the adjustment of age, gender, and body mass index (BMI).

Conclusion: According to the results of this study, there were significant, positive associations between plasma VEGF levels and grades of steatosis in overweight and obese chilen and adolescents.

Keywords: Nonalcoholic Fatty Liver Disease, VEGF, sVEGFR1, Chilen, Adolescents

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Cellular and molecular basis of cancer

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Page | 532

Introduction: several of the pathways significant in cancer carry signals from a cell's surroundings; others are responsible for the cell's interior programs, such as those that control the cell cycle or cell death; still, In addition to epigenetic factors and signaling pathways, the role of tumor suppressor genes and oncogenes can be seen in most malignancies. This study aimed to investigate the most important cellular and molecular basis of cancer. This study aimed to investigate the most important cellular and molecular basis of cancer. Search

Methods: This study with the title cellular and molecular basis of cancer used scientific databases including Science Direct, Springer, Google Scholar, and PubMed.

Results: In reality, research on cancer-causing genes, receptors, GTP-binding proteins, protein kinases, gene regulatory proteins, etc. led to the initial discovery of many of the parts of cell signaling pathways. One of these is a mutation that causes the Ras family of proteins, which are downstream from such growth factor receptors, to improperly activate a receptor tyrosine kinase, such as the EGF receptor.

Conclusion: Generally speaking, mutations that activate particular oncogenes and inactivate particular tumor suppressor genes in the various signaling pathways might be associated with the stages of tumor growth. However, various cancer types and even patients who ostensibly have the same form of the disease might have distinct combinations of mutations, which highlights the random nature of mutations. Oncogenes and tumor suppressor genes, which make up the majority of the genes found to be mutated in cancer, code for parts of the pathways that control the proliferative behavior of body cells, particularly the mechanisms by which signals from a cell's neighbors can cause it to divide, differentiate, or die. Keywords: cellular, molecular, cancer, mutations

Keywords: cellular, molecular, cancer, mutations

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Measuring the ratio of interleukin 10 and 6 and other inflammatory parameters in patients with COVID-19

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Page | 533

Introduction: Inflammatory process activated by rapid viral replication of SARS-CoV-2 can play a vital role in the pathogenesis of multiple organ damage, and be responsible for the COVID-19 patients' amatic outcomes and common abnormal laboratory findings. This study aimed to assess the correlation between various laboratory biomarkers, IL-10/IL-6 ratio, and receiver operating characteristic (ROC) analysis in monitoring COVID-19 patients

Methods: This observational study was conducted in three groups: healthy participants, non-COVID-19, and clinical signs and COVID-19 patients (severe and non-severe). Biochemical (CRP, IL-10, IL-6, and albumin) and hematological (WBC, lymphocytes) parameters were assessed by automated methods. Moreover, IL-10/IL-6 ratio and NLR markers were calculated in mentioned three groups. Statistical analyses were done using R (version 4.1.0). ROC curve was used to validate the predictive value of parameters.

Results: The COVID-19 positive group had significantly higher NEU, CRP, ferritin, and IL-10/IL-6 ratio, while its WBC, absolute counts of lymphocytes, and albumin were significantly lower than the non-COVID-19 patients ($P < 0.001$). Serum ferritin and IL-10/IL-6 ratio level of the severe group was significantly higher than that of the non-severe group ($p = 0.006$ and ($p = 0.011$ respectively). The strongest correlation in all subjects showed between lymphocytopenia and increased NEU ($r = -0.98$, $P < 0.001$). The AUC values of WBC (0.87), lymphocytes (0.81), NEU (0.74) and NLR (0.73) had higher than CRP (0.59) or Ferritin (0.71).

Conclusions: We recommend using IL-10/IL-6 ratio, WBC, and NLR change as simple, helpful, and inexpensive indicators in the early detection of COVID-19 patients.

Keywords: SARS-CoV-2, COVID-19, IL-10/IL-6 ratio, NLR, laboratory biomarkers

A-10-1120-1

The Importance of the Role of Apoptosis in cancer therapy

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Introduction: A significant issue with public health is cancer. Apoptosis was first defined by its morphological features, including cell shrinkage, membrane blebbing, chromatin condensation, and nuclear fragmentation, which are present in some kinds of colon cancer and hematological malignancies. The first tumor suppressor gene associated with apoptosis was p53. Investigating the Importance of the Role of Apoptosis in Cancer was the goal of this investigation. Search **Methods:** This study was conducted in order to investigate the process of apoptosis and its function and role in the occurrence of cancer and based on reliable scientific databases such as Science Direct, Springer, Google Scholar, and PubMed.
Result: Anticancer medications cause apoptosis in both cancers and healthy tissues. In contrast to cancer cells, which are able to avoid programmed cell death and thus achieve immortality, apoptosis is a mechanism that is crucial for the growth and development of organisms. Effective cancer treatment agents must first understand the underlying mechanisms of chemotherapy resistance in cancer. apoptosis, which includes aberrant cross-talk between autophagy and apoptosis as well as downregulation of pro-apoptotic signals and overexpression of anti-apoptotic signals. Chemotherapeutic medications allow cancer cells to undergo pro-apoptotic processes; nevertheless, the overexpression of anti-apoptotic proteins, such as Bcl-2 and IAPs, results in cancer resistance. The chemoresistance is also influenced by death receptors and signaling pathways associated to NF-B, PI3/AKT, and p53. Through the control of autophagic proteins, activation of caspase, and destruction of autophagic material, faulty autophagy may also result in apoptosis avoidance.
 Conclusion: Having a deeper understanding of apoptosis evasion would be beneficial for creating countermeasures against chemotherapy-resistant malignancy. The use of nanoscale ug delivery (nanomedicine), medicines that target numerous targets, and combined chemotherapeutic therapy offer promising potentials to overcome chemoresistance and achieve precision therapy.
Keywords: Apoptosis, Chemotherapeutic, signaling pathways, cancer

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Frequency evaluation of CDKN2B-AS1 gene polymorphism (rs10811661) in gastric cancer patients

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Page | 535

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Gastric cancer is one of the most common human cancers and the sixth most common cancer globally. GC is reported as the third leading cause of cancer death worldwide. Genetic factors are important risk factors for gastric cancer and mainly refer to genes involved in cancer that play an important role in genetic and epigenetic changes. The main components of genetic factors are mutations and polymorphisms that have their effect by changing the expression or function of proteins. The CDKN2B-AS1 gene is one of the most important genes in human cancers, especially gastric cancer, and has a pro-oncogenic role in many cancers. Polymorphisms cause individual differences in susceptibility to disease and response to ug therapy. Therefore, identifying different genotypes predisposing individuals to gastric cancer can be very useful in screening, diagnosis, and treatment. In the current study, the frequency of the CDK2B-AS1 gene polymorphism (rs 10811661) was evaluated in gastric cancer and healthy individuals. In this case-control study, 228 patients (118 patients with gastric cancer as a case group and 110 healthy individuals as a control group) were selected from the Aras Clinic of Imam Khomeini Hospital and Digestive Disease Research Center in Ardabil. Whole blood samples were collected from the subjects for DNA extraction and determination of CDKN2B-AS1 gene polymorphisms using the RFLP technique. Finally, the results were analyzed by t-test and X2. The rs10811661 polymorphism was associated with an increased risk of gastric cancer (OR=2.12, CI= 1.39-5.88, p<0.001 and dominant model: OR=4.12, CI=3.44-9.71, p<0.001). The minor allele frequency (C) was 33.3 % in the total population. In summary, our findings demonstrate that the rs10811661 SNP of the CDKN2B-AS1 gene was related to the occurrence of gastric cancer suggesting its potential role as a prognostic biomarker for the management of gastric cancer.

Keywords: Gastric Cancer, LncRNA, CDKN2B-AS1, Single Nucleotide Polymorphism (SNP)

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Synthesis and evaluation of 4-hyoxy-L-proline derivatives as carbonic anhyase II inhibitors

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Introduction: The carbonic anhyases form a family of enzymes that catalyze the interconversion between carbon dioxide and water and the dissociated ions of carbonic acid (i.e. bicarbonate and hyogen ions. CA isozymes have been broadly studied in many pathological/ physiological processes.

Methods: In the current research, a series of 4-hyoxy-L-proline derivatives were designed and chemically synthetized and interaction of these carboxylic acid-based compounds with hCA II were evaluated in vitro utilizing several spectroscopic and computational techniques.

Results: Results indicated that different derivatives had different potencies on hCAII inhibitory activity and among them, compounds 1-(4-Chlorobenzosulfonyl)-4-hyoxy-pyrrolidine-2-carboxylic acid (3b) and 4-Hyoxy-1-(4-methylbenzosulfonyl)pyrrolidine-2-carboxylic acid (3c) had the lowest IC50 and Kd values than 4-hyoxy-L-proline and other derivatives and therefore had the most affinity to the hCA II. The Kinetic data demonstrated that 3b and 3c inhibit the hCA II esterase activity in a linear competitive way, with Ki values in the low micromolar range. Fluorescence tests showed that the hCA II surface hyophobicity is diminished in the presence of compounds 3b and 3c, as confirmed by the decrease in ANS binding to hCA II in their presence. Docking results revealed that 3b and 3c had more binding energy than 4-hyoxy-L-proline. Furthermore, these compounds could occupy the hCA II active site, where they would interact with critical amino acid residues via non-covalent forces to inhibit hCA II.

Conclusion: Overall, the strengthening of inhibitory activity and the binding power of these carboxylic acid derivatives (3b and 3c) for the hCA II makes these compounds interesting for designing novel hCA II inhibitors.

Keywords: Synthesis, human Carbonic anhyase II, Carboxylic acids derivatives, Competitive Inhibition, DNSA

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Evaluation of mRNA expression of IL8 and IL10 in patients with IBD compared to IBS

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Introduction: Irritable bowel synome (IBS) is a complex, functional gastrointestinal disorder characterized by chronic abdominal pain or discomfort and altered bowel habits. Inflammatory bowel disease causes inflammation of the colon and small intestine. Environmental factors, genetics and immunity play a role in this disease. several studies have suggested the relationship between irritable bowel synome and inflammatory bowel disease. The aim of this study was to evaluate the expression of IL-8 and IL-10 genes in IBS patients compared with IBD. Materials and **Methods:** This case-control study was performed on 33 patients with IBD, 47 patients with celiac disease and 20 controls who referred to the Liver and GI Research Institute. For this purpose, the RNA of patients and control subjects was extracted and after cDNA synthesis, quantitative real time PCR (qRT-PCR) method was used to evaluate and express the target gene.

Results: The results of this study showed that IL-8 expression in UC patients was significantly higher than control subjects (p value: 0.026). while the Comparison of IL-8 gene expression in CD subjects did not show a significant increase compared to controls. Comparison of IL-8 gene expression in three groups of IBS, CD, UC and healthy controls also showed a significant difference (p value: 0.003). IL-10 gene expression also decreased significantly in CD patients compared to control subjects (p value: 0.02). Comparison of IL-10 gene expression in IBS patients compared with control subjects showed a decrease in expression of this gene, but this reduction was not significant.

Conclusion: IL-8 gene can be used as a biomarker to distinguish between celiac, CD, and UC, as well as UC diagnosis from healthy subjects. The IL-10 gene can also be used as a biomarker for CD diagnosis from healthy subjects.

Keywords: IL8, IL10, IBD, IBS

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Pretreatment of exosomes derived from hUCs with LPS ameliorates liver fibrosis by inhibiting Smad3C signaling pathway in the HSC-T6 cell line

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Page | 538

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Introduction: Activated hepatic stellate cells (HSC) by the TGF-β signaling pathway, is likely to worsen liver fibrosis, later-stage of NASH. Along with the HSC activation, the extracellular matrix (ECM) proteins namely collagen- I α and α-SMA will also overexpress. MicroRNA-146a, HSC activation Modulator, affect Smad2/3 phosphorylation. As stated by the up-to-date indications, s-derived exosomes have gained in popularity as it depicts its fruitfulness in the treatment of an array of diseases such as hepatic fibrosis. In the current study, the effects of LPS-stimulated mesenchymal cell exosomes on miR-146a expression and smad3c phosphorylation in the HSC-T6 cell line are inspected.

Methods: Firstly, the HSC-T6 cells were cultivated in DMEM with FBS (10%). Secondly, the separation of s-derived exosomes was performed, using exocib kit. Finally, the expression levels of each collagen- I α, α-SMA, and miR-146a gene were scrutinized through real-time PCR. Western blotting was executed in order to examine phosphorylation levels of smad3c protein.

Results: TGFβ1 treatment increased P-Smad2/3 phosphorylation, α-SMA, and Collagen1α. miR-146a expression, however, was down-regulated by TGFβ1. Treatment with exosomes caused a considerable decrease in p-Smad2/3 phosphorylation levels, α-SMA and Collagen1α1 gene expression, while it up-regulated miR-146a expression.

Conclusion: Owing to our observations, it was s-derived exosomes that decreased the expression levels of genes associated with hepatic fibrosis such as collagen- I α, and α-SMA. In addition, exosomes impede smad3c phosphorylation via increasing miR-146a expression, resulting in averting liver fibrosis progression. Therefore, exosomes should be cherished as an advantageous treatment strategy.

Keywords: Key words: Liver fibrosis, HSC, exosomes, TGFβ1, α-SMA, Collagen1α

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Combination chemotherapy against colorectal cancer cells: co-delivery of capecitabine and pioglitazone by polycaprolactone-polyethylene glycol carriers

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Page | 539

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Introduction: Colorectal cancer causes many deaths despite many treatment options. Capecitabine (CAP) uses as the standard chemotherapy regimen for colorectal cancer, and pioglitazone hyochloride (PGZ) for diabetic disease and cancer treatment. However, free ugs do not induce effective apoptosis. This work aims to co-encapsulate CAP and PGZ and evaluates cytotoxic and apoptotic effects on HCT-119, HT-29 colorectal cancer cells, and human umbilical vein endothelial cells (HUVECs).

Methods: CAP, PGZ, and combination treatment nano-formulations were prepared by triblock (TB) (PCL-PEG-PCL) biodegradable copolymers to enhance ugs' bioavailability as anti-cancer agents. The Ultrasonic homogenization method was used for the preparation of nanoparticles. The physicochemical characteristics of nanoparticles were studied using FTIR, DLS, and FESEM techniques. The zeta potential, entrapment efficiency, ug release, and storage stability were studied. Also, cell viability and apoptosis were examined by using MTT and acridine orange (AO) and propidium iodide (PI), respectively.

Result: The smaller hyodynamic size (236.1nm), polydispersity index (0.159), and zeta potential (-20.8 mV) were observed in nanoparticles. Nanoparticles revealed higher zeta potential and storage stability at 25°C than 4°C in 90 days. The synergistic effect was observed in (CAP-PGZ)-loaded TB nanoparticles in HUVEC, HCT-116, and HT-29 cells. In (AO/PI) staining, the high percentage of apoptotic cells in the (CAP-PGZ)-loaded TB nanoparticles in HUVEC, HCT-116, and HT-29 were calculated as 78%, 71.66%, and 69.31%, respectively.

Conclusion: The (CAP-PGZ)-loaded TB nanoparticles in this research offers an effective strategy for targeted combinational colorectal cancer therapy.

Keywords: Colorectal cancer, Capecitabine, Pioglitazone hyochloride, Micelle, Combination chemotherapy, Apoptosis

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The investigation of the level of iron in serum and genetic polymorphisms of exon 1,2 and 3 of Ferroportin gene in Buffalo

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Page | 540

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Introduction: Current investigation primary goal was to determine iron concentrations in 21 buffalos. The second target was to determine single-nucleotide polymorphism (SNP) in exons 1, 2 and 3 from Ferroportin gene in buffalo. In addition, relationships among those SNPs and animals serum iron concentrations have been investigated. Iron mal-metabolism emanated Clinical presentations, could be assorted into two categories: first group have been investigated based on selective loading of iron in macrophages and the second by considering of iron accumulation in enterocytes. The expression of Ferroportin gene is handled through two Regulatory mechanisms; post-transcription by IRE/IRP and post-translation via hepatic Hepcidin. It has been reported that Ferroportin mRNA is a functional motif of IRE that in cell culture, binding of IRP to IRE at UTR5 results in translation of mRNA in ribosomes. These elements cooperation (IRE/IRP) provides the most efficient hemostasis of Iron even if the iron concentrations is below the Cellular requirement levels.

Methods: Extracted DNA from Buffalos' blood were amplified using PCR methodology and PCR products investigated by gel electrophoresis subsequently. In the following DNA sequencing performed to determine the possible mutations in studied exons through Blast in NCBI. Moreover, iron concentration of blood samples were investigated using a biochemical method (Iron Kit, Pars Azmoon, Iran). Finally, any iron concentration abnormality related Mutations of Feroprotein exons I, II and III were assessed.

Results: Generally, all buffaloes showed low levels of blood iron concentration in compare with available reports (Mean=60.01ug/dl). This may associate with malnutrition and poor diet in terms of trace minerals. PCR and sequencing results illustrated that there is no significant difference and mutation among Feropeotein exons rather than standard gene in NCBI.

Conclusion: SNPs in Exon 1, 2 and 3 are correlated with variations of iron concentrations of blood in the buffalo's under the investigation.

Keywords: Ferroportin, Hepcidin, Iron, Transferrin, Exon, Gene polymorphism

MiRNA-mRNA Regulatory Network in the Molecular Response of Monoclonal Antibody ugs in the Ovarian Cancer treatment: A Systems Biology Approach

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Introduction: Ovarian cancer (OC) is one of the three major malignant tumors of the female reproductive system among worldwide. Monoclonal antibodies such as Trastuzumab and Pertuzumab are used in immunotherapy targeting human epidermal growth factor 2 (HER2) as a suitable therapeutic strategy. Until now, the molecular mechanisms underlying the tumorigenesis, clinical diagnosis and treatment of OC have not been fully understood. The systems biology approach with a holistic method helps to understand the mechanism of action of ugs. As regulators of protein expression, microRNAs (miRNAs) play a role in ug treatments by targeting mRNA. This study aims to investigate the miRNA molecular response of these monoclonal antibody ugs in the interaction network of OC.

Methods : The gene expression profiles (GSE31432) were downloaded from the Gene Expression Omnibus database. Differentially expressed genes (DEGs) were analyzed with GEO2R tools in three groups: Trastuzumab compared with the control group, Pertuzumab compared with control, and Combination compared with control. Then, a defined formula [-log(p.value) × |log (fold change) |] was applied to select the 500-top significant probs in every groups. At last, we integrated all data groups and select the common mRNAs. Additionally, used Toppgene online database to select miRNA targets related to common mRNAs and constructed miRNA-mRNA network by Cytoscape software, and determined mRNA and miRNA with the highest degree of mRNA and miRNA.

Results: A total of 44 DEGs were detected after the analysis of the three groups that response to monoclonal antibody ugs. 85 miRNAs were predicted from toppgene that targeted common mRNAs. After awing the network, 5 hub mRNA (CDKN1A, HOXC4, RASSF6, MMP16, and LFNG) and miRNA (miR-670, miR-4265, miR-4322, miR-325-3p, and miR-200a) with the highest degree were determined.

Conclusion: Our finding investigates the miRNA molecular response to all three trastuzumab, pertozumab, and combined therapy.

Keywords: MiRNA, Monoclonal antibody, Regulatory network and Ovarian cancer

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Identification of hub genes associated with ovarian cancer through systems biology

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Page | 542

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Introduction: Ovarian cancer (OC) is a lethal gynecological malignancy with very complicated pathogenesis. The availability of high-throughput Transcriptomic data and advancements in bioinformatics methods help us to predict gene biomarkers and apply systems biology approaches to get a better diagnosis and prognosis of the OC. The present study aimed to identify significant genes with poor outcomes and their underlying mechanisms.

Methods: Gene expression profiles of GSE36668, GSE40595, GSE69428, and GSE54388 were available from the GEO database. There are 92 OC tissues and 30 normal tissues were selected from the datasets. Differentially expressed genes (DEGs) were analyzed with Transcriptome Analysis Console (TAC) software with a P-value < 0.05 and a |log fold change (FC)| > 2.5. We established a protein-protein interaction (PPI) network of the DEGs through the (STRING) database and use Gephi software to select hub genes and find modules with a crucial role. Next, we made use of the Toppgene database for gene ontology (GO).

Results: A total of 1840 DEGs were detected after the analysis of the four gene expression profiles; of these, 401 were upregulated genes and 1438 were downregulated. Additionally, 10 hub genes (CTNNB1, CCNB1, CCND1, TOP2A, BIRC5, EGFR, CDK1, GAPDH, AURKA, EZH2) with the highest degree and 4 hub genes (FAM153A, FAM153B, FAM198B, FJX1) with highest closeness centrality were determined. The most frequent top 2 gene ontology of molecular function were cytoskeletal protein binding and tubulin binding; in the biological process were cell division and cytoskeleton organization; in the pathway were Aurora B signaling and Ensemble of genes encoding core extracellular matrix including ECM glycoproteins, collagens, and proteoglycans.

Conclusion: In summary, the data may produce new insights regarding OC pathogenesis. Hub genes may improve individualized diagnosis for OC in the future.

Keywords: ovarian cancer, protein-protein interaction, differentially expressed genes

The Emerging role of mir-200 family in Suppressing Wnt/β-catenin pathway in EMT in Cancer

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Introduction: In Endothelial-mesenchymal transition (EMT), epithelial cells lose their polarity and acquire a mesenchymal phenotype. This transition is observed in 3 states of embryonic development, wound healing and cancer progression. In this review, we describe the various signaling pathways involved in cell progression, survival, and apoptosis including TGF-β, Wnt/β-catenin, Hedgehog and Notch Axis. In line with this, several studies have found that disruption of the Wnt/β-catenin signaling pathway through miRNAs is one of the causes of EMT. The miRNAs play an important role in development and progression of cancer cells. Among miRNAs, the expression of mir-200 family that has a negative correlation with tumor invasion and leads to EMT inhibition by targeting the Wnt signaling pathway.

Methods: Keywords such as MicroRNA, Endothelial-mesenchymal transition, Wnt/β-catenin pathway, etc have been searched in the PubMed and Google Scholar database and after reviewing the articles, the results have been summarized.

Result: The occurrence of EMT is associated with increasing mesenchymal markers and E-cadherin's repressors such as ZEB1 (Zinc finger E-box-binding homeobox1) and ZEB2. E-cadherin is one of the effective epithelial markers in maintaining cell junctions, whose expression decreases in EMT. Mir-200 inhibits EMT and prevents metastasis by two mechanisms related to Wnt/β-catenin pathway: First, mir-200 increases E-cadherin and restores epithelial properties in EMT by suppressing ZEB1/2 gene. Second, mir-200 inhibits the overexpression of beta-catenin by binding to the 3'-untranslated region (UTR) of the beta-catenin gene and prevents its accumulation in the nucleus.

Conclusion: Considering the role of in regulating the Wnt axis and consequently reducing cancer invasion and metastasis, the mir-200 overexpression might be as a therapeutic method to reverse EMT and cancer therapy.

Keywords: MicroRNA, Endothelial-mesenchymal transition, Wnt/β-catenin pathway

Prevalence of C677T single nucleotide polymorphism of methylene tetrahyofolate reductase gene and its relationship with serum levels of homocysteine, vitamin B12, folate and cholesterol in Alzheimer's patients

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Introduction: One of the most common types of dementia is Alzheimer's disease in which the patient's mental abilities gradually decline. Many single nucleotide polymorphisms affect the incidence of Alzheimer's disease. The aim of this study was to evaluate the frequency of C677T single nucleotide polymorphism of methylene tetrahyofolate reductase (MTHFR) gene in Alzheimer's patients referred to Poursina Hospital (Rasht) and to determine its relationship with some metabolic factors. Materials and

Methods: This study was performed in two groups of control (n = 80) and patient (n = 80) with a ratio of 1: 1 male to female. ARMS-PCR method was used to study mutations and ELISA was used to measure homocysteine and Chemiluminescence method was used to measure cholesterol, Vit. B12 and folate.

Results: Based on the results of PCR test of MTHFR gene, the incidence rate of mutation in healthy allele was 44.6% and in mutant allele was 27.9% of the total study population. The frequency of mutations at the C677T site was higher in patients than in healthy individuals. In addition, the frequency of mutations in healthy alleles was higher in sick women than in healthy individuals and sick men. In addition, the frequency of mutations in healthy allele was higher than mutated allele in all subjects. On the other hand, the frequency of heterozygous genotype in healthy individuals and patients is more than other genotypes.

Conclusion: Examination of MTHFR gene polymorphism in C677T position showed that the risk of Alzheimer's disease increased in individuals with heterozygous CT genotype and TT homozygous genotype compared to CC homozygous genotype, also, in people with TT genotype, a decrease in serum homocysteine, a decrease in folate and vitamin B12 was observed at the same time. Also it was found that an increase in cholesterol levels is associated with an increased risk of developing the disease.

Keywords: Alzheimer's, SNP, Homocysteine, Vitamin B12, Folate, Cholesterol, C677T, MTHF

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Computational study of antibody evasion of the receptor binding domain of the SARS-CoV-2 Omicron (BA.1) variant

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Page | 545

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Introduction: The recent variant of SARS-CoV-2, Omicron (B.1.1.529), has become globally dominant and a large number of mutations were found in the spike protein of this variant. Since receptor binding domain (RBD) of the spike protein plays significant role in interaction with human angiotensin enzyme (ACE2) and antibody recognition, it is critical to investigate the effects of Omicron (BA.1) mutations in the RBD for the development of effective COVID-19 vaccines.
Methods: In this study, we performed 50 ns Molecular dynamic simulation to evaluate the effect of the RBD mutations on binding to S309 mAb and Eli Lilly (LY-CoV555) mAb. In addition, the free energy binding of Wuhan and Omicron RBD-mAb complexes were calculated by MM/GBSA method.
Results: Based on our results the binding affinity of RBD to Eli Lilly (LY-CoV555) mAb may reduce as a result of Omicron (BA.1) mutations and also, Omicron (BA.1) RBD mutations have minimal impact in decreasing the binding affinity of RBD to S309 mAb.
Conclusion: According to the results, RBD Omicron mutations may reduce the efficacy of S309 mAb and Eli Lilly (LY-CoV555) mAb. Overall, this study can be useful for the development of new therapeutics.

Keywords: COVID-19, SARS-CoV-2, Omicron variant, Receptor binding domain (RBD), Molecular Dynamics Simulation

Bioinformatic study on the function of the Tp53 gene in the vitiligo disease process

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Introduction: Vitiligo is a chronic skin and hair disease manifested by the loss of melanocytes and appears with white and milky spots on the skin. The Tumor protein p53 (Tp53), a tumor suppressor gene encodes a protein that activates transcription, which responds to apoptosis. This study aimed to investigate the effect of the Tp53 gene on vitiligo disease through bioinformatics studies.

Methods: General information about Tp53 and vitiligo was obtained from National Center for Biotechnology Information (NCBI) database. The Database for Annotation, visualization and Integrated Discovery (David) was used to find the correlation of the pathways connected to the gene. The information about the Tp53 gene in the apoptosis pathway was obtained from Kyoto Encyclopedia of Genes and Genomes (KEGG) database. The interaction among proteins was identified in the STRING database.

Results: According to the findings, the expression of Tp53 gene plays a key role in the process of vitiligo disease. The STRING database showed that Mouse double minute 2 homolog or E3 ubiquitin-protein ligase m2 (M2) proto-oncogene and Ataxia-Telangiesctasia Mutated (ATM) serine/threonine kinase have the most interaction with Tp53, and all three are involved in the development of the studied disorder. In addition, mutations in the Tp53 gene cause pathogenesis. The Kegg pathway revealed that stimulation of Tp53 gene could play a critical role in occurrence of disease. According to the favorable regulatory function in the apoptosis process obtained from DAVID, the increase in gene expression is expected to cause pathogenicity.

Conclusion: Our results and previous studies showed that targeting the Tp53 gene as a potential factor to suppress and activate the apoptosis pathway helps control the disease. By identifying the function and expression of the Tp53 gene in the vitiligo process, the pathogenesis and development of the disease would be better understood, which lead to better treatment opportunities.

Keywords: Skin disease, M2, ATM, Bioinformatics

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Liver function test in patients with covid-19 :A Systematic Review

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Page | 547

Introduction: COVID-19 is an epidemic disease usually associated with lung damage and respiratory problems, but it can involve multiple organs, including the liver, and lead to various abnormalities in liver function tests. Since the effect of the coronavirus on the liver and its functional enzymes has not yet been fully and clearly determined, this study aims to investigate the impact of COVID-19 and its therapeutic ugs on liver function tests.

Methods: we searched and studied the articles that were published in PubMed and Google Scholar since last year (2021-2022) for a systematic review by using the keywords of covid-19 , SARS-CoV-2 , Liver biochemical parameters abnormalities ,Liver enzymes ,Liver function tests ,Liver function test abnormalities, and their combinations. The title, full text and abstract of the selected articles were reviewed.

Results: A total of 24 articles were finally included in the systematic review process after exclusion of studies that did not meet the eligibility criteria. According to this study, COVID-19 causes LFT abnormalities, which are more prevalent in patients who are hospitalized in the intensive care unit. These tests make it feasible to predict a person's COVID-19 infection as well as the severity of the disease. In fact, liver dysfunction worsens as COVID-19 becomes more severe. The medications used to treat COVID-19 are another factor that impairs LFT. However, it was noted that abnormal liver function test results usually return to normal after a year.

Conclusion: The use of therapeutic medications, the viral proliferation in the liver cells, and the inflammatory response brought on by the virus can all cause LFT impairment in COVID-19 patients.

Keywords: covid-19 , Liver biochemical parameters abnormalities ,Liver enzymes ,Liver function tests ,Liver function test abnormalities, SARS-CoV-2

Investigating the role of hsa-miR-497-5p as therapeutic targets involved in MAPK- ERK1/2 pathway in Ischemic stroke

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Introduction: Ischemic stroke (IS) is the leading cause of death worldwide with a high rate of disability and mortality which is classified as the second cause of death that arises from the sudden occlusion of small vessels in the brain with consequent lack of oxygen and nutrients in the brain tissue. Following an acute ischemic event, the cascade of events promotes the activation of multiple signaling pathways responsible for irreversible neuronal damage. MiRNAs play an important role in the pathogenesis IS that can regulate protein translation by either complete or incomplete pairing with the target gene, or by inhibiting expression of downstream target proteins .So this study purposes to evaluate the association between hsa-miR-497-5p and MAPK- ERK1/2 pathway.

Methods: Specifications of miRNAs were obtained through mirbase, HD and miRdSNP. To identifying target genes, miRTarBase and MIRWALK2.0 were used. Venn diagram used to identify common target genes. The signaling pathways for target genes which had high expression difference were observed from the DAVID database and the pathways associated with IS were stored for interpretation.

Result: The result demonstrated the expression levels of related proteins in the PI3K-Akt-mTOR pathway in which hsa-miR-497 -5p prevents cell growth and proliferation by activating JNK which blocks AKT in which microRNAs inhibit MTOR by blocking NF-κB and AKT and effect on adhesion increasing by preventing cell survival and proliferation.

Conclusion: Some miRNA are dysregulated in IS, influencing its pathogenesis through an altered regulation of the MAPK pathway which can modulate processes occurring after stroke such as inflammation, oxidative stress, and cell death. Here we found that the role of hsa-miR-497-5p in IS is associated with the MAPK- ERK1/2 pathway that might be a novel bio-marker for IS that act as regulators of mechanisms of inflammation, apoptosis, angiogenesis, and neurogenesis through the modulation of the MAPK-ERK1/2 pathway.

Keywords: Ischemic stroke, Signaling pathways, MicroRNA, Target genes

A-10-1496-1

Green synthesis of cerium oxide nanoparticles using Lepidium sativum extract and its anti-tumoral effects in prostate cancer

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Introduction: There has been a growing interest in using nanoparticles for different biomedical applications such as bioimaging, targeted ug delivery, and cancer therapy, over the last few years. Presently, cerium oxide nanoparticles (CeO2-NPs) have been widely applied in nanomedicine science due to their exceptional physico-chemical and biological properties. This study aimed to describe a simple and eco-friendly method for the green synthesis of CeO2-NPs using Lepidium sativum extract as a capping agent and to evaluate their anti-cancer effects on human prostate cancer cells (PC3).

Methods: CeO2-NPs have been synthesized in Lepidium sativum extract by sol-gel method. The phyto-synthesized CeO2-NPs were characterized by UV–visible spectroscopy, X-ray diffraction (XRD), transmission electron microscope (TEM), Fourier transform infrared spectroscopy (FTIR), and energy-dispersive X-ray spectroscopy (EDX). Moreover, the in vitro anti-cancer effects of CeO2-NPs against PC3 cancer cells were evaluated utilizing resazurin-based cytotoxicity assay and Real-Time PCR analysis.

Results: UV-Vis spectra of CeO2-NPs was showed an optical absorbance peak at about 313 nm. Furthermore, the XRD pattern confirmed the crystalline structure of green synthesized CeO2-NPs. Spherical shape of CeO2-NPs was detected by TEM image, and according to TEM image, average size of nanoparticles was reported to be about 16 nm. In biological experiments, the results of the resazurin assay indicated the significant cytotoxic activity of CeO2 NPs against PC3 cells in a dose-dependent manner with an IC50 at 113.6 µg/ mL. Additionally, the Real-Time PCR findings suggested that the biosynthesized CeO2 NPs could suppress cell metastasis, and promote cell cycle arrest as well as apoptosis in prostate cancer cells.

Conclusion: Collectively, these findings suggest that the CeO2 nanoparticles green-mediated by Lepidium sativum extract can be used or considered as novel anti-cancer agents in the treatment of human prostate cancer.

Keywords: Cerium Oxide Nanoparticle, Green Synthesis, Lepidium sativum, Prostate Cancer

A-10-1339-1

Circular RNAs in Glioblastoma, the Contribution of circRNAs to Cancer Development-Their Diagnostic and Therapeutic Potential

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Introduction: Glioblastoma multiforme (GBM), as a fatal brain cancer and an incurable disease, is fast-growing type of tumour of the brain or spinal cord, affecting both chilen and adults. Despite significant advances in neurosurgery, radiotherapy, and chemotherapy, high rates of cellular heterogeneity, and multiple genetic alterations in molecular processes associated with cancer complicate treatment and lead to therapeutic resistance; so that the median survival for patients with glioblastoma multiform is still less than two years. Circular RNA (circRNA), as a group of non-coding RNAs, with covalently closed loop and high stability, regulates cancer-related processes such as proliferation, apoptosis, invasion, and chemoresistance, and has been introduced as an effective treatment for GBM. This review summarized the publications related to the biological roles of circRNAs in glioblastoma.

Methods: PubMed and Web of Science databases were used to search publications related to circRNA and glioblastoma with the following keywords: (circRNA), molecular mechanism and glioblastoma.

Results: Studies have shown that dysregulated circRNAs are involved in angiogenesis, metastasis, tumor growth and ug resistance in glioblastoma, which indicates the potential of circRNAs as biomarkers or therapeutic targets for glioblastoma.

Conclusions: Herein, we clarified the functional, prognostic, and predictive roles of circRNAs in glioblastoma and believe that one day significant progress will be made in the treatment of glioblastoma using circRNAs in diagnosis and treatment.

Keywords: Glioblastoma multiforme, Circular RNA, Signaling pathways, Diagnosis, Treatment

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Oxidative Stress Induction By Pesticides May Cause Lung Cancer Incidence

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Introduction: and aims: Pesticides are nowadays known as one of the most important causes of human disorders worldwide. The aim of the present study was to investigate the role of organochlorine pesticides (OCPs) and organophosphorus pesticides (OPPs) in the development of lung cancer.

Methods: We determined the levels of seven derived OCP residues (α-HCH, β-HCH, γ-HCH, 2,4 DDT, 4,4 DDT, 2,4 DDE, and 4,4 DDE) and enzymatic antioxidant biomarkers including paraoxonase-1 (PON-1), erythrocyte's acetylcholinesterase (AChE), glutathione peroxidase (GPx), superoxide dismutase (SOD), catalase (CAT), and non-enzymatic antioxidant biomarkers including total antioxidant capacity (TAC), protein carbonyl (PC), malondialdehyde (A), and nitric oxide (NO) in the blood samples of 51 lung cancer patients and 51 healthy subjects as controls. Furthermore, the effects of OPP exposure on the development of lung cancer and oxidative stress (OS) are indirectly assessed by measuring AChE and PON-1 enzyme activities.

Results: The average values of all the measured OCPs were significantly higher in lung cancer patients when compared with healthy control subjects. AChE, PON-1, GPx, and CAT activity levels as well as the amounts of PC, A, and NO were higher in patients with lung cancer than in the control subjects, while TAC values were lower in the patients. Moreover, our data showed a significant association between OCP concentrations and OS parameters.

Conclusion: The results suggest that OCPs and OPPs may have a role in lung cancer incidence in southeastern Iran, and at least one of the mechanisms by which OCPs and OPPs may contribute to increasing the development of lung cancer in the studied area is through OS generation.

Keywords: Acetylcholinesterase, Lung Cancer, Organochlorine, Organophosphorous

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Development of Simple Protocol for Generation of Functionally Active Hepatocyte-like Cells from Human Adipose Tissue-derived Stem Cells

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Page | 552

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Introduction: and Aims: Human adipose tissue-derived stem cells (hASCs) are considered as an attractive source of regenerative stem cells, mainly because of their higher proliferation rate, more accessibility and hepatocyte like properties as compared to mesenchymal stem cells isolated from other tissues. Numerous studies have described the beneficial use of adipose tissue-derived stem cells for generating hepatocyte-like cells. However, due to the lack of appropriate culture conditions, most of the produced cells exhibit poor functionality. The aim of the present study was to establish a new protocol for the efficient hepatic differentiation of hASCs. Materials and

Methods: hASCs were cultured in hepatic differentiation medium containing fibroblast growth factor 4, hepatocyte growth factor, dexamethasone and oncostatin M using a three-step protocol up to 21 days. Then, the functionality of the treated cells was evaluated by analyzing specific hepatocyte genes and biochemical markers at various time points.

Results: A significant upregulation in albumin, alpha-fetoprotein, cytokeratin 18 and hepatocyte nuclear factor-4α expressions was observed in differentiated cells relative to day 1 of differentiation protocol. Moreover, the finding of glycogen deposits increased urea production and positive immunofluorescence staining for albumin and alpha-fetoprotein in hepatocyte-like cells suggesting that most of the cells differentiate into hepatocyte-like cells.

Conclusions: Our report has provided a simple protocol for differentiation of hASCs into more functional hepatocyte-like cells.

Keywords: Fibroblast growth factor, Hepatic differentiation, Hepatocyte-like cells Mesenchymal stem cell

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A-10-1749-1

Chemical composition of Glycyrrhiza Glabra.L leaves and Its extract's Cytotoxicity on Chronic Myeloid Leukemia cells (K562) in vitro

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Page | 553

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Introduction: Chronic myeloid leukemia (CML) accounts for approximately 15% of adult leukemias. However CML can be treated, ug resistance is one of the main challenges and in some cases it can not be treated. Recently, Many attention focused on herbal medicine to increase efficacy of chemotherapeutic ug. Glycyrrhiza glabra.L(G.glabra) belongs to fabeaceae family. It contains important phytoconstituents which are responsible for its medicinal characteristics. In spite of many studies that have been done on its roots, the effects of its leaves are unknown. In this study we determined the chemical composition of G.glabra leaves and its extract's cytotoxicity on the K562 cells.

Methods: G.glabra was collected in May from Shiraz. Then its extract was prepared in suitable conditions (away from direct sun light). Phytochemical study of the plant was done on extract. Chemical composition was determined by quantifying tannin, flavonoid ,alkaloid , phenol and terpenes contents. Then, K562 cancer cell lines in their exponential phase (passage 3) were treated with different doses of leave's extract for 72 hours. Finally, Percentage of viability was assessed by resazurin colorimetric assay.

 Results: The active constituents of the G.glabra leaves extract were Flavonoids and terpenes compound that may be responsible in part for the activity of the extract. K562 Cell survival was reduced with increasing concentration of G.glabra extract compared to control samples by resazurin test. Viability result demonstrated approximately 65% of cells treated with 2mg/ml dose of extract, remained alive.

Conclusion: It may be concluded that because of flavonoid content, G.glabra extract has anti-cancer activity. However, purification should be done and the effective substance of this plant should be found.

Keywords: Chemical composition,Glycyrrhiza Glabra.L leaves, Cytotoxicity ,K562 cell line

A-10-1664-2

The expression analysis of SMAD4 and lncRnaH19 genes in the intestinal wall cells of mice treated with artemisinin

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Page | 554

Introduction: Artemisinin extracted from the wormwood plant is an effective anti-malarial substance and valuable in the treatment of cancer. In this research, by feeding mice with a diet containing artemisinin, the expression profile of two important genes in the process of proliferation and metastasis of colon cancer was investigated. Studies have shown that high expression of lncRnaH19 is significantly associated with cancer progression and tumorigenesis intensity. Also, SMAD4 signaling pathway is one of the most important pathways deal with the colorectal cancers. **method**: Two groups of mice under standard diet (N = 7, Control Group) and 1µL/g Artemisinin (N = 7, Treatment Group) were treated for 21 days. Intestinal tissue was separated and total RNA was extracted and followed by cDNA synthesis. Realtime RT-PCR was performed using specific primers against SMAD4 and LncRNAH19 genes, and finally the expression changes were calculated based on the 2-ΔΔCT method. Regard to the gene expression analysis, Cytoscape software was applied for gene network design.

Result: Our result showed an elevated level of smad4 gene expression after the treatment with artemisinin (Sig.= 0.00, $P \leq 0.05$, FC=2.78), however, we detected a non-significant decrerase in the expression of LncRNAH19 gene compared with the control group.

Conclusion: It seems that nutrition can strongly influence the expression of intestinal wall genes. In this research, we showed that wormwood plant extract, which contains artemisinin, can be useful in modulating the expression of genes in favor of preventing colon cancer.

Keywords: Artimisinin, SMAD4, LncRNAH19, Colorectal cancer, gene expression

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A-10-1247-1

Comparative effect of co-administration of apigenin and porous silica nanoparticles containing doxorubicin with apigenin and doxorubicin on expression of P53 gene in chronic human myeloid leukemia cells (k562)

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Introduction:One of the main causes of death is cancer in worldwide Leukemia is a type of blood and bone marrow malignancy.Doxorubicin(DOX)is an anticancer ug. The antitumor activity of DOX is increased by using nanoparticles made with it. Apigenin is one of natural effective substances which its modulator effect with anticancer ug reported.In the present study, we compared the effect of co-administration of apigenin and porous silica nanoparticles containing Dox with co-administration of apigenin and Dox.

Methods: For the synthesis of porous silica nanoparticles,first the surfactant is dissolved in the solvent with the presence of a catalyst,then the silica precursor is added to the surfactant solution, and then the surfactant is removed.Then doxorubicin is loaded on porous silica nanoparticles.In order to determine the survival percentage of cells with different doses(10μM porous silica nanoparticles containing doxorubicin with 60μM and 80μM apigenin)simultaneously and different doses of apigenin and DOX(60μM and 80μM of apigenin with 10μM DOX)were treated for 24 hours and viability determined by MTT colorimetric method.Finally,using Real-Time PCR,the expression of P53 gene in treated cells was assessed and compared with β-actin gene as an internal reference gene.

Results: Viability of K562 cells treated with apigenin and DOX demonstrated higher reduction than K562 cells treated with apigenin and porous silica nanoparticles containing DOX. Furthermore, the RT-qPCR results showed that the expression of P53 gene in the cells treated with DOX and apigenin at the same time was higher than the combined effect of porous nanoparticles containing DOX and apigenin at the same time.

Conclusion: Considering that the effect of P53 gene expression in cells treated with dox and apigenin at the same time was greater than the effect of the combination of porous nanoparticles containing dox and apigenin at the same time,this finding is probably due to the lack of resistance of K562 cells although further investigation was needed.

Keywords: K562 cell line, P53 gene, doxorubicin

A-10-1638-1

Analysis of gastric cancer gene expression data based on personalized pathways

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Introduction: Gastric cancer (GC) is the fourth leading cause of cancer-related deaths. The incidence of GC gradually increases with age. Carcinogenesis is a multi-stage disease process characterized by the progressive development of mutations and epigenetic changes in the expression of various genes. Signaling networks allow cells to process information from their environment and respond to incoming signals in appropriate ways. These networks comprise a collection of interacting proteins. Changes in the activity of these proteins throughout the network transmit signals from the cell membrane to downstream elements, which ultimately leads to a specific phenotypic response. Traditionally, these networks are organized into "canonical pathways" corresponding to a set of proteins involved in the transduction of a particular signal. Considering the poor effectiveness of biomarkers as differentially expressed genes, researchers have provided some approaches to determine potential pathogenic pathways, which increase the robustness and accuracy when these pathways are used as biomarkers. The Pathifier algorithm quantifies pathway deregulation and generates continuous features that can be used to characterize pathway function during disease progression.

Methods: Gastric cancer expression data were obtained from The Cancer Genome Atlas (TCGA) portal, and pathways were obtained from Kyoto Encyclopedia of Genes and Genomes (KEGG). To determine Pathway Deregulation Score (PDS), we used the Pathifier package and calculated the PDS score.

Results: The PDS algorithm assigns a score between 0 and 1. Values close to 0 correspond to samples whose expression levels are like controls. Samples with higher values present higher differences in expression levels compared to the control group. Our results clearly showed that pathways were deregulated in GC, including metabolic pathways.

Conclusion: By providing single-sample-level models of dysregulation in GC, we can better characterize tumor behavior. This approach, combined with targeted therapy, could create an opportunity for the design of personalized diagnostic, prognostic, and therapeutic strategies.

Keywords: Keywords: gastric cancer, pathway deregulation scores, prognostic pathways

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A-10-1751-1

Apelin is associated with the development of cardiovascular diseases: A systematic review and meta-analysis

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Page | 557

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Introduction: The objective of this systematic review and meta-analysis was to determine if patients with cardiovascular diseases (CVDs) and controls have different circulating levels of apelin, an essential regulator of cardiovascular homeostasis.

Methods: To find the studies adessing apelin in CVD, a thorough search was conducted in electronic databases including PubMed, Scopus, EMBASE, and Web of Science up to April 5, 2021. The standardized mean difference (S) and its 95% confidence interval (CI) were stated as the overall effect size because the included studies used various units to assess the apelin levels in the blood. Ss were pooled using a random-effects model that included the DerSimonian and Laird methods.

Results: Twenty-four articles (30 studies), including 1416 controls and 1793 cases were included. The blood samples from the patients had considerably lower apelin concentrations than those from the control groups, according to combined results using a random-effects model (S= -0.72, 95% CI: -1.25, -0.18, P= 0.009; I2= 97.3%, P<0.001). The subgroup analyses demonstrated that the apelin levels in studies with a cohort or cross-sectional design, plasma body fluid, without medical comorbidities of diabetic/metabolic synome (MetS), studies conducted in Europe or Asia, and patients with other diseases were statistically significant as compared to other strata.

Conclusion: The association of apelin with CVDs is different based on the disease subtypes and geographic location. These findings give credence to apelin's potential value as a further biomarker for the detection of CAD and CVD in diabetic patients.

Keywords: Apelin, Cardiovascular diseases, Coronary artery disease, Meta-analysis.

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The Effects of Aqueous- Ethanolic Extract of Nigella sativa Against Rhabdomyolysis - Induced Kidney Damage in Male Rats

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Page | 558

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Introduction: Rhabdomyolysis, or destruction of skeletal muscle, is the release of the contents of skeletal muscle cells into the plasma, which can be filtered through the glomeruli and lead to acute renal failure by various mechanisms. In the present study, the protective effect of Nigella sativa on acute renal injury due to rhabdomyolysis in rats was investigated.

Methods: There were three groups rats (n=8): Control, rhabdomyolysis and Nigella sativa extract (200 mg / kg) + rhabdomyolysis. The duration of the study was seven days and on the third day of the study, 50% glycerol (10 ml / kg) was injected intramuscularly into both legs for induction of rhabdomyolysis. Renal function parameters on the first, fourth, and seventh days of the experiment were assessed.

Result: In the rhabdomyolysis group, on day four (24 hours after glycerol injection), serum levels of CPK, urea and creatinine and urine output showed a significant increase compared to the control group. In group treated with Nigella sativa extract (200 mg/kg) on days 4 and 7 of the study, serum levels of CPK, urea and creatinine, and urine output on day 7 were significantly reduced compared to the rhabdomyolysis group.

Conclusion: Nigella sativa had a good protective effect on renal function in animals with rhabdomyolysis.

Keywords: Nigella sativa extract, Rhabdomyolysis, Kidney Failure

Toxicity and effect of Sophora pachycarpa extract on P53 gene expression analysis in U266B1 cells

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Introduction: Over the last decades, many researches has made on herbal medicine and their therapeutic properties. Sophora pachycarpa (S.pachycarpa) is one of herbal medicine which have anti-inflammatory, immune-regulating, and anti-cancer properties.The second most frequent hematologic malignancy, multiple myeloma (MM), accounts for 10% to 15% of all blood disorders. In present study, we investigated the toxicity of extract of S.pachycarpa fruit on U266B1 cells. RT-qPCR was used to assess the expression of P53 gene in present study.

Methods: In this study, S.pachycarpa fruit was collected from Torbat Hydariyyeh and its hyoalcoholic extract was prepared. Then, U266B1 cells in exponential phase were treated (for 24 and 72 hours) with various concentration of its extract (0.5-1 mg / ml) and % of viability was determined by resazurin assay. Then, expression of P53 gene was evaluated by Real-Time PCR, in comparison to the β-actin gene as an internal reference gene.

Results: Viability results demonstrated about 92% and 62% of cells treated with 1mg/ml dose of extract, remained alive after 24 and 72 hours in comparison to control respectively. Furthermore, expression level of P53 increased ($p \geq 0.05$) in cells treated with extract for 24h.

Conclusion: It can be concluded that hyoalcoholic extract of S.pachycarpa fruit demonstrated low cytotoxicity on U2666B1.However, more investigations should be done to determine the chemical composition of the extract and its exact mechanism of action.

Keywords: U266B1, Sophora pachycarpa, P53 gene

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Multi-targeting of angiogenic pathways by antagonistic peptides effectively suppresses tumor growth in a murine mammary carcinoma model

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Introduction: The vascular endothelial growth factor receptor 1, 2 (VEGFR1 and VEGFR2), and fibroblast growth factor receptor 1 (FGFR1) are the critical angiogenic receptors. Therefore, these are potential targets for suppressing tumor angiogenesis and metastasis and treating cancer. In our previous studies, we designed antagonistic peptides targeting VEGFR1/R2 and FGFR1 and showed their efficacy in suppressing 4T1 mammary carcinoma tumors. In the present study, we examined the combinatory effect of these peptides on repressing tumor growth and compared it to the effect of each peptide.

Methods: The combinatory effect of the peptides on tumor growth was examined utilizing a murine 4T1 tumor model. Under ketamine (100 mg/kg, i.p.) and xylazine (10 mg/kg, i.p.) anesthesia, the cancerous tissue was cut into fragments <0.3 cm3 and subcutaneously transplanted into the right flank of the female BALB/c mice (6–8 weeks old). Mice-bearing tumors, when the tumor volume reached ~150 mm3, were randomly divided into control and treatment groups (6 mice/group). The treatment groups received 0.2 mg/kg of VEGFR1/2 or/and 10 mg/kg FGFR1 antagonistic peptides (every two days, i.v.), whereas the control (vehicle) group daily received equivalent volumes of phosphate-buffered saline (PBS). Every seven days, tumor size was calculated utilizing the formula: Tumor Volume = $0.52 \times$ length $\times$ width2. Two-way repeated-measures ANOVA supported by Tukey's post hoc test was used to estimate the peptide efficacy on the tumor growth, and data were provided as mean ± SEM. $P < 0.05$ was considered significant.

Results: In vivo study indicated that combination therapy with the antagonistic peptides could more efficiently than therapy with each one inhibit the growth of 4T1 tumors.

Conclusion: Our results show that combination therapy with the designed peptides targeting the angiogenic receptors VEGFR1, VEGFR2, and FGFR1 can be a potentially efficient strategy for suppressing human breast tumor growth and metastasis.

Keywords: Breast cancer, VEGF receptors, FGFR1, Antagonistic peptides, Tumor suppression

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New formulation of Doxo/5-Fu niosome and evaluation of its effect on cancerous cells

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Page | 561

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Introduction: In recent years, many studies have been conducted on ug delivery systems to decrease the obstacles of anticancer medicines such as low selectivity, side effects, high toxicity, water insolubility and poor stability. Naturally derived nanoparticles target specific tissues and cells and deliver bioactive molecules and ugs to them, becoming important intelligently engineered ug delivery systems. Doxorubicin (DOX) is one of the anthracycline chemotherapy ugs, and alone or in combination with other first-line chemotherapy ugs. 5-fluorouracil (5-FU) has become one of the most used anti-metabolite chemotherapy ugs recently. This compound has been used as a first-line anti-neoplastic agent in the treatment of many cancers.

Methods: For ug delivery, we used Niosome, which we made by the method of thin film hyation technique. In this method. We used Span40(0.7 ml), Twin40(1.1 ml), Cholesterol (0.9 ml) and we mixed them in Rotary device, so evaporation happened. Then, last stage in rotation was hyation (adding ugs). And we captured photos of niosome under the light microscope. After this stage Niosomes were divided into two groups, the first type was niosomes that were sonicated for 3 minutes and the second type was niosomes without sonication. then we gave the sample into DLS device (Nano DS SN 165) to measure size of two types of Niosomes.

Results The above preparation suspension was evaluated by light microscopy as indicated in photo 1. A high percentage of niosomes in the figure1 are equal in size and multilayered. As indicated in table 1, medium size of type number 1 is D50= 0.6 nm and DLS size distribution in the polydispersity index is 0.00034 and in type number 2 medium size is D50= 5.0 nm and polydispersity index is 0.00280.

Conclusion: We can conclude from this results that obtained formulation is very good for preparation and ug delivery uses of niosome.

Keywords: Doxorubicin, 5-Flurouracil, Niosome, Cancerous cells

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Effects of Astaxanthin and Metformin Combined therapy on the glycemic indices and glucose metabolism via GLUT4, Adiponectin and GLUT-4 in type 2 diabetes mellitus patients - a randomized controlled trial

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Introduction: :Due to some dose-dependent adverse effects of anti-diabetic ugs and the advantages of the combination of natural and pharmacological therapies to more effective treatment of diabetes mellitus, The aim of the present study was to determine the effects of Astaxanthin (AST) supplementation as a recommended potent beneficial antioxidant on type 2 diabetic (T2DM) patients and to evaluate the effectiveness of AST-metformin combined therapy to control glycemic indices in this patients.

Methods: This randomized clinical trial was conducted on 50 T2DM cases receiving metformin for 12 weeks. Patients were divided into the test group (n = 25; who consumed 10 mg/day AST plus metformin) and the placebo group (n = 25; the same amounts placebo plus metformin). GLUT-4 and adiponectin gene expression and glycemic indices were evaluated by standard methods. Furthermore, to find a mechanistic relationship, the level of AMP-activated protein kinase was assessed as well.

Results: GLUT-4 and adiponectin gene expression were increased significantly in the AST group as well as the AMPK level. Fasting blood sugar and total cholesterol also significantly decreased after combination therapy. However, insulin concentration, HbA1c, HOMA-IR, and the other lipid profiles did not significantly change.

Conclusion: The combination therapy of metformin-AST significantly modifies some FBS and total cholesterol via inducing the gene expression of GLUT-4 and adiponectin as well as AMPK levels.

Keywords: Astaxanthin, type 2 diabetes mellitus, adiponectin, glucose transporter type 4, AMP-activated protein kinase

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Investigate the TAGLN2 gene expression level as a potential target for Alzheimer's disease early diagnosis and treatment

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Introduction: Alzheimer's disease (AD) is a progressive neurologic disorder that causes the brain to shrink (atrophy) and brain cells to die. The early signs of the disease include forgetting recent events or conversations. Medications may temporarily slow progression of symptoms but there is no treatment that cures AD. Certainly, genes have a potential role in various processes of this disease. In this study, TAGLN2 (Transgelin 2) expression levels, related genes and genetic pathways in AD were investigated using bioinformatics databases.

Methods: In this bioinformatic study, the GEO database was used to determine related genes and validation of the TAGLN2 gene. Subsequently, the DAVID database was used to genetic pathways evaluation. Furthermore, TAGLN2 gene was structurally analyzed in GeneCards. Eventually TAGLN2-related single nucleotide polymorphisms (SNPs) and microRNAs were found in miRdSNP database.

Results: TAGLN2 gene is a protein coding gene and located on chromosome 1q23.2. This gene has the highest expression in the cytosol, also the analysis of the RNA-Seq data derived from brain cells shows that this gene is highly expressed in the brain endothelial cells of healthy people and has low express in severe Alzheimer's disease. TAGLN2 makes actin filament binding permanent and stabilizes immune T cells. The analysis showed that the occurrence of the SNP:rs11556953 can lead the damaged brain cells to recovery and repair and affect the involved hsa-miRNA-133 family in this process. When miRNA-133b/133a bind to 3'UTR of TAGLN2 mRNA, increase gene expression and seriously reduce the symptoms of AD by brain nerve cells durability.

Conclusions: The current study shows that, the TAGLN2 gene plays a fundamental role in the suppression of Alzheimer's disease and the resistance of nerve cells and can be used as potential treatment targets. Furthermore, hsa-miRNA-133 family can be offered as neuroprotective biomarkers in early diagnosis.

Keywords: Alzheimer's disease, TAGLN2, hsa-miRNA-133

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Evaluation of the effect of asprin and TGF-β1 inhibitor on the expression of angiogenic and apoptotic factors in HT29 cell line

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Introduction: Aspirin plays a crucial role in chemoprevention and restraint of colorectal cancer. however, the Fundamental Mechanism of its action still remains ambiguous. Aspirin has long been prescribing for primary CVD Prevention in The United states, and more recently it has also been presumed for colorectal cancer (CRC) Prevention. One the Other hand TGF-β1 as a factor that involves in angiogenesis and wound healing may stimulate Tumorgenesis by inducing angiogenesis. PDGF-BB as another suspicious factor for participating in tumorgenesis Have been analyzing. PDGF and TGF- β1 have been marked as mediators of mesangial cell proliferation and Matrix expansion.

Methods: MTT analysis was used to evaluate the effect of aspirin (ASA) treatment on the proliferation of HT29cells. TGF-β1, PDGF-BB mRNA expression has been analyzed by RT-PCR in HT29 on Aspirin treatment versus a control group. The role of Aspirin in the modulation of PDGF-BB expression was analyzed by western blot and RT-PCR assays and rate of apoptosis was evaluated by flow cytometry

Results: The expression of TGF-β1 have been decreased during the ASA treatment. the rate of Pdgf-BB expression has Been decreased in the group that took co-treatment of ASA and SB431542 as a TGF-b blocker, this group compare to other groups have been shown a remarkable op. As follow the result of RT-PCR, western blot verified the previous experiment. In the next step rate of BAX and BCL-2 have been measured by RT-PCR that have been increased and decreased Respectively, it leaves a seal of approval on the assertion that ASA increase apoptosis by restraint TGF-β1.

Conclusion: In the present study, a newly-characterized association among aspirin, transforming growth factor TGF-β1 and CRC inhibition was identified. ASA have oriented Ht29 cells toward apoptosis by reducing TGF-β1 and Pdgf-BB, both as two double edged sword factors.

Keywords: TGF- β1, PDGF-BB, Aspirin

17th National Congress of Biochemistry & 8th International Congress of Biochemistry & Molecular Biology August, 23-26, 2022 - Tehran, Iran

Page | 565

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Evaluation of the status of fasting blood sugar (FBS), 2 hour post prandial (2hpp) blood sugar, glycosylated hemoglobin (HbA1c) and urine glucose reporting in the general population referring to the affiliated laboratories of Shiraz University Of Medical Sciences

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The prevalence of type 2 diabetes is increasing worldwide. Considering the importance of prevention and regular follow-up of diabetes and to answer the existing questions including the average fasting blood sugar and related tests in the Iranian population, in this study, we examined the relationship between HbA1c, FBS, and 2hpp in the general population referred to affiliated laboratories of Shiraz University of Medical Sciences. This study was performed on the laboratory data of the general population referred to affiliated hospitals between July 2016 to January 2022. After extracting the relevant data of FBS, 2hpp, HbA1c, and urinary glucose, each data was statistically analyzed in its own category and then the relationship between each factor was compared in pairs and then in multiples. The experimental data of 172,041 patients were analyzed. The mean age of participants was 41.69 ± 14.51 years. The mean FBS in the studied population was 102.30 ± 34.63 mg/dl, 2hpp was 168.94 ± 90.38 mg/dl and HbA1c was $6.48 \pm 1.90\%$. The correlation between all these tests was statistically significant and the highest correlation between the two variables FBS and 2hpp was 0.848. The best cut-off point for HbA1c was 6.55% with an AUC of 0.88 and for FBS was 127.50 with an AUC of 0.92 (with a criterion of 2hpp≥200). The best cut-off points of HbA1c, FBS, and 2hpp for glycosuria analysis were 7.15%, 156.50, and 205.50, respectively. The average of different blood sugar criteria is higher in men than in women. The best tests to distinguish diabetics from non-diabetics in the present study are FBS, 2hpp, and HbA1c, respectively. Since the probability of external error due to 2hpp is higher, it can be concluded that FBS is the best diagnostic test for diabetes. The best cut-off point for glycosuria is 7.15% for HbA1c, 156.50 and 150.50 mg/dl for FBS and 205.50 mg/dl for 2hpp.

Keywords: Diabetes ،Fasting blood sugar ،Two-Hour Postprandial Glucose ،Urine Sugar

Evaluation of changes in the expression Na/H antiporter gene and oxidative stress parameters during copper sulfate toxicity in kidney of male rats treated with ascorbic acid

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Introduction: Copper is an essential element for the body. High amounts of copper cause the production of free radicals, which can cause various diseases, including kidney failure. Also, the effect of antioxidants on the elimination of free radicals in the body is always important. In this study, the effect of copper sulfate as a poison on the parameters of oxidative stress and the expression of the antiporter sodium/hyogen gene in the kidney tissue of male rats during treatment with vitamin C was investigated.

Methods: 24 rats were randomly divided into 4 groups (n=6). Groups: control (A), recipient of copper (10mg/kg) (B), recipient of vitamin C (100 mg/kg) (C), recipient of vitamin C and copper sulfate (D). After ten days of treatment, the kidneys were removed from the body and examined to measure the parameters of oxidative stress and changes in gene expression. Gene expression was measured by RT-PCR technique.

Results: The observations showed that the Glutathione peroxidase enzyme level did not change significantly, the Total Antioxidant Capacity(TAC) parameter in group d had a significant difference ($p < 0.01$) compared to the control group. The expression level of sodium/hyogen antiporter gene also changed in group d compared to group b ($p < 0.01$)

Conclusion: it can be concluded that copper poisoning caused a change in the expression of sodium/hyogen antiporter gene in the kidney as well as the occurrence of oxidative stress in cells.vitamin C as an antioxidant reduces oxidative stress parameters.

Keywords: kidney ،Nephrotoxicity ،Copper ،Oxidative stress

Docking Study on Interaction of Taurine and Ellagic Acid as Anti-Inflammatory Agents with Pro-Inflammatory Proteins, IL-1β, TNF-α, and NF-κB

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Introduction: Inflammation is a process that protects organs against various potentially harmful stimuli and enables repair. Dysregulated inflammation, however, damages tissues and leads to disease, including cancer and autoimmunity. Dysregulated inflammation is characterized by excessive production of pro-inflammatory cytokines, such as IL-1β, TNF-α, and NF-κB. Targeting these inflammatory mediators is considered as a therapeutic strategy. The aim of this study is to evaluate the interaction of taurine and ellagic acid antioxidants with the target proteins.

Methods: The 3D structures of two antioxidants and ug were retrieved from the PubChem database. The structure of proteins was designed using homology modeling and energy minimized by Gromacs 2021.4. Finally, the compounds were docked into IL-1β, TNF-α, and NF-κB using the Autodock 4.

Results: The docking interactions demonstrated that EA had the lowest binding energies with IL-1β (-4.64 kcal/mol), and TNF-α (-5.81 kcal/mol), while TAU presented the strongest affinity with NF-κB (-5.35 kcal/mol).

Conclusion: Based on the results obtained from the present study, it can be concluded that taurine and ellagic acid can influence the inflammation process while interacting with important amino acids located in the active site of pro-inflammatory proteins.

Keywords: Docking, Ellagic acid, IL-1β, NF-κB, TNF-α, Taurine

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Detection of antiproliferative role of Diamond nanoparticles on human cervical carcinoma HeLa cells with Raman Spectroscopy

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Introduction: Nanodiamnod has recently received considerable attention because of the various possible applications in the medical field such as the ug delivery system. In this research, we offered a delivery system containing nanodiamonds to the cervical cancer cells (HeLa Cell line) and tracked them with Raman spectroscopy, as a noninvasive protocol.

Methods: Hela cell line and nanodiamonds were purchased. Raman spectroscopy and MTT cytotoxicity assay were applied for tracking the synergic effect of nanodiamonds on the Hela cell line.

Results: After treating Hela cells with nanodiamonds, the relative survival rate of the cells decreased in a dose-dependent manner. After the addition of nanodiamonds, a lower cell growth rate was observed ($p < 0.05$). The results of Raman spectroscopy indicated that nanodiamonds can enter cells and induce cell death.

Conclusion: The nanodiamonds have an inhibitory effect on the growth of HeLa cervical cancer cells. It was also concluded that Raman spectroscopy could be used to track the entry of nanodiamonds by comparing significant wavelengths.

Keywords: Cervical cancer cells, Nanodiamonds, Raman spectroscopy

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Synergistic anti-cancer effects of silibinin-etoposide combination against human breast carcinoma MCF-7 and A-MB-231 cell lines and breast cancer mouse model

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Introduction: Recently, there is a significant focus on combination chemotherapy for cancer using a cytotoxic ug and a phytochemical compound. We investigated the effect of silibinin on etoposideinduced apoptosis in MCF-7 and A-MB-231 breast carcinoma cell lines. Materials and **Methods:** The cytotoxic effects of silibinin and etoposide were determined using MTT assay after 24 and 48 hr incubation with these ugs individually and combined. The mRNA expression of Bax and Bcl2, and protein levels of P53, phosphorylated p53 (P-P53), and P21 were determined using real-time PCR and western blot analysis, respectively. The caspase 9 activity was measured using an ELISA kit.

Results: Silibinin and etoposide alone and combined significantly inhibit cell growth in a dose and time-dependent manner in both cell lines. The strongest synergistic effects in terms of MCF-7 cell growth inhibition [combination index (CI) = 0.066] were evident. The silibinin-etoposide combinations cause a much powerful apoptotic death (47% and 40%) compared with each compound individually in MCF-7 and A-MB 231 cells, respectively. Additionally, the silibinin-etoposide combinations significantly increased the expression of P53, P-P53, and P21 in MCF-7 cells. Neither silibinin nor etoposide individually increased the level of P53 and P-P53 in A-MB-231 cells, but both of them individually and combined increased the level of P21.

Conclusion: Since the silibinin-etoposide combination induces apoptosis in both cell lines with and without expression of p53, thus, it is suggested that this combination may be a successful therapeutic strategy for breast cancer regardless of P53 status.

Keywords: Apoptosis Breast cancer ug synergism Etoposide MCF-7 cells Silibinin

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PDL1 Positivity Rate between Triple-negative and Non-luminal Her2+ Cases

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Introduction: Triple-negative breast cancer cases with no available targeted therapy and advanced cases of luminal and HER2+ that become resistant to available state-of-the-art treatments are priorities in cancer research. Immune checkpoint blockade, particularly PDL1/PD1 inhibition, is suggested as a potential option for these patients suffering from several other types of cancers, such as melanoma. However, the exact subpopulation of breast cancer patients that overexpress PDL1 is yet to be completely identified. Additionally, reports on the value of PDL1 as a biomarker for the prognosis of cancer and its correlation with clinicopathological features of malignancy are diverse.

Methods: In this study, we performed immunohistochemistry on 60 breast cancer, including 22 triple-negative and 38 HER2+ cases, and 20 paired lymph node samples.

Results: PDL1 expression was present in 21. 6% (13/60) of breast cancer samples. PDL1 expression is significantly associated with ER/PR negativity and the grade of the tumor. The association between PDL1 positivity and recurrence and the overall survival of patients was not significant.

Conclusion: PDL1 expression is similar between triple-negative and non-luminal HER2+ cases, thus some of the advanced non-luminal HER2+ cases might be benefitted from immune checkpoint blockade.

Keywords: Breast cancer, triple-negative, PDL1, HER2-positive, immunohistochemistry, tumer.

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Evaluation of Serum levels of NGAL, KIM-1, and L-FABP Chronic Kidney Disease patients

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Introduction: Chronic kidney disease (CKD) is one of the most threatening and important disorders worldwide. Its prevalence is increasing among industrial and developing countries. Neutrophil Gelatinase-Associated Lipocalin (NGAL), Liver-type Fatty Acid Binding Protein (L-FABP), and Kidney Injury Molecule-1 (KIM-1) are three factors that are suggested as biomarkers for diagnosis and progression of the CKD. Because of the lack of enough efficiency of the creatinine in the prognosis of CKD, we performed this study to determine the association between these three factors and CKD occurrence and determine if they could be valid biomarkers. **Methods:** A case-control study was designed enrolling 42 patients with confirmed CKD referred to the Imam Khomeini hospital of Kangan and 42 age and sex-matched healthy volunteers. Blood samples were obtained. NGAL, KIM-1, and L-FABP were measured by ELISA using commercial kits (Bioassay Technology Laboratory). Serum creatinine was detected by applying Jaffe's method.

Results: There were significant differences in serum levels of all of the four factors between CKD patients and the control group, in which the serum levels of NGAL (specificity: 87.6%, sensitivity: 79.3%, and AUC: 0.89) and L –FABP (specificity: 83.3%, sensitivity: 78.3%, and AUC: 0.86) and KIM-1 (specificity: 85.7%, sensitivity: 78.6%, and AUC: 0.88) and creatinine were significantly higher in CKD patients as compared with controls. Also, there was a significant correlation between serum levels of NGAL, L-FABP, and KIM-1 in both patient and control groups.

Conclusion: NGAL, L-FABP, KIM-1, and creatinine could be used as independent biomarkers for the diagnosis of CKD.

Keywords: Chronic kidney disease, Liver-type Fatty Acid Binding Protein, Kidney Injury Molecule-1, Neutrophil Gelatinase-Associated Lipocalin

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Levels of organochlorine pesticides, methylation of P16, P15, and MGMT gene promoters, and histone modifications in chilen with acute lymphoblastic leukemia

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Introduction: Epigenetics is the science of altering gene expression without changing nucleotide sequences and may be induced by various environmental factors, including pesticides. This study aimed to investigate the relationship between the level of organochlorines (OCs) and epigenetic changes such as P15, P16, and MGMT promoter's methylation and histone changes of H3K9ac, H4K16ac, H4K20me3, and H3K4me3 in leukemia.

Methods: A total of 181 patients with leukemia were considered the patient group and 232 healthy individuals without underlying diseases were considered as the healthy group. The evaluation of OC levels, promoter methylation, gene expression, and expression of histone modifications were performed by gas chromatography (GC), methylation-specific polymerase chain reaction (MS-PCR), and reverse transcription PCR (RT-PCR), and western blotting, respectively.

Results: The results indicated that 76.2% of P15 promoters and 85.1% of MGMT promoters were hypermethylated in patients with leukemia compared to healthy individuals. In addition, the relative expression of P15, MGMT, H4K16ac, and H3K4me3 showed a significant decrease in patients with leukemia compared to healthy individuals. Levels of OCs in patients with leukemia were significantly higher than in healthy individuals. Furthermore, the results revealed that the rise in the OC levels was associated with an increase in methylation at the promoter level of P15 and MGMT as well as a decrease in the relative expression of H4K16ac and H3K4me3.

Conclusion: Therefore, it can be concluded that exposure to OCs induces epigenetic changes at the DNA and histone levels, which may lead to the disruption of transcriptional activity and cell cycle regulation, ultimately resulting in the development of leukemia.

Keywords: Organochlorine pesticides, methylation, P16, P15, MGMT, histone modification, leukemia.

MicroRNAs as Prospective Recognition Strategy in Cancer Patients with COVID-19

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Page | 573

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Introduction: Nowadays, miRNAs are found in liquid biopsies such as saliva, tears, urine, and plasma, and one of the reasons they are used in plasma from recovered COVID-19 patients is the presence of antiviral miRNAs to antibodies from previous SARS-CoV-2 infection. Furthermore, a cutting-edge approach known as "Salivaomics" may assess the genome, transcriptome, proteome, and biomarkers such as miRs in oral diseases and cancers. This review aims to introduce some potential miRNAs in diagnosing SARS-CoV-2 infection in cancer patients.

Methods: This review was conducted using keywords such as microRNAs, miRNAs, COVID-19, SARS-CoV-2 Infection, Diagnosis, Biomarkers, Therapeutic approaches, in PubMed, Scopus, Medline, Science Direct, and Web of Science based on the Cochrane Highly Sensitive Search Strategy.

Results: The human miRs can be used as biomarkers for viral infection and cancer diagnosis because they are regulators and impact gene-related expression. For instance, miR-338–3p (Liver, lung, and gastric cancers), miR-4778–3p (Cervical cancer radioresistance), miR-6864–5p (Urothelial Carcinoma of the Bladder), miR-5197–3p (Squamous cell lung carcinoma), miR-548c-5p (Colorectal Cancer), miR-548d-3p and miR-409–3p (Osteosarcoma), miR-30b-5p (Esophageal squamous cell carcinoma), miR-505–3p (Prostate cancer), miR-23c (Hepatocellular carcinoma), miR-30d-5p and miR-5197 (Non-small cell lung cancer), miR-4684–3p (Colorectal cancer), miR-518a-5p (Gastrointestinal tumors), miR-3934 (Colon cancer, lung cancer, NSCLC, rectal carcinoma mucosa), and miR-1468–5p (Glioma, hepatocellular carcinoma) can be utilized in the diagnosis of cancer patients who are suffering from COVID-19 disease.

Conclusion: Undoubtedly, microRNAs have versatile functions in the cell and molecular biology. Alternation in human miRs' expression, including overexpression or mimic replacement, inhibition, or suppression, helps block viral entry or replication in host cells. In contrast, decreasing human miRs against SARS-CoV-2 infection provides more viral replication and accessibility to the immune system. This study listed the potential miRNAs for detecting COVID-19 in cancer patients.

Keywords: microRNAs, SARS-CoV-2 Infection, COVID-19, Cancer, Biomarker

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The Role of Quantum Dots (QDs) in the Diagnosis of Oral Cancer: A Systematic Review

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Introduction: Oral cancer is the sixth most prevalent malignant tumor worldwide, and the five-year survival rate is calculated at 50%. Quantum dots (QDs) are semiconductor nanocrystals that typically have a diameter of between 1 and 10 nm and are made up of elements from groups II-IV, IVVI, or III-V. QDs may be used as probes or ug delivery vehicles in cancer treatment, but they can also create reactive oxygen species (ROS) or produce heat when exposed to radiation, killing cancer cells. This systematic review was performed to illustrate the utility and ability of QDs in detecting and treating oral cancer.

Methods: This review was conducted using keywords such as nanoparticles, quantum dots, oral cancer diagnosis, oral cancer therapy, and semiconductor nanocrystals in PubMed, Scopus, Medline, Science Direct, and Web of Science based on the Cochrane Highly Sensitive Search Strategy.

Results: Scientists have labeled Tca8113 cells using QDs and the FITC labeling approach, noting that QDs are more suited for long-term dynamic monitoring of cell physiological changes than FITC due to their superior fluorescence intensity and photostability. Another group fabricated EGFR-antibody-conjugated QD800 for the targeting and in vivo imaging of the human BcaCD885 cell line in an OSCC animal model. Xue et al. have studied the formation of Cav-1 protein in carcinogenesis and the development of tongue SCC by semiconductor QDs-IHC. They suggested that Cav-1 protein is an oncogene in the carcinogenesis and development of tongue SCC. Xue and his colleagues used the QDISH method to look at the link between OSCC and HPV. The results showed that QDISH was more sensitive than in situ hybridization.

Conclusion: This in-depth analysis shows that QDs have the potential to be used as an indicator of oral cancer and are highly expected to be used overall in the forthcoming years.

Keywords: Oral cancer, Quantum dots, Semiconductor nanocrystals, Cancer Diagnosis

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The effect of probiotic supplementation on the glycemic index in NAFLD patients: a systematic review and meta-analysis

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Introduction: & objective(s): Novel pandemic of this era is obesity and its cooccurance overnutrition diseases, as Nonalcoholic fatty liver disease (NAFLD) could be named as one of them and one of the most prevalent chronic liver disorders across the world. Although this disease has no pharmaceutical remedy, but lifestyle and diet changing are the best ways to control the situation. Supplementation with probiotics has been related to reduced concentrations of the glycemic index and could be a supplementary remedy for enhancing the state of disease. Concerning clinical findings, the noticeable results have been controversial. In the present meta-analysis, a review investigates the effectiveness of probiotic supplementation on the glycemic index in NAFLD patients.

Method: The literature search included PubMed, Scopus, and Cochrane up to February 2022 to obtain the relevant published intervention. Effect sizes of included studies were pooled using Comprehensive Meta-Analysis (CMA) V3 software.

Result: eleven trials were included in the meta-analysis of glycemic endpoints. The combined findings, using a random-effects model, showed that supplementation with probiotic supplementation significantly improved insulin S [-1.10; 95% CI -2.12, -0.087; p = 0.033], and HOMO-IR S [-0.59; 95% CI -1.07, -0.12; p = 0.014], however our results show that probiotic supplementation not significantly effect on FBS concentration S [-0.34; 95% CI -0.73, 0.036; p = 0.07] .

Conclusion: Current findings suggest probiotic supplementation is a suitable choice in managing the glycemic index in NAFLD patients, although future researches are necessary

Keywords: HbA1c, FBS, insulin, NAFLD

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Effect of atorvastatin on liver histopathology in animal model of NAFLD in rats

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Introduction: Nonalcoholic fatty liver disease (NAFLD) is characterized by significant lipid accumulation in the hepatocytes. Fibrosis can progress over time, resulting in severe scarring of the liver and leading to the development of cirrhosis

Methods: Twenty-four male rats were divided randomly into seven groups: 1) control, 2) HFFD (high fructose/fat diet) control that received fructose, olive oil, and CCl4 and, 3) HFD + Atorvastatin that received Atorvastatin 20 mg/kg. Interventions have been done for 23 weeks. Hepatic fragments were fixed in formaldehyde 4% and embedded in paraffin for H&E analysis. The histological features were grouped into three broad categories: steatosis, inflammation, and hepatocellular injury.

Results: Compared to HFFD, the lipid oplet accumulation was decreased in the liver of rats treated with atorvastatin. The lobular inflammation was decreased in atorvastatin. Atorvastatin therapy led to a reduction in NAFLD activity score.

Conclusion: Atorvastatin has effectiveness in the management of dyslipidemia and liver function being considered crucial for attenuating the progression of NAFLD although more studies are needed.

Keywords: NAFLD, Atorvastatin, Rat, High fructose/fat diet, liver

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Studding the gene expression pattern of Toll like receptor and histamine during methamphetamine addiction in the brain stem of rats

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Introduction: Methamphetamine is an amphetamine-like brain stimulant that has been widely abused in recent years. ug addiction can change the hemostasis of neurotransmitters in brain. Toll-like receptor signaling is modified during addiction. Involvement of the brain histaminergic system in addiction is proposed. In this study the gene expression pattern of Toll like receptor and histamine was studied in the brain stem during methamphetamine addiction and treatment with buprenorphine.

Methods : The male Wistar rats weighing 200-220 gr were randomly divided into control, methamphetamine (10 mg / kg for 5 days), and buprenorphine group at a dose of / 6 kg for 5 days and withawal group. 32-72 hours after the last use of methamphetamine, the first signs of withawal appear, which increase after 98 hours. The method of injection was intraperitoneal. Brain stems were sampled from all animals. Then the expression level of TLR1 and histamine genes was measured using real-time PCR technique. One-way ANOVA and SPSS software version 22 were used to analyze the data.

Results: The level of TLR1 gene expression is increased in meth group ($p < 0.05$). Also the level of histamine gene is increased in withawal group ($p < 0.05$).

Conclusion: It seems there is an active relationship between nervous system and immune system. During addiction this interaction is changed by modifying special molecules like histamine and Toll like receptor as a bridge between this two systems.

Keywords: Methamphetamine, Toll like receptor, histamine, gene expression, brain

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SIRT1 activation attenuates palmitate induced apoptosis in C2C12 muscle cells

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Introduction: Insulin resistance is a major feature of type 2 diabetes, which occurs mainly in skeletal muscle. Studies have shown that SIRT1 is involved in processes related to the insulin signaling pathway. However, the molecular mechanisms of the role of SIRT1 in the induction of apoptosis by palmitate fatty acid are not very clear.

Results: Here we show that SIRT1 is reduced in C2C12 skeletal muscle cells under palmitate induction of apoptosis and also activation of SIRT1 reduces the harmful effects of palmitate induced apoptosis of muscle cells. The results of this study showed that induction of apoptosis by palmitate decreased mitochonial biogenesis by decreasing PGC-1α expression while increasing SIRT1 expression improved mitochonial biogenesis by increasing PGC-1α expression. On the other hand, SIRT1 inhibitor, sirtinol, reduced mitochonial biogenesis in similar conditions. This study also showed that the amount of ROS increases in the condition of induction of apoptosis by palmitate and ROS inhibitor can reduce the induction of apoptosis by palmitate. The results of this study showed that increasing the expression of SIRT1 by reducing the amount of ROS can reduce the induction of apoptosis in skeletal muscle cells.

Conclusion: In general, the results of this study showed that SIRT1 attenuates the harmful effects of apoptosis induced by palmitate in skeletal muscle cells through various mechanisms and has the potential to improve insulin resistance in type 2 diabetes and to reduce the level of lipoapoptosis and improve mitochonial biogenesis in skeletal muscle cells.

Keywords: apoptosis, Muscle cells, palmitate, type 2 diabetes, SIRT1, Resvertrol

A-10-1754-1

Investigating the expression of miR-155 in the tissue of breast cancer patients compared with healthy tissue

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Introduction: breast cancer is a multifactorial disease and has the fatal attribute. In spite of increased progresses regarding the diagnosis, it is still the main reason of death among women. The aim of this study is the investigation and expression of miR-155 in the people with breast cancer compared to normal tissue.

Methods: 60 tissue specimens from cancer-suffered people were investigated which 30 specimens were taken from the central part of masses and the other 30 specimens were from the partial parts. Quantitative RT-PCR was used to determine the expression of miR-155 in both tissues with and without cancer.

Results: the results showed that CEA mRNA marker was positive in the central parts of cancer masses with 25 specimens of 30 and 10 of 30 specimens in the partial parts. The statistical comparisons were represented the significant differences between these two groups (P-value < 0.001). MiR-155 marker in the 22 specimens of 30 central parts of masses was positive, while in the partial normal tissues, this rate was six of 30 specimens. The statistical comparisons showed significant differences between two groups (P-value < 0.001).

Conclusion: overall, it can be concluded that the results of this study, which is related to breast cancer markers, can be considered as the diagnosis-screening test for the disease discovery. To further supportive of the results carried out in this study, comprehensive and more developed studies with more specimens are recommended.

Keywords: Breast Cancer, marker tumor, miR-155, quantitative RT-PCR

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Anticancer Effects of Turmeric and White Tea Silver Nanoparticles Against MCF-7 Cancer Cells

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Page | 580

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Introduction: Hyperproliferation is one of the outstanding apoptosis-inducing stresses. Cancer proliferation is considered by the loss of inhibition of apoptosis, comprising caspase-3 activation. Silver nanoparticles (AgNps) have several important implications including cytotoxic properties. This research aimed to study effect of turmeric and white tea green AgNp on the MCF-7 cells apoptosis.

Methods: MCF-7 cells were cultured with prepared ugs of AgNp, 3% turmeric extract and a combination of that with 3% white tea extract in concentrations of 0, 25, 50, 75 and 100 µg/ml for 24 Hr. Cell viability was detected by MTT technique. Thereafter, the caspase-3 of the supernatants was measured by ELISA.

Results: Upon 24Hr of treatment in group A (AgNp) with 25, 50, 75 and 100µM of the total 2mM concentration of AgNps, the cell viability of MCF-7 cells were 92.5, 85.5, 76.7 and 69.0 respectively. In group B (AgNp + white tea) the findings were 60.3, 65.4, 72.9 and 74.9 respectively. In group C (AgNp + white tea + turmeric) correspondingly 10.6, 12.3, 15.0 and 39.4 of cells were viable. Also, the average concentration of produced caspase-3 (nM) in cells treated by 100µM of groups A, B and C were 18.29, 17.18 and 15.94, respectively.

Conclusion: AgNp alone has lethal properties. White tea is known to have antioxidant activities; and this protective role might explain how application of white-tea-AgNps with higher portion of white tea show higher cell viability. However, the combined effect of white tea and turmeric AgNps suppress the viable cells more than that of AgNps and white-tea-AgNps alone. The activation level of caspase-3 has a reverse link with apoptosis and adding turmeric induces higher rate of apoptosis-inducing stresses and lower levels of caspase-3. The high synergistic potential of these green AgNps can be considered as a promising strategy in the treatment of cancer.

Keywords: Cancer, Apoptosis, Caspase-3, MCF-7

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Prospect of Circular RNA in Acute Kidney Injury: Is a Potential Biomarker?

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Introductions: The kidney play a vital role in regulating acid–base homeostasis, maintaining the balance of water, fluids and electrolytes. Despite extensive and significant advances in the control of acute kidney injury (AKI), it still has high morbidity and mortality for important reasons, including difficulty in identifying renal damage and delayed diagnosis. CircRNAs are a new class of non-coding RNAs that have different effects on cellular signal processes. CircRNAs have closed covalent structures and are thus protected against RNA exonucleases. Studies have shown that various kidney diseases, including AKI, are associated with circRNAs.

Methods: Performed a search of online database including "Scopus, PubMed and Web of Science" and collected published data by following keywords: "Acute kidney injury, Circular RNAs, Biomarker."

Results: AKI is characterized by a sudden or rapid decrease in glomerular filtration rate. The diagnosis of AKI is often based on an assessment of creatinine levels, but this test sometimes does not accurately detect kidney function. Therefore, the identification of new biomarkers that have specificity, sensitivity, and non-invasiveness is under investigation. CircRNAs have been gradually introduced as ideal biomarkers for disease diagnosis due to their presence in various tissues and their stability. The unique structure of these molecules makes them resistant to RNA exonucleases. On the other hand, studies have shown that circRNAs circulate in body fluids. Therefore, they can act as good candidates as diagnostic biomarkers.

Conclusion: Although CircRNAs, due to their structural stability and tissue specificity, have great ability to detect AKI in the early stages by changing the contents of urine and blood, but more studies are needed to identify circRNAs that change specifically during AKI. Basic studies on the relationship between circRNA levels and disease severity are also essential.

Keywords: Acute kidney injury, Circular RNAs, Biomarker

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The intensity of microRNA-429 expression in respect with guppy skin color

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Introduction: MicroRNAs are a kind of small non-coding RNAs that have been shown to play a key role in vital cellular processes, including evolution and differentiation through post-transcriptional regulation. The miRs are involved in regulating melanogenesis and their role in determining skin color in fish shows that miR429 is a potential regulator of skin pigments. The miR429 directly modulates Foxd3 expression by targeting the 3'untranslated region (3'UTR). So, to investigate the difference of miRNA429 expression level between red and white skin guppies, the Poecilia reticulata family was selected as a model organism and miRNA429 expression was analysed by RT-qPCR method.

Methods: For this purpose, red male and white female guppies' skin were sampled and Total RNA was extracted with YTZOL. Primers were designed using sRNAprimerDB site with stem loop RT-qPCR method. Then cDNA was synthesized with Sinaclon kit and the expression of miR429 gene was estimated using SYBR Green dye RT-qPCR in the presence of 5SrRNA gene as internal control. The final results showed that the expression of miR429 gene was significantly different in the skin of male and female guppies and it was expressed about 10 times more in male fishes.

Keywords: Poecilia reticulata, melanogenesis, different expression, RT, qPCR, YTZOL

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Identifying an upregulated lncRNA and its associated gene in breast cancer using bioinformatics analysis

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Introduction: and objective: Breast cancer is the most prevalent cancer and the second leading cause of cancer death in women. Despite advances in the diagnosis and treatment of breast cancer, the disease remains a challenge for global research. Long non-coding RNA are a class of non-coding RNAs that most of them lack the ability to encode proteins and play essential roles in various biological processes. This study intended to identify an upregulated lncRNA and its associated gene in breast cancer using bioinformatics analysis.

Methods: 12727 lncRNAs expression profiles of 837 breast cancer samples and 105 normal breast samples were downloaded from TANRIC database. Expression data were subsequently imported into iDEP website and then we performed analysis including heatmap and DEGs on the data. First we excluded lncRNA with lgFC>1 as upregulated lncRNAs and those with lgFC<-1 as downregulated lncRNA, and in both cases, we considered F<0.01. Then we collected lncRNAs involved in breast cancer using LncBook database. Finally, we shared information from two databases with VENNY diagram. After selecting the desired lncRNA, prediction of the most gene associated with this lncRNA was performed using the lncHUB website.

Results: Heatmap analysis revealed that the expression profiles of different lncRNAs, were able to distinguish tumor samples from normal tissue samples, wich indicates the logic of the data.Through the DEG analysis, we found a total of 64 lncRNAs displayed differential expression in tumor tissues compared to normal tissues, including 18 upregulated lncRNAs and 46 downregulated lncRNAs. After sharing data from two databases, TANRIC and LncBook, we detected two common lncRNAs called MRPS30-DT and DSCAM-AS1. Finally we found MRPS30 gene as the most related gene with MRPS30-DT, using lncHUB database.

Conclusion: Findings of the study suggested that MRPS30-DT and MRPS30 may have a potential role in breast cancer, wich requires further studies.

Keywords: Breast cancer، lncRNA، MRPS30-DT، MRPS30

A-10-1794-1

The efficacy of human amniotic membrane in prevention of post-operative tendon adhesion band

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Introduction: Tendon regeneration and reduction of peritendinous adhesion are among the most common ailments of the musculoskeletal system. Peritendinous adhesions are complications known to occur after surgery and cause chronic pain and disability. Anti-adhesion barriers are currently one of the best options for this medical complication. The aim of this study was to evaluate the efficacy of the human amniotic membrane (HAM) in decreasing tendon adhesion.

Methods: In this study, male Wistar rats (weighing 200-250 g) were divided into 3 groups: sham, control, and experiment. A full-thickness Achilles tenotomy was performed, and the tendon was repaired using a modified Kessler suture. In the experiment group, HAM wrap was used as a treatment. Bio-mechanical, Histological (hematoxylin/eosin (H&E) or Masson's trichrome staining) and quantitative evaluation of inflammation, and total fibrosis scores (Tang et al. and Ishiyama et al. adhesion scoring system) were graded and measured.

Result: Human amniotic membrane could significantly decrease adhesion formation and inflammation. In addition, biomechanical properties of the Achilles tendon, such as ultimate load, ultimate stress, and ultimate strain were improved in the HAM group.

Conclusion: The results showed that HAM wrap around the tendon repair site could significantly reduce post-surgical adhesion band and result in better tendon healing.

Keywords: human amniotic membrane, Peritendinous adhesion, Peritoneal fibrosis, Post-surgical adhesion bands

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The effect of overexpression of Yap1 on the production of heterologous glucose oxidase in Pichia pastoris

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Page | 585

Introduction: Metabolism of methanol in methylotrophic yeast Pichia pastoris increases the amount of ROS (reactive oxygen species). During adaptation to the methanol medium, the yeast antioxidant defense system activates under the control of various transcription factors to overcome the destructive effects of ROS. Among them, PpYap1 activates the expression of the glutathione redox system by promoting the upregulation of glutathione reductase 1 (Glr1). In this study, the expression of glucose oxidase in presence of overexpressed PpYap1 was examined.

Methods: The correlation between the expression of Yap1 and AOX1 in Pichia pastoris under different feeding conditions was in-silico studied using a gene co-expression network-based analysis. The Yap1 gene under the control of AOX1 and GAP promoters was transferred into a heterologous glucose oxidase (GOX) producing Pichia pastoris strain. The expression and secretion of GOX, cell viability, and intracellular ROS in Yap1 overexpressed strains were investigated in presence of 1 to 8 percent Methanol as an inducer.

Results: The gene co-expression network-based analysis showed that the expression of the Yap1 and AOX1 genes have a 0.90 positive correlation. The overexpression of Yap1 under the control of both AOX1 and GAP promoters showed a similar 50% increment in secretory production of heterologous GOX in the 4% methanol medium. Also, it significantly elevated the viability of yeast cells in all media and astically decreased intracellular ROS.

Conclusions: This study showed that the elevation of oxidative stress tolerance in P. pastoris is a notable strategy to increase heterologous protein production in higher percent methanol media.

Keywords: ROS, heterologous protein production, oxidative stress, yeast, Pichia pastoris.

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The effect of overexpression of PpPMP20 on the production of heterologous glucose oxidase in Pichia pastoris

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Introduction: Peroxisomes as specialized organelles for methanol metabolism produce large amounts of ROS in methylotrophic yeast Pichia pastoris. PpPMP20 (peroxisomal glutathione peroxidase) is the most important antioxidant enzyme in the glutathione redox system as a central compartment of the ROS reduction machinery in peroxisomes. In this study, using overexpression of PMP20, the effects of increment of the capacity of the glutathione reduction system in a glucose oxidase producing P. pastoris is investigated.

Methods: A gene co-expression network-based methodology was used to investigate the association between the expression of PMP20 and AOX1 in P. pastoris. The PMP20 gene was transferred into a glucose oxidase (GOX) producing P. pastoris under the control of the AOX1 and GAP promoters. In the presence of 1 to 8% Methanol as an inducer, the production of GOX, cell survival, and intracellular ROS in pmp20 overexpressed strains were studied.

Results: The gene co-expression network analysis revealed a 0.98 positive connection between the expression of the pmp20 and AOX1 genes. Inductive and continuous overexpression of pmp20 showed a 60% and 80% increase in the secretion of GOX into the culture media containing 4 percent of methanol, respectively. It also increased the viability of yeast cells in all conditions and reduced intracellular ROS.

Conclusions: This research demonstrates that increasing oxidative stress tolerance in P. pastoris is an effective strategy for increasing heterologous protein production in higher percent methanol environments.

Keywords: ROS, heterologous protein production, oxidative stress, yeast, Pichia pastoris.

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Kinetics studies of Bovine Liver Catalase in presence of Glucose

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Introduction: Bovine Liver Catalase (BLC) is an enzyme that catalyzes the H_2O_2 into harmless water and molecular oxygen. Due to many industrial and medical applications of BLC, its stability and activity are important. Organic osmolytes such as glucose, preserve proteins from destruction by the conservation of their folded and functional states under different unfavorable conditions. **Method**: Determination of the BLC activity was done by checking the reduction of the absorbance values at 240 nm and the temperature of 37 °C by using a UV-Vis spectrophotometer; this could help to detect the amount of H_2O_2 consumed in both absence and presence glucose for the steady-state kinetics. The values related to Vmax, Km, Kcat and Vmax/kcat were calculated.

Results: To identify the effects of glucose on the enzyme kinetic, at first, the catalytic activity was studied in the absence and presence of various concentrations of glucose and substrate at the temperature of 37 °C and pH 7.4. Based on the Lineweaver–Burk curve, Glucose could influence the activity of BLC. Upon glucose binding, the value of the maximum velocity (Vmax) of the enzyme was increased, thus the enzyme activity could be increased. With the addition of the glucose, the affinity of the BLC for H_2O_2 was reduced (Km was increased).

Conclusion: There was a direct correlation between the BLC activity and the concentration of glucose. As a result, glucose could be regarded as an activator.

Keywords: BLC, Spectrophotometer, Glucose

A-10-1801-1

Effect of Oleuropein on Apoptosis, mir-21 expression and PTEN/PI3K/Akt Signaling Pathway in Azacitidine-treated Acute Myeloid Leukemia cells.

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Introduction: Acute myeloid leukemia (AML) is the most common type of acute leukemia in adults, which often gets worse quickly if left untreated. One of the key factors in the development of AML is miRNAs, which can be modulated by chemical ugs or natural agents. Oleuropein is a natural polyphenol with anti-cancer properties that can be used alone or with another chemical agent. Azacitidine is a hypomethylating agent for use in certain hematologic malignancies, particularly AML.

Methods: The present study was performed to evaluate the therapeutic effect of Oleuropein by modulating mir-21 as an important oncogene and one of the factors that reduce the response to Azacitidine and its effect on the PTEN/PI3K/AKT as an important pathway in multiple biological processes. Human leukemia cells (HL-60) were grouped as follows: Control (HL-60 cells without treatment), HL-60 cells with Oleuropein treatment, HL-60 cells with Azacitidine treatment, and HL-60 cells with a combination of these treatments. Bioinformatics assays were performed to analyze the association between mir-21 and PTEN, the MTT method was used to measure cell proliferation and IC50 determination, flow cytometry for apoptosis, RT-PCR for detection of mir-21 and PTEN expression, and Western blot was used to detect PTEN, P13K, and AKT protein expression.

Results: Oleuropein and Azacitidine treatment, alone or in combination, decreased the expression of mir-21, PI3K, and AKT compared to untreated cells. Furthermore, the expression of PTEN and apoptosis was increased. MiR-21 targets PTEN, the key protein in the PTEN/PI3K/AKT signaling pathway, thereby inhibiting apoptosis of cancer cells. In addition to increased apoptosis, Oleuropein suppresses the PTEN/PI3K/AKT pathway in Azacitidine-treated cells by reducing the expression of mir-21.

Conclusions: In summary, our study demonstrated that oleuropein could enhance the response to Azacitidine and increase the ug's efficacy by decreasing the expression of mir-21 and inhibiting the PTEN/PI3K/AKT pathway.

Keywords: Leukemia, Oleuropein, Azacitidine, mir-21, PI3K, PTEN, AKt

Investigating the effects of metformin on ovarian cancer

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Introduction: Ovarian cancer is one of the most common cancers in women, and the effects of metformin on this cancer have received less attention. This study was conducted with the aim of investigating the effect of metformin on ovarian cancer

Methods: In this review, the keywords metformin, ovarian cancer, and polycystic ovary synome were used in Google Scholar, SID, Science direct, Madlib, and Pubmed databases to search for articles

Result: Metformin generally has long-term effects on certain diseases, its progression and ovarian cancer patients, and it reduces the occurrence of ovarian cancer in women with polycystic ovary synome and diabetes. Metformin limits the growth and proliferation of ovarian stem cells in invitro and invivo environments. Metformin causes apoptosis in ovarian cancer cells and Skov-3 cells by reducing the expression of Bcl-xl and Bcl2 regulators and increasing the expression of Bax and cytochrome C regulators. Apoptosis induction by metformin can be increased by a combination including cisplatin and paclitaxel as auxiliary agents.

Conclusion: Metformin significantly limits the growth of cancer cells in vitro by increasing the effects of platinum, and FAGS analysis confirms the effect of metformin in reducing the activity of the aldehyde dehyogenase enzyme of ovarian cancer cells, as well as metformin in the formation of cells in the environment. It inhibits the growth of pathogenic tumors

Keywords: metformin, ovarian cancer, polycystic ovary synome

A Novel Approach to Type 3 Diabetes Mechanism: The Interplay between Non-Coding RNAs and Insulin Signaling Pathway in Alzheimer's Disease

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Introduction: In recent years, several studies indicated that there's a linkage between patients having type 2 diabetes (T2D) and development of Alzheimer disease (AD). In fact, several T2D related mechanisms such as insulin resistance (IR), inflammation, oxidative stress and mitochonial dysfunction can aggravate AD in people aging over 65 years old. In this regard, type 3 diabetes is a new term for patients diagnosed with AD while having symptoms of T2D and IR. Today, countless studies have confirmed the role of non-coding RNAs including microRNAs (miRNAs) and long non-coding RNAs in development of AD due to their ability to regulate insulin signaling pathways.

Methods: In the present study the electronic data bases of PubMed, Google Scholar and science direct from 1996 to 2021 were searched for these keywords: Alzheimer disease, type 3 diabetes, miRNAs, lncRNAs, insulin signaling pathway.

Results: Results of this study indicate the effects of dysregulated levels of ncRNAs in AD pathogenesis through targeting insulin signaling pathways subunits. For example, here the neuroprotective role of ncRNAs like miR-21, miR-425-5p, miR-539-5p, miR-132 and miR-212 was portrayed. Additionally, it was reviewed that higher levels of some miRNAs such as miR-27b and miR-128 can stimulate AD development. This review article has also consistently brought a brief insight into diagnosis and treatment approaches available for AD patients. In this regard, gene therapy and using some compounds namely, Isovitexin seems to be promising treatments for managing and prevention of AD.

Conclusion: Here the intrinsic interplay between different ncRNAs and targeted proteins in insulin signaling pathways were reviewed. This study might be a cornerstone for new approaches of the early diagnosis and treatment of AD patients. However, finding solutions for current problems and suggesting a practical strategy in the clinical setting are still a challenge.

Keywords: Alzheimer disease, type 3 diabetes, miRNAs, lncRNAs, insulin signaling pathway

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Effect of Nigella sativa on the lipid profile in Type 2 diabetes mellitus: a systematic review and meta-analysis of randomized controlled trials

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Page | 591

Introduction: Type 2 diabetes mellitus (T2DM (is a group of metabolic disorders and is currently growing alarmingly. Accumulating evidence has been described the effect of N. Sativa, as a natural polyphenolic compound, conditions such as cancer, hypercholesterolemia, hypertension, gastrointestinal disorders, inflammation, and diabetes; however, findings are controversial. Here we performed a systematic review and meta-analysis to evaluate the effect of N. Sativa on lipid profile levels in T2DM.

Methods: Online research was conducted in the following database: MEDLINE, EMBASE, Cochrane Library, Web of Science databases, and Scopus. This systematic review and meta-analysis of randomized controlled trials (RCTs) were conducted to investigate the potential effects of N. Sativa supplements on lipid profile level among patients with T2DM. The meta-analysis was performed using Comprehensive Meta-Analysis (CMA) V3 software.

Results: Six RCTs met the inclusion criteria and were selected for the current meta-analysis. The results of the present study demonstrated that N. Sativa significantly decreases serum levels of total cholesterol (W: −13.4 mg/dl; 95% CI, −19.82 to -6.99; P = 0.00; I2: 65.64%), LDL-cholesterol (W: −13.49 mg/dl; 95% CI, -19.25 to -7.74; P = 0.00; I2: 68.42%), and increased HDL-cholesterol concentrations (W: 1.67 mg/dl, 95% CI: 0.27, 3.06; P = 0.02; I2: 17.86%) in patients with type 2 diabetes. While we found no significant effect of resveratrol intake on triglycerides (W: −10.34 mg/dl; 95% CI, -24.62 to 3.93; P = 0.11; I2 = 40.92%; P = 0.04) concentrations. **Conclusion:** Our results recommend that N. Sativa be used as a potential therapy in patients with T2DM by reducing lipid profile level.

Keywords: T2DM, lipid profile level, N. Sativa

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The role of caveolin-1 and endothelial nitric oxide synthase polymorphisms and NO serum level in susceptibility to prostate cancer

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Introduction: Prostate cancer continues to be the most frequently diagnosed neoplasm. Caveolin-1(cav-1) is overexpressed in prostate cancer (PC) and associated with prostate cancer aggressiveness. We decided to study the effects of CAV1-T29107A and endothelial nitric oxide synthase (eNOS) G894T polymorphisms on the serum levels of testosterone, NO and prostate-specific antigen (PSA) in patients with PC.

Methods: This case-control study was conducted on 100 PC patients and 150 healthy participants selected from among the western population of Iran. SNP rs1799983 and SNP rs7804372 genotypes were determined by PCR-RFLP and T-ARMS-PCR methods, respectively, and were confirmed by DNA sequencing technique. Testosterone serum level was determined by ELISA method, and serum levels of Nitric oxide was determined by Grease method.

Results: The results showed the mean serum nitric oxide and testosterone in PC patients was significantly lower than that of control group (p<0/001). The mean nitric oxide and testosterone serum in patients suffering from prostate cancer, with GT and GT+TT genotypes from SNP rs1799983, was lower than control group, indicating a significant difference (p<0/001). Further, the mean nitric oxide and testosterone serum in PC patients with AA and AT+TT genotypes from SNP rs7804372, was lower than control group, showing a significant difference (p<0/001). Moreover, the serum nitric oxide and testosterone in patients with low Gleason greed was lower than that of patients with high Gleason greed but the difference was not statistically significant (p=0/07).

Conclusion: The findings of this study indicated an association between reduced serum nitric oxide and testosterone induction of prostate cancer. Moreover, SNP rs7804372 of encoding gene Cav-1and SNP rs1799983 variants of encoding gene eNOS were found to be correlated with serum level of nitric and testosterone

Keywords: Prostate cancer, nitric oxide, Caveolin-1, eNOS, Gleason greed

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Effects of Scopolamineon on Neuronal Response of Pyramidal Neuron of the CA1 Hippocampus in Rat Model of Parkinson's Disease

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Introduction: Some people with Parkinson's disease (PD) experience mild cognitive impairment. Scopolamine (Scp), a muscarinic receptor antagonist, produces a blocking of the activity of the muscarinic acetylcholine receptor, and the concomitant appearance of transient cognitive amnesia and electrophysiological changes, which resemble those observed in Alzheimer's Disease (AD). So far, a specific study of the effects of Scp on the molecular neurons in the CA1 region has not been done. The current study aimed at evaluating the effect of Scp on pyramidal neuron response in CA1 region of a rat model of PD.

Methods: In this experimental study, adult male Wistar rats were randomly divided into five groups: Substantia nigra pars compacta (SNc) lesion (the lesions were induced by IP injection of Rotenone 2mg/kg/19day/48h) and four groups of Scp (lesions plus 0.5, 1, 2 and 4 mg/kg ip of Scp). Spontaneous neural activity was recorded for all groups in the CA1 region of the hippocampus.

Results: The obtained results showed that IntraPeritoneal (IP) injection of Scp (0.5 & 1 mg/kg) decreased neuronal spontaneous activity in the rat model of PD.

Conclusion: The current study results suggested that Small amounts of Scp decreased neuronal response in CA1 region of hippocampal in a rat model of PD that is probably through interference from the cholinergic receptors.

Keywords: Keywords: Electrophysiology, Parkinson's disease, Rats, Rotenone, Scopolamine

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Preparation of L-asparaginase from bovine liver and measuring the effect of Melissa officinalis essential oil on its kinetic parameters

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Introduction: L-asparaginase (EC3.5.1.1), due to hyolyzing the amide bond of the L-asparagine side chain and converting it to L-aspartate and ammonia is one of the most important anti-cancer ugs in the world. Also this enzyme include antiviral effect, reduction of acrylamide levels in food industry and anti-inflammatory effect in the treatment of autoimmune diseases. Iranian Melissa officinalis is a herbaceous plant with antioxidant, analgesic, anti-inflammatory, anti-diabetic properties.

Methods: 10 g of fresh bovine liver were homogenized with 0.05 M Tris-HCl buffer. After precipitation with acetone, centrifugation and dialysis, the partially purified asparaginase was prepared. Enzyme activity was measured by Nesslerization method. The protein concentration was determined by Bradford method. Then the enzyme activity was measured at different concentrations of L-asparagine as substrate and Michaelis-Menten and Lineweaver-Burk diagrams were awn. Essential oil extraction was performed by distillation using Clevenger apparatus. Then, the constituents of the essential oil were identified using GC/Mass spectrometry.

Results: Enzyme activity and specific activity were 55.39 U/ml and 11 U/mg, respectively. Km and Vmax for the enzyme were 0.437 mM and 0.0278 mM/min, respectively. The most constituents of M.officinalis were identified as caryophyllene, palmitic acid, alpha citral, triconetane, linolenic acid and thymol. By adding 20-100 μl of M.officinalis essential oil, Km and the maximum velocity were 0.76 mM and 0.021 mM, respectively. The Ki of the enzyme in presence of M.officinalis essential oil was also calculated to be 0.038 mM. Therefore, incubation of M.officinalis essential oil with the enzyme showed inhibitory effect by reducing the affinity and maximum velocity of the enzyme.

Conclusion: Since the enzyme L-asparaginase plays an important role in the treatment of cancers and also the reduction of acrylamide in the food industry, its inhibition by the essential oil of M.officinalis or its ingredients is recommended for further studies in pharmaceutical and industrial purposes.

Keywords: Essential oil, Kinetic parameters, L-Asparaginase, Lamiaceae, Partial purification

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Prevalence and Antibiotic Resistance of ESKAPE Pathogens Isolated from Blood Samples in Two University Hospitals in Tehran, Iran.

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Introduction: ESKAPE is an acronym for a group of life-threatening nosocomial pathogens; Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa and Enterobacter spp. Global efforts on controlling multiug-resistant (M) organisms have been hampered by their ability to escape antibacterial ugs. This study was conducted to determine the prevalence of ESKAPE pathogens and antibiotic resistance patterns isolated from blood specimens in two university hospitals.

Methods: A total of 412 bloodsamples were processed for the isolation and identification of ESKAPE pathogens following standard microbiological procedures. These isolates were subjected to antimicrobial susceptibility testing. Test for M, extended-spectrum β-lactamase (ESBL), metallo-β-lactamase (MBL), methicillin-resistant Staphylococcus aureus (MRSA), vancomycin-resistant Enterococcus (VRE) was done by the disk diffusion and E-test methods. In the case of VRE, molecular detection was done for vanA and vanB genes.

Results: The percentage distribution of Enterococcus faecium was 5.5%, S. aureus 33.4%, K. pneumoniae 33.0%, A. baumannii 8.6%, P. aeruginosa 18.6%, and Enterobacter aerogenes 0.9%. MRSA was 57.6%, and vancomycin resistance among Enterococcus faecium was 20%. ESBL- and MBL-producing K. pneumoniae were 16.1%, and 8.1%, A. baumannii 10.3% each and P. aeruginosa 10.7% and 8.3%, respectively. Linezolid was the ug of choice for VRE. Ampicillin-sulbactam was most useful against A. baumannii apart from polymyxins, whereas piperacillin-tazobactam was effective against other Gram-negative bacteria. VanA gene was detected in all the VRE isolates.

Conclusion: This study estimates the burden of the ESKAPE organisms and their antimicrobial resistance pattern in a hospital setting. A high percentage of ug resistance was noted; hence antimicrobial resistance surveillance targeting ESKAPE pathogens should be incorporated into the infection control policy throughout Iran.

Keywords: extended-spectrum β-lactamase, ESBL, ESKAPE pathogens, metallo-β- lactamase, MBL, methicillin-resistant Staphylococcus aureus, MRSA, vancomycin-resistant Enterococcus, VRE

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The protective effect of gamma oryzanol on lipopolysaccharide-induced oxidative stress and inflammation in adult mice liver

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Introduction: Rice (Oryza sativa L.), the main food source for more than half of humankind, is rich in phytochemicals and antioxidants with several biological activities. Among these compounds, gamma oryzanol (ORY), extracted from rice bran oil, exhibits both antioxidant and anti-inflammatory properties. The purpose of this study was to evaluate the protective effects of ORY on hepatic oxidative damage induced by systemic lipopolysaccharide (LPS) in adult male mice.

Methods: Adult male BALB/c mice (n=36) intraperitoneally (i.p.) received either LPS (0.75 mg/kg/day) or saline for a week. Meanwhile, animals were supplemented with ORY (100 mg/kg/day, gavage) or vehicle for 2 weeks (a week before injecting LPS and a week co-treated with LPS). After treatment, animals were sacrificed and the markers of liver injury including ALT and AST were evaluated in blood samples, in addition to the measurement of oxidative stress and inflammatory markers including lipid peroxidation (A), tumour necrosis factor alpha (TNF-α), interleukin 1 beta (IL-1β), interleukin 6 (IL-6) and nuclear factor kappa B (NF-κB) in hepatic tissue.

Results: Systemic LPS injections induced oxidative stress in liver tissue of treated animals, characterized by the increased A, with significantly decreased catalase and total free thiol. Besides, the serum levels of ALT and AST increased compared to the control group. These findings were accompanied by the increased hepatic expression levels of IL-6, IL-1β, TNF-α, and NF-κB. Furthermore, pathological evaluation of tissues exhibited that LPS induced microvesicular steatosis. Interestingly, ORY supplementation for two weeks could reverse the mentioned deficits induced by LPS.

Conclusion: In summary, our results demonstrate that LPS-induced hepatic damage can be mitigated by ORY supplementation in adult mice. These findings support the idea that natural products can be beneficial against hepatotoxicity.

Keywords: hepatotoxicity, natural products, oxidative stress

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Association between the expression levels of microRNA-101, -103, and -29a with Autotaxin and Lysophosphatidic Acid Receptor 2 expression in gastric cancer patients

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Introduction: Gastric cancer (GC) is regarded as the most prevalent malignancy with the high mortality rate, worldwide. However, Gastroscopy, a biopsy of suspected sample, and detecting CEA, CA19-9, and CA72-4 are presently used, but these diagnostic approaches have several limitations. Recently, microRNAs as the most important member of non-coding RNAs (ncRNAs) have received attention; recent evidence demonstrates that they can be used as the promising candidate biomarkers for GC diagnosis. We aimed to investigate the association between the microRNA-29a, -101, and -103 expression and autotaxin(ATX) and lysophosphatidic acid receptor 2(LPA2) expression in GC patients. Material &

Methods: The present study was conducted on 40 paired samples of primary GC tissue and adjacent non-cancerous tissue. The gene expression levels of miR-101, -103, -29, ATX, and LPA2 were analyzed by quantitative reverse-transcription PCR (qRT-PCR). Besides, the protein levels of ATX and LPA2 were evaluated using western blot.

Results: The expression levels of miR-29 and miR-101 were significantly lower (p.value<0.0001), but the miR-103 and LPA2 were significantly higher in gastric tumor samples compared to the corresponding non-tumor tissues (p.value<0.0001.

Conclusion: It seems, that determining the expression level of miR-101, -103, -29, as the novel diagnostic biomarkers, have diagnostic value to distinguish GC patients from healthy individuals.

Keywords: MicroRNA, Gastric Cancer, Diagnostic Biomarker, Autotaxin, lysophosphatidic acid receptor 2

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The potential of the CCL1 gene as a therapeutic capacity factor in Multiple Sclerosis disease.

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Abstract Multiple sclerosis (MS) is a disabling autoimmune disease of the central nervous system. The impaired function of immune cells causes them to overwhelm the myelin sheath of nerves, leading to nerve demyelination and eventual nerve deterioration. The chemokine CC motif ligand 1 (CCL1), released from several types of immune cells, acts selectively through the CC motif chemokine receptor 8 (CCR8). The presence of this receptor in white blood cells, such as regulatory T cells (Treg), supports the role of CCL1 in immune regulation. In fact, CCL1 is one of the major Treg-attracting chemokines, and this action supports its role in autoimmunity. The aim of this study was to inquire about the effects of the potential microRNAs (miRs) on the 3'UTR of the CCL1 gene through MS disease. To achieve this goal, the influential miRs obtained from the HMDD database were analyzed in the miRdSNP database to identify the relationship between CCL1 gene and associated Single Nucleotide Polymorphism (SNP) in MS disorder. The miRNASNP database also searched for the targeted mRNA gain or loss. Moreover, the Kegg database was studied to find the possible related pathways to MS disorder. The results showed that SNP:rs3136682 could change the function of miR-106a, founded on the CCL1 3'UTR region, which is involved in the migration of leukocytes. This miRNA, affects out breaking the MS disorder and might be effective in regulating the expression of the CCL1 gene. The study concluded that rs3136682 mutation decreases the binding of has-miR-106a to the CCL1 3'UTR region, resulting in an increase in CCL1 expression. At the same time, it seems that the overexpression of CCL1 abate the migration of leukocytes and inflammation. Therefore, this data identifies the hsa-miR-106a as a potential therapeutic biomarker for Multiple Sclerosis.

Keywords: MS, CCL1, Chemokine, T Cell, MicroRNA, SNP

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The effect of thyroid hormones on central nervous system development

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Hormones play an essential role in the development and differentiation of body tissues. One of these important hormones is T3 (triiodothyronine) and T4 (tetraiodothyronine), which are from the family of thyroid hormones and are secreted from the thyroid gland. They play an important role in the development and differentiation of the central nervous system of the fetus and adult in such a way that it affects brain differentiation processes such as myelination, axon and dendrite growth, and synaptogenesis. Deficiency of these hormones in the neonatal and fetal period leads to cretinism, which is retardation. It leads to mental retardation and deafness. T4 is the dominant form and T3 is its active form. In this case, T4 is converted into T3 form by the deiodinas enzyme in body tissues, including the brain. Astrocytes and tanycytes in the brain convert the T4 form to T3 by expressing deiodinas2. Hormone receptors Thyroid cells are inside the nucleus, which changes the expression of genes when the hormone binds to the receptor. It is concluded that any deficiency and change in the amount of thyroid hormones or disorder in the thyroid gland causes irreparable damage in the development and neurogenesis of the fetus and adult, and it can be prevented by examining the effect of these hormones on the brain and nervous system. Treated neurological and neurological disorders.

Keywords: T3 hormone, T4 hormone, deiodinas enzyme, central nervous system

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Quercetin targeted delivery with a pH-responsive agarose-based nanocarrier to treat breast cancer

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Quercetin (QC) has long been used in treating various cancers, especially breast cancer. Yet, using quercetin as a free drug is challenging due to low sustainability, poor solubility, and lack of target tissue recognition. In this study, a pH-sensitive nanocarrier was synthesized using agarose (AG) as a polysaccharide and polyvinylpyrrolidone (PVP) as a biocompatible polymer. Hydroxyapatite nanoparticles (HAP) were also incorporated into the fabricated pH-responsive platform, improving loading efficiency. A comparison of drug release in pH=7.4 and pH=5.4 during 96 hours confirmed the pH-sensitive feature of the nanocarrier. FTIR analysis was used to investigate the chemical bonds and the presence of components in the nanocomposite. FESEM images demonstrated the appropriate dispersion and homogenous spherical surface of the nanocarrier. The zeta-potential study confirmed the stability of nanocarriers. MTT assay analysis was used to assess the level of induced toxicity on the MCF-7 cells treated by the nanocarrier. Overall, the results of the present study showed that the quercetin-loaded pH-sensitive AG/PVP/HAP platform is a promising option to ameliorate constraints associated with using quercetin as an anti-cancer drug, opening a new avenue toward targeted delivery of quercetin to tumor cells with minimal damage to normal neighboring cells.

Keywords: Breast cancer, PH sensitive drug delivery, Quercetin, polyvinylpyrrolidone, Hydroxyapatite nanoparticles

A-10-1707-1

Increased peripheral NLRP3 gene expression is associated with the reduced duration of rapid eye movements sleep and sleep continuity in chronic insomnia patients

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Introduction: NLRP3 inflammasome is among the main activators of inflammatory cytokines that can play a critical role in CNS physiopathology as a proinflammatory mediator. In this regard, studying the correlation between aspects of sleep structure and expression of NLRP3 inflammasome markers in patients with the difficulty in initiating and/or maintaining sleep, is warranted. Here we measured the expression of NLRP3 inflammasome components in peripheral blood mononuclear cells (PBMCs) and also association between them and polysomnography parameters in chronic insomnia patients.

Methods: 22 patients with chronic insomnia disorder (6 males, mean age 41.7 ± 11.4 years, range 19-65) were identified based on Pittsburgh Sleep Quality Index (PSQI) and full-night videopolysomnography (V-PSG). Furthermore, 22 healthy individuals (8 males, mean age 42.3 ± 12.1 years, range 21-63) were selected as a control group based on PSQI.The inflammasome activation was evaluated using real time PCR of NLRP3, ASC, and Caspase1.

Results: We found that patients with chronic insomnia had significant higher gene expression levels of NLRP3, ASC, and caspase-1 in PBMC compared to controls. Furthermore, the results of correlation analysis indicated that NLRP3 inflammasome gene expression had a significant negative correlation with REM sleep duration ($p < 0.05$, $r = -0.615$) and sustained sleep efficiency ($p < 0.05$, $r = -0.641$).

Conclusion: This evidence suggests that NLRP3 inflammasome is involved in the pathogenesis of the sleep disorders. Based on this results, inhibitors of the NLRP3 inflammasome may be promising therapeutic agents in sleep deprivation and sleep fragmentation.

Keywords: Chronic insomnia, NLRP3 inflammasome, REM sleep

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Investigating the relationship between oxidant factors and missed miscarriage in pregnant women referred to Assalian Hospital in Khorram Abad

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Introduction: Abortion refers to the termination of pregnancy before the 20th week of pregnancy or birth with a weight of less than 500 grams. Forgotten abortion is called this because of the absence of symptoms of other abortions, such as bleeding and abdominal pain. The diagnosis of forgotten abortion is made when there is no heartbeat of the fetus during the examination. Ultrasound evidence of miscarriage can include an empty gestational sac with a size of 25 mm or more or a fetal bridge of 7 mm or more or a fetus without cardiac activity.

Methods: In order to conduct the research, 28 pregnant women with a gestational age of 6-14 weeks who were candidates for legal termination of pregnancy due to a missed abortion confirmed by two ultrasounds. After explaining the objectives of the research to them and obtaining informed consent, they will voluntarily enter the research and be included in the subject group. 5 cc of venous blood was taken from each of the research samples and will be sent to the biochemistry laboratory to measure the oxidant compounds and the level of oxidant factors was investigated. **Results:** The results of the research indicated that the level of oxidant factors increases in the blood of people who have had a forgotten abortion.

Keywords: pregnancy, abortion, forgotten abortion, oxidants

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Improving the antibacterial performance of bacterial cellulose using carbon structure for wound dressing

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Bacterial cellulose has been taken as an alternative to conventional dressings today. However, bacterial cells alone do not have antibacterial properties. Accordingly, in this study, by adding quantum carbon nanoparticles and copper nanoparticles that have antibacterial properties, they try to increase the performance of this nanobiocomposite. Scanning electron microscopy (SEM) analysis was performed to investigate and form structures in the cellulosic layer. Various infrared (FTIR) analyses and light dynamic subtraction (DLS) were performed on the nanosystem. Measurements No growth by disk method containing two bacteria Staphylococcus aureus and Escherichia coli against the antibacterial properties of mineral quantum carbon nanoparticles and compared with antibiotic samples in order to determine cell growth against carbon nanoparticles, copper was performed in vitro. The results showed that this wound dressing, which is produced for the first time, can be an alternative to traditional methods.

Keywords: Bacterial cellulose, Wound dressing, Carbon quantum dot, and Anti-bacterial

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Evaluation of cytotoxic properties of co-glycolic acid polylactic nanoparticles (PLGA) loaded with Kambucha) Auricularia auricular (extract against human ovarian cancer cells (A2780)

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Cancer is progressing rapidly around the world. So far, nano-therapy strategies have been designed to increase the effectiveness of cancer treatment by using nano-based drugs to improve the harmful effects of chemotherapy. Nanotechnology has this capability to increase the selectivity and power of chemical, physical, and biological approaches causing cancer cell death, while minimizing lateral toxicity. Kambucha is an abundant natural source of glucuronic acid. Due to the presence of glucuronic acid, it not only prevents cancer cells but also stops the growth of cancer cells. Kambucha tea has anti-tumor properties due to its polyphenols content. In this study, the cytotoxic effects of PLGA nanoparticles loaded with kambucha extract were evaluated using MTT methodCancer is progressing rapidly around the world. So far, nano-therapy strategies have been designed to increase the effectiveness of cancer treatment by using nano-based drugs to improve the harmful effects of chemotherapy. Nanotechnology has this capability to increase the selectivity and power of chemical, physical, and biological approaches causing cancer cell death, while minimizing lateral toxicity. Kambucha is an abundant natural source of glucuronic acid. Due to the presence of glucuronic acid, it not only prevents cancer cells but also stops the growth of cancer cells. Kambucha tea has anti-tumor properties due to its polyphenols content. In this study, the cytotoxic effects of PLGA nanoparticles loaded with kambucha extract were evaluated using MTT method.

Keywords: Co-glycolic acid PLGA polylactic nanoparticles, Kambucha extract, Toxicity, Ovarian cancer

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A new method of chemotherapy by nano-drugs

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Breast cancer is one of the most common cancers in women. Cisplatin is one of the conventional drugs used in chemotherapy which has a potent antitumor function. However, due to the dangerous side effects, including the damage to the DNA of the normal cells, its clinical use is limited. The aim of this study was to prepare and characterize nanoliposome containing cisplatin. We optimized liposome formulations through the modification of the proportion of SPC80 (soybean phospholipids with 75% phosphatidylcholine) and cholesterol content. Then, novel PEGylated liposomal formulations containing SPC80: cholesterol: DSPE-mPEG (at ratios of 85:10:5) were designed and developed to serve as a therapy to achieve more improved pharmaceutical efficiency. Zeta Sizer showed that PEGylated nanoliposomes had a mean diameter of 119.7 ± 2.1 nm, a zeta potential of -26.03 ± 1.34 mV, and entrapment efficiency of $96.65 \pm 3\%$. The optimum formulations represented sustained, thermo-sensitive release, and augmented cellular uptake. The cytotoxic effect of the liposomal drug was higher than the free medication drug confirming the efficiency of cellular uptake. This study suggests that nanoliposome-loaded cisplatin plays a vital role in improving drug efficacy and the reduction of dosage.

Keywords: breast cancer, chemotherapy, cisplatin, nanoliposome

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Evaluation of the effect of Daunorubicin on HNF4alpha protein by molecular docking method

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Introduction: Daunorubicin is an anthracycline antineoplastic antibiotic with therapeutic effects similar to those of doxorubicin. Daunorubicin exhibits cytotoxic activity through topoisomerase-mediated interaction with DNA, thereby inhibiting DNA replication and repair and RNA and protein synthesis. In this study, we try to investigate the effect of this drug binding to the protein HNF4alpha Investigate the interaction between this protein and the drug by molecular docking

Methods: In this descriptive-analytical project, we first downloaded the most suitable three-dimensional structure of HNF4alpha protein in terms of resolution and number of suitable chains from the uniprot site in pdb format. We see some specifications of this protein below. This protein has 5 chains A, C, G, E, I was. resolution =3.70A Then, protein chains were examined using Chimera software. The most suitable chain was c chain, which had more amino acids than other chains, and the largest protein chain was HNF4alpha. Through this software, water molecules and all We removed the solvents from this chain and hydrogen ions and charge bar were added to the chain and finally saved in pdb format in the next step, we downloaded the structure of Daunorubicin from Pubcheem site in SDF format. The information about Daunorubicinwas as follows: Molecular formula: $C_{27}H_{29}NO_{10}$ to perform the docking process, pyrx software was used. In this software, after entering the protein as a receptor and the drug Daunorubicin as a ligand, we obtained the binding site through the Deepsite site, the specifications of which were as follows: Center c= 33.92 Center y=-10.29 Center z=30.23

Result: After docking with Pyrex software, 10 models were suggested, the first three models being the best docking modes, the results of which were obtained in the table below model Binding affinity kcal/mol Rmsd 1 -6.4 kcal/mol 0.00 2 -6.4 kcal/mol 2.985 3 -6.2 kcal/mol 2.832

Keywords: Daunorubicin, HNF4alpha, docking

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Cancer vaccines as a targeted immunotherapy approach for breast cancer: an update of clinical evidence

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Page | 607

Introduction: Breast cancer (BC) is the first common neoplastic malignancy and the second leading cause of death in women worldwide. Conventional treatments for BC are often associated with severe side effects and may even lead to late recurrence. For this reason, in recent years, cancer immunotherapy (e.g. cancer vaccines), a novel approach based on the specificity and amplification of acquired immune responses, has been considered as a potential candidate in particular to treat metastatic BC. Areas covered: In this review, we summarize and discuss the recent development of therapeutic vaccines for BC, use of specific BC cellular antigens, antigen selection, and probable causes for their insufficient effectiveness. Expert opinion: Despite development of several different BC vaccines strategies including protein/peptide, dendritic cell, and genetic vaccines, until now, no BC vaccine has been approved for clinical use. Most of the current BC vaccines themselves fail to bring clinical benefit to BC patients and are applied in combination with radiotherapy, chemotherapy, or targeted therapy. It is hoped that with advances in our knowledge about tumor microenvironment and the development of novel combination strategies, the tumor immunosuppressive mechanisms can be overcome and prolonged immunologic and effective antitumor response can be developed in patients.

Keywords: Cancer immunotherapy, DNA-based vaccine, breast cancer, dendritic cell vaccines, peptide-based vaccine.

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Effectes of Plant Kandall Mountain (Bilhar) (Dorema aucheri) in Diabetes and Oxidative stress in Patients with type 2 Diabetes.

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Introduction: The aim of this study was to investigate the Effect of Dorema aucheri (Plant Kandall Mountain) (Bilhar) in Diabetes and Oxidative stress in patients with type 2 Diabetes.

Results: After 6 weeks (45 days), Dorema aucheri powder induceda significant 6.8% and 31.2% reduction in FBS, 9.1% and 23.7% reduction in TC, 10.2 % and 25.6 % reduction in TG, 18.9 % and 31.9 % reduction in ALT, 13.2% and 29.2 % reduction in AST, 13.6% and 35.3 % reduction in LDL-C, 11.6% and 23.4 % reduction in urea and 13.3 % and 18.4 % reduction in creatinine , respectively, in group 2 (100 mg capsules) and 3 (capsules , 500 mg) compared with the beginning of the study were observed (P<0.05) .changes in total protein and albumin concentration of uric acid in any groups also was not significant (P> 0.05). In Group 3 significantly decreased in 7.8% in systolic blood pressure of 7.7% in diastolic blood pressure, and 1.3% by weight patients compared with the beginning of the study were observed (P<0.05). Serum HDL-C in the intervening period in Group 2 and Group 3 significantly to the 11.7% and 23.2% higher than the control group (P <0.05). In the present study in the intervening period the Group 2 and Group 3, respectively, 17.3%, and 37.5% significant reduction in the ratio of triglycerides to cholesterol-HDL (atherogenic index of plasma) had (P <0.05).

Conclusion: The findings Administration of Dorema aucheri powder could be improving and reducing blood sugar and blood fats (lipid profiles) and as well as lower blood pressure and total antioxidant capacity and Antioxidant Gap, in patients with type 2 diabetes should have a positive impact.

Keywords: Type 2 diabetes, blood sugar, blood lipids, total antioxidant capacity, Antioxidant Gap, hemoglobin A1C and Dorema aucheri (Bilhar)

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The Effect of Continuous Aerobic Exercise with Low Carbohydrate Diet on the Serum Immunoglobulins G and M among Overweight Adult Men

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Introduction: The goal of this research was determine the effect of Continuous aerobic exercise with low carbohydrate diet on immunoglobulins G and M levels in adult men with overweight.

Methods: 30 men with age average 36-50 and BMI between 25-30 Kg/m2 were selected and divided in three groups with 10 persons randomly. Blood samples were collected of each group before induction of exercise and diet from brachial vein. The diet with limitation of carbohydrate was applied for 8 weeks. Continuous aerobic exercise performed for 8 weeks and 3 sessions in a week. In the following, the second blood samples were collected after 8 weeks. At the end by using ELISA method, Pars Azmon, the levels of immunoglobulins were measured. The level of significance was set at $P \leq 0.05$.

Results: The results of this research revealed that 8 weeks continuous aerobic exercise with low carbohydrate diet was caused significant reduction in serum level of immunoglobulins G and M in adult men with overweight ($P < 0.05$).

Conclusion: So performing Continuous aerobic exercise accompanied by low carbohydrate diet causes suppression of the humoral immunity, one of most important parts of the immune system.

Keywords: Continuous aerobic exercise, diet limitation of carbohydrate, IgG, IgM.

Homocysteine intracerebroventricular injection induces apoptosis in the Substantia Nigra cells and Parkinson like behavior in rat

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Parkinson Disease is a degenerative disorder of the central nervous system. The motor symptoms of Parkinson's disease result from the death of dopamine-generating cells in the substantia nigra, a region of the midbrain; the cause of this cell death is unknown. Homocysteine (Hcy) is a non-protein amino acid. It is a homologue of the amino acid Cysteine. Elevated levels of homocysteine in plasma have been associated with a number of disease states. Hcy (2 μ mol / μl) was injected intracerebro ventricular (i.c.v) in rat, five days later, locomotor activity was measured with open field apparatus, also apoptosis was investigated in Substantia Nigra cells by immunohistochemical analysis. Hcy could decrease locomotor activities significantly in rats as well as it could induce apoptosis in Substantia Nigra cells. These results suggest that Hcy is a neurotoxic metabolite and may induce cell death in some nuclei in the brain. Parkinson Disease is a degenerative disorder of the central nervous system. The motor symptoms of Parkinson's disease result from the death of dopamine-generating cells in the substantia nigra, a region of the midbrain; the cause of this cell death is unknown.. Hcy could decrease locomotor activities significantly in rats as well as it could induce apoptosis in Substantia Nigra cells. These results suggest that Hcy is a neurotoxic metabolite and may induce cell death in some nuclei in the brain.

Keywords: Homocysteine, parkinson disease, locomotor activity, substantia nigra, immunohistochemistry.

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The interaction of Carotenoids (β-carotene) with lysozyme: Molecular dynamics and spectroscopic insights

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β -carotene is a carotenoid with a yellow-red color that is insoluble in water and very slightly soluble in edible oils. Because of its pro-vitamin A and antioxidant properties, -carotene consumption has been studied. When ingested in sufficient amounts, carotenoids are a group of natural pigments with numerous health advantages. B-carotene, in particular, has been demonstrated to protect against cancer, cardiovascular disease, and macular degeneration. Lysozyme is a class of enzymes (EC3.2.1.17) that catalyzes the hydrolysis of 1, 4--linkages between N-acetylmuramic acid and N-acetyl-D-glucosamine to breakdown the cell wall of Gram-positive bacteria. Lysozyme has long been employed as a preservative in the food sector for the long-term storage of vegetables, milk, fish, and meat. In the pharmaceutical industry, the enzyme is also employed in wound healing creams, eye drops, and anticancer treatments. UV–Vis spectroscopy, intrinsic fluorescence spectroscopy , thermal stability, kinetic methods, were used to investigate the effects of -carotene on the structure and activity of lysozyme. Fluorescence spectroscopy studies demonstrated that -carotene binding produced changes in lysozyme tertiary structure. Thermodynamic findings demonstrated that -carotene interacts with lysozyme by hydrophobic forces spontaneously. The circular dichroism spectral finding indicates that secondary structural alterations have occurred. The β -turn structure's content increased. β -carotene decreased the activity of lysozyme, according to kinetic characteristics.

Keywords: Keywords: β-carotene, lysozyme, fluorescence spectroscopy

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Ligation of caspase-9 to split luciferase domain and its expression study in E. coli

Apoptosis is a programmed and physiological cell death that involves extracellular and intracellular cascading signalling pathways and is essential for embryonic growth, destruction and regeneration of cellular structures, cellular homeostasis, and removal of damaged cells. The induction of apoptotic death results in the activation of members of the cysteine protease family (caspases) that break down the substrate at the carboxyl Asp site. Caspase 9, as a initiating caspase, is one of the key agents in the internal or mitochondrial pathway. Forms the active apoptosome complex. The family of apoptosis inhibitory proteins (IAPs) inhibits apoptosis by inhibiting the enzymatic activity of both initiating caspases and activating caspases. Bioluminescent systems are used as strong reporting analytical systems for biodegradation. They have special properties such as relatively high quantum efficiency and photon emission in a wide range of colours from green to red, and protein-protein interactions are important for studying the biological activity of cells. Studies are the interaction of two or more proteins. In this study, wild and mutant caspase 9 gene was ligated and cloned into luciferase fragments and their expression in E. coli host was evaluated. The recombinant proteins were then purified and their activity was measured after evaluating the purity of the proteins. The interaction of suitable recombinant proteins with complementary structures in the laboratory was evaluated.

Keywords: Apoptosis, Caspase 9, Luciferase, Bacterial expression, Purification

A-10-1421-1

Encapsulation of letrozole (femara) for the treatment of breast cancer

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Nano is currently being developed in all fields of medicine and the field, especially in this field. On the other hand, the eyes and the eyes of every one and more are removed from it. In general, the methods of treatment from chemotherapy, radiators, and other cases that are effective, are the same. Hence, they are looking for ways to reach the valleys. Encapsulation of anticancer drugs in medicine promises to solve many medical problems and cancer patients. The use of a drug delivery system is a helpful factor that allows a therapeutic substance to enter the body and by controlling the drug release agents, managing its speed, time and place improves its effectiveness. The aim of this study was to encapsulate letrozole for breast cancer to be one of the important achievements in drug delivery systems and new drug delivery systems in cancer treatment. In addition to increasing the efficiency and targeting drug delivery, the toxicity and side effects on healthy cells can be reduced by loading the drug in question or making it specially functionalized. In this study, acrylic base monomers were used to encapsulate letrozole.

Keywords: Breast Cancer ،Encapsulation ،Controlled drug release ،Letrozole ،Acrylate based polymer ،Mini-emulsion polymerization ،Nanostructure

Fisetin-loaded Grape-derived nanoparticles Improve Anticancer Efficacy in MOLT-4 cells

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Introduction: Fisetin (FIS) is a natural flavonoid with anti-proliferative and anti-apoptotic effects on different human cancer cell lines and can be considered a therapeutic agent for ALL treatment. However, FIS has little aqueous solubility and bioavailability, limiting its therapeutic applications. Thus, novel drug delivery systems are needed to improve solubility and bioavailability of FIS. Plant-derived nanoparticles (PDNPs) could be considered a great delivery system for FIS to the target tissues. In this study, we investigated the anti-proliferative and anti-apoptotic effect of free FIS and FIS-loaded Grape-derived Nanoparticles (GDN) FIS-GDN in MOLT-4 cells.

Methods: In this study, MOLT-4 cells were treated with increasing concentration of FIS and FIS-GDN and viability of cells were assessed by MTT assay. Additionally, cellular apoptosis rate and related genes expression were evaluated using flow cytometry and Real Time-PCR methods, respectively.

Results: FIS and FIS-GDN decreased cells viability and increased cells apoptosis dose-dependently, but not time dependently. Treatment of MOLT-4 cells with increasing concentrations of FIS and FIS-GDN considerably increased the expression of caspase 3, 8 and 9 and Bax level, and also decreased the expression of Bcl-2. Results indicated an increased apoptosis after increased concentration of FIS and FIS-GDN at 24, 48 and 72 hours.

Conclusion: Our data proposed that FIS and FIS-GDN can induce apoptosis and have antitumor properties in MOLT-4 cells. Furthermore, compared to FIS, FIS-GDN induced more apoptosis in these cells by increasing the solubility and efficiency of FIS. Additionally, GDNs increased FIS effectiveness in proliferation inhibition and apoptosis induction.

Keywords: Acute Lymphoblastic Leukemia, Apoptosis, Drug Delivery, Fisetin, Plant-derived Nanoparticles

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Total antioxidant capacity as a marker of severity of COVID-19 infection: Possible prognostic and therapeutic clinical application

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Page | 615

The pathogenesis of SARS-CoV-2 infection, causative pathogen of the known COVID-19 pandemic is not well clarified. In this regard oxidative stress is one of the topics that need to be investigated. Therefore, the present research was performed to explore the relationship between the oxidant/antioxidant system and COVID-19 exacerbation. Sera were collected from 120 patients with COVID-19 infection and 60 healthy volunteers as the control group. The patient group consisted of 60 cases with mild disease and 60 severely ill patients. Serum levels of total antioxidant capacity (TAC) and nitric oxide (NO) as well as serum activities of the two main antioxidant defense enzymes, superoxide dismutase (SOD) and catalase (CAT), were measured. TAC levels were considerably lower in patients compared with healthy individuals ($p < 0.05$) and also between patients with mild and severe diseases ($p < 0.05$). A rather decreasing trend was also found in NO concentration as well as SOD and CAT activity, though, the observed differences were not statistically significant ($p > 0.05$). These findings suggest that COVID-19 patients may be susceptible to depleted total antioxidant capacity. Moreover, showing such variations in blood samples of infected individuals could be considered as a predictive marker of COVID-19 severity.

Keywords: antioxidant enzyme, COVID-19, oxidative stress, TAC

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Review of gerobiotics and inflammaging

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Introduction: It is thought that inflammaging which is one of the leading causes of aging could be affected by unique strains of probiotics that can beneficially increase health span. Studies showed that gerobiotics could modulate cellular senescence and promote longevity.

Methods: A systematic review was performed for collecting evidence regarding the association between gerobiotic and inflammaging. Three databases of Pubmed, Scopus, and Web of science were systematically monitored, and eight appropriate articles were retrieved.

Results: Studies has been revealed that the use of gerobiotics is associated with reduced senescence markers like p16, p53 and reduced inflammation markers like p-p56, COX-2, p-FOXO3a and iNOS. Gerobiotics could also increase the number of mitochondria and muscle mass.

Conclusion: The literature reviewed proposes gerobiotics usage could modulate the inflammaging and alleviate age-related diseases and affect the quality of life by decreasing physiological aging processes.

Keywords: gerobiotic ،inflammaging ،health span

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Effects of thioridazine and perphenazine on the catalytic activity of human recombinant matrix metalloproteinase-9 (MMP-9)

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Abstract the extracellular matrix(ECM) is a critical regulator for neural network development and flexibility.The ECM stabilizes synaptic contacts, while its slit plays an active role in regulating flexibility.Matrix metalloproteinase9(MMP-9) is a member of a large family of zinc-dependent endopeptidases that can break down ECMs and multiple cell surface receptors,allowing reorganization at the synaptic and orbital levels.It is becoming increasingly clear that the regulated activity of MMP-9 is critical for development of the central nervous system (CNS).The MMP-9 can regulate sensory-mediated local circuit reorganization through its ability to control axonal routing , and myelination.Although MMP-9 dependent activation at specific synapses plays an important role in multiple flexibility mechanisms across the CNS, enzyme mediated activation plays a role in a number of neurodegenerative disorders,including traumatic brain injury multiple sclerosis,and Alzheimers disease.This study aimed to investigate the effects of thioridazine and perphenazine as two drug which are prescribed in defferent neural disease on catalytic activity of MMP-9 enzyme. For this purpose,recombinant MMP-9 gene expressed by E.coli BL21(DE3) cells having PET21a-MMP-9.After producting and prefication of the enzyme ,protease activity of MMP-9 was measured in the presence and absence of drugs by using casein as substrate .Results confirmed both of the drugs could inhibit catalytic acivity of the enzyme with different efficiency.Evaluated IC50 values for thioridazine and perphenazine were calculated as 18 and 12 micromolar respectively.Enzyme activity assay in the presence of increasing concentration of inhibitors showed inhibition pattern is competitive for perphenazine and is mix type of inhibition for thioridazine.Molecular docking analysis also was used to investigate the possible

Keywords: Keywords: Thioridazine-Perphenazine-Matrix Metalloproteinase 9 MMP-9))

Effects of Oleracein E and Oleracein L from Portulaca oleracea on Cell Survival, Antioxidant and Antidiabetic Efficacy on β-TC-6 Pancreatic Cell Line

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Page | 618

Oleracein E and oleracein L are the major bioactive isoquinoline alkaloids in Portulaca oleracea. Here, the effects of these alkaloids on cell survival, the activity of superoxide dismutase, catalase, and glutathione peroxidase, factors associated with oxidative stress such as malondialdehyde and dityrosine, carbohydratehydrolyzing enzymes α-amylase and α-glucosidase, insulin secretion levels and glucose uptake ability were investigated. The β-TC-6 pancreatic cell line was incubated with oleracein E and L at concentrations of 0, 50, 100, 200 and 400 µM and tested separately. All biological assays were based on UV/Vis spectrophotometric and/or high performance liquid chromatography methods. Oleracein E and L at 100 µM concentrations increased antioxidant activity of enzymes. In addition, the total oxidative damage biomarkers ablated significantly in 50 and 100 µM concentrations, which could be due to the positive effect of antioxidant enzymes on biomarker level. Similar inhibition properties were shown by α-amylase and α-glucosidase and consequently, the investigated alkaloids could exhibit the high hypoglycemic effect. Furthermore, glucose uptake and insulin secretion were enhanced by these compounds. Hence, these alkaloids have considerable antioxidant and potential hypoglycemic effects on the pancreatic cell line and they could be suggested for future studies in the treatment of diabetes mellitus.

Keywords: Antioxidant enzyme, antidiabetic indicators, oxidative stress levels, oleracein E, oleracein L, β-TC6 cell line

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Designing modified nanocarriers containing selenium nanoparticles extracted from the Lactobacillus acidophilus and their anticancer properties

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Page | 619

Introduction: This study investigated the new design imaging nanocapsules (NCs) gallium@deferoxamine/folic acid/chitosan/polyaniline/polyvinyl alcohol (Ga@DFA/FA/CS/PANI/PVA) containing Moras nigra extract and selenium produced of Lactobacillus acidophilus for applying on cancer cells. Ga uses as an anti-tumor substance by binding to PVA, which has a very high absorption rate. Also, PANI is a conductive agent in the drug, and it can work well together with CS/PANI. Different antibiotics test on a variety of microbes. They investigated the resistance of NCs to other systems. MIC/MBC tests conduct. In clinical applications, NPs have selective and rapid accumulation in the target tissue, targeted, effective transfer of therapeutic agents, biocompatibility and safety, and non-production of toxic by-products.

Methods: PVA (Mw=72000, 99%, Hydrolyzed), chitosan with medium molecular weight (75–85% degree of deacetylation), polyvinyl alcohol, and polyaniline purchase from Sigma-Aldrich Co. (USA). Ga, Tween 80, and Gelatin are obtained from Merck Company (Germany). M. nigra was purchased from a market selling herbal drugs in Germany.

Results: The concentration of Ga@DFA/FA/CS/PANI/PVA (6 ml), pH=5.5, buffer (20 ml), suitable solvent and surfactant (acetone and Tween 80), and time of reaction (3 h) was the best condition. All sections confirmed what is find here using SEM, XRD, ZPS, EDX, FT-IR, UV-Vis spectra, and cytotoxicity on cancer cells. The experimental section is optimizing with the RSM method. The relationship between buffer and DFA is directly related to NCs. In vitro (MTT assay) was examined. According to ZPS data, NCs are compatible with the human body. Antibiogram testing on NCs killed Pseudomonas aeruginosa bacteria. q

Conclusion: We created Se-NPs that bind to metals and reduce the risks posed by the bacterium L. acidophilus. Ga with this technique can do less harm to the body.

Keywords: Imaging contrast agent, nanoparticles, Response surface method, Lactobacillus acidophilus, Selenium

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Renal, Cardiac, Neurological, Cutaneous and Coagulopathy Manifestations of Covid-19 after Recovery

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Page | 620

Introduction: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) caused the novel global coronavirus (COVID-19) disease outbreak. Its pathogenesis is mostly located in the respiratory tract. However, other organs are also affected. Hence, realizing how such a complex disturbance affects patients after recovery is crucial. Regarding the significance of control of COVID-19-related complications after recovery, the current review has designed to evaluate the cellular and molecular mechanisms linking COVID-19 to significant long-term signs including renal and cardiac complications, cutaneous and neurological manifestations, as well as blood coagulation disorders.

Methods: Online electronic databases including PubMed, Google scholar, Web of Science, Embase, and SCOPUS were searched to identify initial studies until February 2022.

Results: This virus can directly influence on the cells through Angiotensin converting enzyme 2 (ACE-2) to induce cytokine storm. Acute release of IL1, IL6 and plasminogen activator inhibitor (PAI-1) have been related to elevating risk of heart failure. Also, inflammatory cytokines like IL-8 and Tumor necrosis factorα (TNF- α) cause the secretion of von Willebrand factor (VWF) from human endothelial cells and then VWF binds to Neutrophil extracellular traps (NETs) to induce thrombosis. On the other hand, it can damage the blood–brain barrier by increasing its permeability and subsequently enter into the central nervous system (CNS) and the systemic circulation. Furthermore, SARS-induced ACE2-deficiency decreases desArg9-BK degradation in kidneys to induce inflammation, thrombotic problems, fibrosis and necrosis. Notably, the angiotensin II-angiotensin II type 1 receptor (ANGII-AT1R) binding causes an increase in aldosterone and mineralocorticoid receptors on the surface of dendritic cells (DC) cells, leading to recalling macrophage and monocyte into inflammatory sites of skin.

Conclusions: All the pathways play a key role in the pathogenesis of these disturbances. Nevertheless, more investigations are necessary to determine more pathogenesis mechanisms of the virus.

Keywords: Blood Coagulation Disorder, Cardiac Disease, COVID-19, Kidney, Mechanisms, Neurological Disorder.

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Introduction of effective medicinal plants in the treatment of inflammatory eye diseases from the perspective of traditional Iranian medicine

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Page | 621

From the traditional point of view, the eye has several layers. There are four types of eye diseases: one is simple malaise, the second is substance abuse, the third is the Separation of eye layers such as injuries and inflammation, and the fourth is combined diseases such as eye protrusion. There are four different types of treatment. In this article, we review the treatments for inflammation in Iranian medicine. In different types of inflammation, different treatments have been described, some of which are herbal. Sometimes these treatments are to reduce pain and sometimes to reduce inflammation, we found the herbs that were recommended to reduce inflammation from the books of traditional Iranian medicine, such as Akbari medicine and Khwarazmshahi reserve, and searched in Google Scholar and PubMed. A number of plants have already been studied and proven to be useful. Saffron plant had the highest frequency in inflammation prescriptions, this plant has been studied in different doses in the laboratory, and the positive effect of this plant for inflammation of different layers of the eye has been proven orally. The benefit of aloe vera in the form of herbal drops for inflammation of the outer layers of the eye has been proven. Gum arabic and violet have the following ranks of Repetition in prescriptions, the anti-inflammatory properties of these plants have been studied in other diseases, it is recommended to be checked for inflammatory eye diseases as well.

Keywords: Inflammation, Traditional Iranian medicine, Medicinal plants, Saffron, Aloe vera.

A-10-1355-1

Inhibition of EZH2 as a tumor suppressor expression through Nano formulated Paclitaxel in combination with Curcumin

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Lung cancer is the leading cause of cancer-related deaths, worldwide. Non–small cell lung cancer is the most prevalent lung cancer subtype. Up-to-date findings show the functions of the enhancer of zeste homolog 2 (EZH2) in cell proliferation, apoptosis, and senescence and its important role in cancer initiation, progression, metastasis, and drug resistance. EZH2 is an enzymatic catalytic subunit of Polycomb repressive complex 2 (PRC2) that can alter gene expression as a mediates gene silencing, by trimethylation of Lys-27 in histone 3 (H3K27me3). Activating EZH2 mutations or aberrations of the SWI/SNF complex can lead to aberrant histone methylation, oncogenic transformation, and a proliferative dependency on EZH2 activity. Paclitaxel (PTX) is a tricyclic diterpenoid compound that promotes the assembly of tubulin into microtubules and prevents the dissociation of microtubules, blocking cell cycle progression, preventing mitosis, and inhibiting the growth of cancer cells. However, owing to its poor solubility and non-selective toxicity, it's serious problems. To solve these problems, we decided to combine PTX with curcumin (CUR) by loading in PEGylated niosome nano-particles (PEG-NPs), as a novel effective method in chemotherapy. CUR is a natural promising anticancer drug that has antitumor effects in many tumors. Drugs nano formulated in PEG-NPs through an applying thin-film hydration assay. characterization of the PEG-NPs by applied DLS, FTIR, TEM, and FE-SEM techniques. Also, the MTT-Assay evaluated the cytotoxic effect of this agent, and mir-EZH2 expression in A549 cell lines, which was amplified by primers was analyzed using qRT-PCR. The average particle sizes of PEG-NPs were less than 200 nm. According to the results, the EZH2 expression level highly decreased in a PTX-CUR/PEG-niosome relative to the free form of PTX-CUR ($p < 0.05$) and had the most effect on concentrations 0.005:5.

Keywords: EZH2 - Paclitaxel - curcumin - lung cancer

Sickle cell disease and COVID-19: Susceptibility and severity

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We surveyed published papers and an intrenational sickle cell disease (SCD) registry to detect suscetibility and clinical course of coronavirus disease 2019 in SCD patients. Covid-19 presentation was mild in children and moderate in many SCD adults. Regarding increased comorbidities with age, it seems severe Covid-19 to be more common in older SCD patients. Although the overal outcome of Covid-19 was favorable in SCD children, a high rate of pediatric intensive care unites admission shoule be considered in managing these patients. To explain Covid-19 outcome in SCD patients, the possible benefits of hydroxyurea therapy could be considered. The obtained results should be interpreted, considering low cases from sub-Saharan people, younger age of SCD patients compared to general population, a bias toward registry of the more severe from of disease, the effect of pre-existing comorbidities with multisystem organ damage, and the role of health socio-economic determinants.

Keywords: Covid-19, Hb F, hydroxyurea, hypercoagulation, sickle cell disease, splenectomy

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Diagnostic Performance of Blood Test profile for Predicting In-hospital Mortality in COVID-19 Patients; Experience from Yazd, Iran

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Page | 624

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Identifying clinical features or scoring system to predict in-hospital mortality in patients with Covid-19 or similar viral infectivity can be of great value for health decision makers. Our goal was to identify demographic and laboratory differences in patients with COVID-19 so that we could provide a diagnostic model that predicts which patients will have severe problems and will require intensive care in the future.

Keywords: COVID-19, Blood profile, Biochemical tests, Hematology tests, Yazd

A glance assessment illustrates a challenging hypothesis | If it becomes a fact, who will be in charge of this negligence?

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Introduction: Is it possible to consider an absolute end to this pandemic? It has been almost four years since people tried to find an ultimate treatment for a well-known disease (Covid-19), and still, we are asking what is happening next. However, it is not fair to ignore those remarkable successes of scientists in restricting the complications caused by this global challenge. Among all those successions, various studies have been conducted on the association between Covid-19 disease and vitamin D deficiency in individuals. In this study, we try to examine the possibility of the aforementioned theory, in comparison with the Iranian health system's capacity when we are dealing to control the disease with all of our possessions and power.

Case Presentation: During this study, which lasted about four months, the samples of 180 patients were recorded, and according to the questionnaire, two separate groups were created. The first group was named Normal Control that Vit D results were estimated in the normal range during the period, and the second one was titled susceptible group, in which their Vit D reports were evaluated under the scale of the Normal Control group. Additionally, each group gathered based on 50 individuals and was also given their permission. Statistical studies have been done considering the ONE-WAY-ANOVA method, and the obtained observations are reported regarding SD and Mean parameters.

Conclusion: In Conclusion, the deficiency of essential vitamins such as vitamin D in our country (IRAN) is an undeniable fact for many years. If we accept the hypothesis of a direct link between the occurrence of Covid-19 and vitamin D deficiency, the main question is how many people might be infected due to simple ignorance, and how should the health system cope with this pressure again?

Keywords: 1,25-Dihydroxyvitamin D, Vitamin D Deficiency, Covid-19, SARS-CoV-2 virus

Construction of a eukaryotic DNA vector harboring a main oncogene of human Papillomavirus linked to small heat shock protein

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Introduction: Development of an effective therapeutic vaccine against human papillomaviruses (HPVs) is critical for the control of a variety of cancers such as cervical cancer. Among therapeutic HPV vaccines, DNA-based vaccine is of-interest strategy due to its safety, stability and ability to induce antigen-specific immunity. Among HPV proteins, E6 and E7 oncoproteins have been known as main target antigens for design of therapeutic DNA vaccines. Moreover, the potency of DNA vaccines could be increased using heat shock proteins (HSPs) as an adjuvant. In this study, a recombinant DNA vaccine candidate was constructed based on the linkage of E7 gene of HPV type 16 to mammalian small heat shock protein B1 (Hsp B1) gene.

Methods: HPV16 E7 and Hsp B1 gene sequences were obtained from the National Center for Biotechnology Information (NCBI), and synthesized in a cloning vector. The HspB1-E7 fusion gene was subcloned into the pcDNA3.1 eukaryotic vector using BamHI/NheI restriction enzymes. Then, the recombinant pcDNA3.1-HspB1-E7 vector was prepared by plasmid purification kit. Finally, its purity and concentration was assessed using NanoDrop spectrophotometry.

Result: The recombinant pcDNA3.1-HspB1-E7 vector was confirmed by digestion with BamHI/NheI restriction enzymes as the clear bands of ~ 975 bp for HspB1-E7 gene, and ~ 5427 bp for pcDNA3.1 (-) vector. The concentration and purity of the recombinant DNA vector was ~ 210 ng/ μL for 10 mL of culture and 1.86, respectively.

Conclusion: DNA construct encoding HspB1-E7 gene can be used as a therapeutic DNA vaccine candidate against HPV infection in near Future. Keywords: Human papillomavirus, E7, small heat shock protein, DNA-based vaccine

Keywords: Human papillomavirus, E7, small heat shock protein, DNA-based vaccine

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Molecular association between Huntington's disease and Schizophrenia based on GEO analysis

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Page | 627

Introduction: Huntington's disease (HD) is a neurodegenerative disease caused by the CAG repeat elongation of the Huntingtin gene (HTT), involving a complex network of pathogenic mechanisms. Schizophrenia (SC) is a serious mental disorder with a series of complex signs and symptoms that cause serious disabilities in adolescents. Schizophrenia has a strong genetic component with a heritability of about 80%, but there are also widespread environmental contributors and stressors associated with the disease's development and neuropathology. In this study, the relationship between SC and HD was investigated by GEO analysis with regard to circulating non-coding RNAs(ncRNAs) involved in their coincidence.

Method: we obtained the blood gene expression profiles of nine patients with HD, five with SC, and eight healthy individuals from the Gene Expression Omnibus (GEO) database under the accession number of GSE167630. Then the data was analyzed by R software. Finally, common ncRNAs were detected by mirPath v.3 database and string database, to understand molecular interactions and respective targets.

Result: we identified 32 ncRNAs that were differentially and chronically expressed in HD and SC samples (P-value < 0.05). Then mirpath v3 software was used for further functional analysis in the GO and KEGG databases. Axon guidance was chosen as the most common pathway between KEGG and GO, revealing that the ncRNAs of hsa-miR-3148, hsa-miR-1206, hsa-miR-4302, hsa-miR-4323, hsa-miR-3171, hsa-miR-890, hsa-miR-4263, hsa-miR-3180, hsa-miR-1912, and hsa-miR-556-5p were involved in axon guidance. These ncRNAs target 99 genes related to axon guidance.

Conclusion: it seems that there are common ncRNAs between HD and SC, which can role in the development and exacerbation of both diseases. These ncRNAs also play an important role in cellular signaling and intracellular metabolism in neurons and associated cells, especially axon guidance. These ncRNA can be reliable biomarkers for identifying and leveling both diseases.

Keywords: HD, SC, circulating non-coding RNAs, neurons, axon guidance

The efect amyloid beta on mir-98 and mir-27a expression in astrocytes isolated from C57BL/6J mice

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Introduction: Objective: Cholesterol homeostasis dysregulations can lead to aggregation of amyloid beta (Aβ) senile plaques in extracellular of neuron cells, causing neuronal death, memory deficits and eventually neurodegenerative disorder like Alzheimer disease. MiRNAs are small noncoding RNAs which can regulate gene expression. In this study the impact of amyloid beta (Aβ) on microRNAs expression participated in cholesterol trafficking and homeostasis via their target genes, ApoE and CYP46A1, has been investigated.

Methods: Astrocytes were isolated from newborn C57BL/6J mice brain, then cultured and treated with 0.5 µM amyloid beta (Aβ) to analyse expression levels of mir-98 and mir-27a by real time PCR method based on the IRNdb, TargetScan, and RNAhybrid softwares.

Results: In comparison to control, Aβ treatment group resulted in a significant increment in mir-27a and significant decrement in mir-98 expression level as ApoE and CYP46A1 regulators respectively.

Conclusion: ApoE and CYP46A1 expression level as targets of mir-27a and mir-98 respectively, change due to the alteration of their relevant MicroRNAs. Therefore, Aβ peptides can influence cholesterol homeostasis by exerting alteration in MicroRNAs expression. Furthere in vitro and in vivo studies are required to investigate the role of MicroRNAs in regulation of cholesterol homeostasis and potential usage of these biomarkers in future therapeutic approaches.

Keywords: APOE, CYP46A1, MicroRNA, Astrocytes, Amyloid beta

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Gastrointestinal, liver, pancreas, oral and psychological long-term symptoms of COVID-19 after recovery

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Introduction: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) caused the novel global coronavirus (COVID-19) disease outbreak in December 2019 and has resulted in a global pandemic. The pathogenesis of the disease is mainly located in the respiratory tract. However, other organs and tissues are also principally affected. Thus, understanding how such a complex multisystem disorder affects people's physical and mental health is crucial. Due to the importance of control and prevention of COVID-19-correlated long-term symptoms, the present review article has summarized what was currently known regarding the molecular and cellular mechanisms linking COVID-19 to important long-term complications including psychological complications, liver and gastrointestinal manifestations, oral signs as well as even diabetes.

Methods: Online electronic databases including PubMed, Google scholar, Web of Science, Embase, and SCOPUS were searched to identify initial studies until February 2022. The combination of MESH and non-MESH terms were used for the search.

Results: COVID-19 can directly affect the body cells through their Angiotensin converting enzyme 2 (ACE-2) to induce inflammatory responses and cytokine storm. The cytokines cause the release of reactive oxygen species (ROS) and subsequently initiate and promote cell injuries. Another way, COVID-19-associated dysbiosis may be involved in the GI pathogenesis. Moreover, SARS-CoV-2-mediated endoplasmic reticulum stress induces de novo lipogenesis in hepatocytes, which leads to hepatic steatosis and inhibits autophagy via increasing mTOR. In pancreas tissue, the virus damages beta-cells and impairs insulin secretion.

Conclusions: All the pathways mentioned above can play a crucial role to the pathogenesis of the disease and related comorbidities. However, more studies are needed to clarify the underlying mechanism of the pathogenesis of the new coming virus.

Keywords: COVID-19, Inflammation, Long-Term, Mechanisms, liver, diabetes

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P-tau Nuclear Translocation is Accompanied with Robust Neurodegeneration

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Introduction: Tauopathies are a class of neurodegenerative disorders common in tau protein abnormalities. Except for a small amount of tau in the nucleus and dendrites, tau is an axonal protein that attaches to and stabilizes microtubules. It has been recently shown that axonal tau translocates into a nuclear compartment in the tau-overexpressing cellular model resulting in neuronal dysfunction. Yet, the fundamental mechanism underlying tau translocation pathogenicity remains uncertain.

Methods: Here we employed starvation stress in primary neurons and ssTBI (Single Severe Trumatic brain injury) in mouse brains as tauopathy models and studied the nuclear displacement of different P-tau epitopes (cis P-tau, AT8, and AT100 P-tau) at various time points by immunostaining and immunoblotting. We also examined p53 stabilization, neuron viability, and fibrillarin (nucleolar protein) during P-tau nuclear translocation.

Results: While all P-tau traveled into the somatodendritic compartment upon stress conditions, cis P-tau moves much faster than the other species. Interestingly, P-tau nuclear translocation was accompanied by profound p53 apoptotic stabilization and nucleolar dispersion. Moreover, cismAb effectively decreased neuron death upon P-tau nuclear accumulation.

Conclusion: Taken these observations together, our findings reveal that P-tau nuclear translocation resulted in p53-dependent apoptosis and neuron death in tauopathy models, reflecting neurodegeneration. This model may explain why nuclear P-tau is extremely neurotoxic and cis mAb efficient in revitalizing stressed neurons.

Keywords: nuclear translocation, nucleolar stress, p53, tauopathy, neurodegeneration

Soluble uric acid promotes LPS-induced endoplasmic reticulum stress markers, inflammation, and ROS production in human peripheral blood mononuclear cells

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Introduction: It has been of particular interest to unravel the exact role of alteration in uric acid (UA) levels in the context of inflammation since hyperuricemia is strongly associated with inflammatory disorders. Recently, the endoplasmic reticulum (ER) stress pathway has been considered a possible mechanism linking hyperuricemia to inflammation. We aimed to examine the role of UA in the presence or absence of a second stimulus, LPS in human peripheral blood mononuclear cells (PBMCs), and analyzed ROS production as well as expression of ER stress markers; GRP78 and CHOP, and transcripts of inflammatory cytokines.

Methods: PBMCs were isolated using Ficoll gradient centrifugation from healthy volunteers. Cell viability was measured by MTT assay. PBMCs were treated with an increasing concentration of soluble UA (0, 5, 12, and 20 mg/dl) for 20 h, followed by the addition of 100 ng/mL of LPS or vehicle for another 4 h. Real-time-PCR was performed to investigate the mRNA expression of GRP78, CHOP, TNF-α, IL-1β, and IL-6, and western blot was used to investigate the protein levels of GRP78 and CHOP. Finally, intracellular ROS production was determined using fluorescent probes (DCFH-DA).

Results: High concentrations of UA either alone or combined with LPS increased the protein levels of GRP78 and CHOP. On the other hand, LPS alone increased the protein levels of GRP78 and CHOP. However, there was no significant difference between the mRNA expression of GRP78, CHOP, TNF-α, IL-1β, and IL-6 when PBMCs were treated with UA. High concentrations of UA augmented LPS-stimulated IL-1β transcript levels in PBMCs culture. Moreover, high concentrations of UA along with LPS significantly increased intracellular ROS production.

Conclusion: It seems that a high concentration of UA not only induces the protein levels of ER stress markers in PBMCs but also augments the impact of LPS-induced inflammation and ROS production.

Keywords: Uric acid, Endoplasmic reticulum stress, Inflammation, Reactive oxygen species

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Bioinformatics of estrogen receptor 1 gene in breast cancer

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In spite of dramatic advances in cancer research, breast cancer remains a major health issue, and it is a top priority for biomedical research. In the coming years, breast cancer is expected to become one of the most common cancers affecting women around the world. Breast cancer is caused primarily by noncoding RNAs that play an important role in regulating the expression of certain genes. Few studies have investigated how long noncoding RNAs and microRNAs regulate transcription, and most studies have defined the regulatory functions of long noncoding RNAs and microRNAs. Using a bioinformatics computational approach, a lncRNA-miRNA-mRNA network was constructed based on the breast invasive carcinoma dataset at cBioPortal. 601 nodes and 706 edges formed the network, which represented the complicated interactions between lncRNAs, miRNAs and target genes. miR-18a was shown to be the most potent miRNA controller and gene regulator, as shown in the present study. The expression of miR-18a is associated with ER-negative breast tumors exhibiting a high degree of inflammation. This expression is potentially associated specifically with macrophages. These results suggest that miR-18a may play a role in the systemic immunological response in ER tumors. It may help refine biomarker predictions and be used to develop new therapeutic approaches for breast cancer by studying the network of lncRNA-miRNA-mRNA interactions.

Keywords: Breast Cancer- noncoding RNAs - microRNAs- bioinformatics computational- miR-18a-lncRNA-miRNA-mRNA

Isolation, characterization, and genome investigation of vB_SenS_TUMS_E1

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Introduction: Salmonellosis is a critical, common infectious disease afflicting people and animals caused by Salmonella bacteria. With bacteria showing antibiotic resistance, new methods should be introduced to prevent and treat infections. To that end, bacteriophages are good choices.

Methods: In this study, phage vB_SenS_TUMS_E1 was isolated from poultry wastewater against Salmonella enteritidis. Phage characteristics were determined, including plaque formation, transmission electron microscopy, structural proteins profile, host range, and growth curve. The extracted genome was sequencing and annotated using standard bioinformatics tools.

Results: Following morphological analysis, phage vB_SenS_TUMS_E1 belonged to the Siphoviridae family. Phage vB_SenS_TUMS_E1 worked on various clinical and environmental strains of Salmonella but did not affect bacteria of other genera. The burst size was approximately 182 plaque-forming units per cell (PFU/cell). The genome of vB_SenS_TUMS_E1 is a linear dsDNA molecule of 43,017 bp whose G+C content stands at 49.7%. Out of 60 detected putative protein-coding genes, 43 gene products with known functions were found in database searches. Neither tRNA genes nor genes associated with antibiotic resistance, virulence factor, and lysogen formation were detected in the vB_SenS_TUMS_E1 genome.

Conclusion: The findings indicate that the lytic polyvalent vB_SenS_TUMS_E1 is an antibacterial agent that could control Salmonella in food samples and helps with Salmonellosis prevention and treatment.

Keywords: Bacteriophages, Antibiotic resistance, Salmonella enteritidis, Siphoviridae, Antibacterial agents,

Role of FGFR3 gene in exosome as a novel biomarker for bladder cancer

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Introduction: Bladder cancer is the tenth most common cancer worldwide, occurring four times more often in men than women. Based on the tumor stage, there are two types of non-invasive bladder cancer (NMIBC) and invasive muscle cancer (MIBC) and it includes 4 levels. Exosomes are extracellular vesicles that act as intercellular messengers and transmit biomolecules. Recently, the role of exosomes has been used as potential sources of non-invasive biomarkers for the diagnosis and monitoring of bladder cancer. Fibroblast growth factor 3 (FGFR3) plays a key role in various cellular processes such as angiogenesis, wound healing, embryonic growth, and endocrine signaling pathways in both health and disease. Changes in the FGFR3 pathway can activate the PI3K / AKT and MAPK / RAS pathways, which contribute to tumor progression and growth. In vitro studies have shown that activation of the FGFR3 mutation via S249C can increase cell proliferation and decrease apoptosis. In recent years, several studies have shown that exosomes can provide new non-invasive diagnostic and prognostic biomarkers in patients affected by cancers, including bladder cancer (BC). This study aimed to investigate the association between exosome and FGFR 3 gene and its application in the early detection of bladder cancer.
Methods: This research is based on the contents of NCBI biopharmaceuticals, GOOGLE SCHOLAR, and PUBMED have taken place. Results FGFR3 gene expression is inversely related to tumor progression and can predict the progression of NMIBC in the early stages.
Conclusion: Due to the unique characteristics of exosomes, it is predicted that the study of FGFR3 mutation in exosomes can provide more accurate and ideal results, especially for early diagnosis of the disease and early prediction of tumor recurrence. FGFR3 could be a new biomarker in the early detection of bladder cancer

Keywords: Exosomes, bladder cancer, FGFR3

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Bioinformatics study on the role of TCF7L2 gene in type 2 diabetes mellitus

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Introduction: Type2 diabetes mellitus (T2DM) is identified by chronic hyperglycemia due to insufficient compensatory insulin secretion by pancreatic β cells. Both insulin resistance and β cell dysfunction are thought to result from the complex interact of many different pathways under the combined control of environmental and genetic factors. The transcription factor7-like 2 (TCF7L2) is the most potent locus for T2DM risk and the first locus to have been strongly reported by genomic linkage studies. The aim of this study was to find the role of TCF7L2 gene in the process of T2DM.

Methods: For this purpose, The GSE25724 obtained from GEO datasets, was used to evaluate the status of TCF7L2 gene regulation between diabetic and non-diabetic individuals; the information about the TCF7L2 gene in the WNT signaling pathway was extracted from KEGG pathways; the GeneMANIA database was used to reveal the involvement of TCF7L2 in association with T2DM and insulin secretion.

Results: The results indicated the upregulation of TCF7L2 in diabetic patients in comparison to non-diabetic individuals. The TCF7L2 participates in the WNT signaling pathway and modulates MYC proto-oncogene, bHLH transcription factor (MYC) expression by binding to its promoter in a sequence-specific manner. TCF7L2 acts as a repressor in the absence of catenin beta1 (CTNNB1), and as activator in its presence, also expression of dominant-negative mutants results in cell-cycle arrest in G1. According to the fact that TCF7L2 is a critical element in the WNT signaling pathway, and its proven function in T2DM, it can be estimated that there might be connections between this cycle and T2DM. Although the mechanisms over which TCF7L2 exerts its effect on T2D are still not well understood, overexpression of TCF7L2 gene may cause pancreatic β cells to stop in G1.

Conclusion: In conclusion, insulin secretion reduces due to this outcome and causes T2DM.

Keywords: TCF7L2, type2 diabetes mellitus, WNT signaling pathway, mutants

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Designing new Integrase inhibitors against human T-cell leukemia virus type 1

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Page | 636

Introduction: The human T-cell leukemia virus type 1 (HTLV-1) is the etiologic factor of the malignancy of adult T-cell leukemia (ATL) and initiates the neurodegenerative HTLV-1- associated myelopathy/tropical spastic paraparesis (HAM/TSP). HTLV-1 infection is endemic in northeast Iran. Prevalence of HTLV-1 infection in Neyshabour and Mashhad showed that about 3% and 7.2 % of the participant were positive for HTLV-1, respectively. To date, several studies have investigated the drugs targeting viral enzyme integrase as a treatment regimen for patients with human immunodeficiency virus type 1 (HIV-1). Moreover, previous research has established that HIV-1 integrase inhibitors can inhibit HTLV-1 integration in vitro. However, no clinically useful inhibitors have been developed against the HTLV-1 integrase.

Method: At first, the integrase homology model was constructed using MODELLER 9.22 and mapped to the cryo-EM structure of HTLV-1 intasome by Coot 0.9.4. The protein structure refinement server (3Drefine) was applied for model refinement. Ligand-, and structure-based approaches was done for new inhibitors designed against HTLV-1 integrase. Then, through virtual screening approaches, new small-molecule inhibitors of HTLV-1 integrase were identified. The binding mode and total free energy changes upon receptor-ligand binding were predicted using Genetic Optimization for Ligand Docking (GOLD) Suite 5.2.2 software. The drug-like and chemical absorption, distribution, metabolism, excretion, and toxicity (ADMET) properties were predicted for all compounds.

Result: Finally, among predicted virtual screening and structure based design compounds, seven potential lead compounds were suggested with high affinity that forming various bound interaction (hydrogen, halogen, etc) with important HTLV-1 Integrase residue and viral DNA. In addition, these molecules have favourable predicted ADME, and lower ki values than the parent molecules.

Conclusion: Therefore, these structures can be used for development of effective drugs for HTLV-1 integrase inhibition.

Keywords: Integrase inhibitors, HTLV-1, Virtual screening

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Investigating the causes of the diversity of clinical findings in people with β gene mutations

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Page | 637

Introduction: Thalassemia is the most common single-gene disorder with different prevalence worldwide. B-thalassemia is the most common form with significant clinical symptoms in the affected people. So far, more than 200 mutations have been reported in the β-globin chain. This study investigates the causes of the clinical findings diversity in a population affected with beta-thalassemia gene mutation.

Method: In this review study, the clinical findings in people with β-mutations in heterozygous, intermediate and homozygous forms, as well as the experiences gained, have been reported.

Results: The findings showed that clinical symptoms in β mutation carriers are related to the type of mutation in the β gene, its coincidence with α mutation and other anemias. While, in people with intermedia thalassemia, in addition to the type of β mutation inherited from the parents, its coincidence with α mutations and factors modulated the expression of hemoglobin F (such as some Single Nucleotide Polymorphisms) involved in the clinical findings. In major thalassemia patients, in addition to α and β mutations inherited, it depends on treatment protocols such as hemoglobin level at the time of blood transfusion, ferritin level, type of chelator therapy, time of starting to use chelator and the regular medical care and examinations.

Conclusion: By performing relevant laboratory and molecular tests and standard treatment protocols, the quality of life in β-thalassemia patients can be improved.

Keywords: Thalassemia, clinical findings, β gene mutations

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Generating a mutant luciferase (S284T) with maximum emission above 600nm for animal imaging in cancer research

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Page | 638

Introduction: Animal model is important tools in Cancer research. A big challenge in use of animal model is how the tumor development and spread in body. One solution of this challenge is Bioluminescence imaging that is high-throughput, cheap and scalable. Although these undeniable advantages, a big problem in this technology is quenching of light wave under 600nm by hemoglobin.

Method: in this study we review known mutation that cause red-shift in emission spectrum of luciferase. Finally, we select conversion mutation of serine at locus 284 to threonine. We create mutant luciferase S284T by site directed mutagenesis on pgl-3 vector then confirm cloning by Sanger sequencing. Then plasmid contain mutant luciferase gene transfect to the HEK293T cells.

Result: Spectrum of luciferase record 48-hour post transfection and confirm that maximum emission of mutant luciferase S284T is above 600nm.

Conclusion: The main purpose of present study is investigation of tumor developing in animal model by using mutant luciferase S284T.

Keywords: imaging ‹luciferase ‹S284T

A beta- secretas inhibitor

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Page | 639

Introduction: Beta-secretase is an aspartic acid protease that cleaves amyloid precursor protein. Cleft products content transmembrane sequence called C99 and a extracellular sequence. Gamma secretase cut the C99 sequence and product 40 or 42 amino acids of beta amyloid. Accumulation of these beta amyloids in brain neurons leads to Alzheimer's disease. Inhibition of aspartic acids 32 and 228 in the active site of beta-secretase enzyme has been the goal of many researches to treat Alzheimer's.

Methods: Beta-secretase enzyme models with codes 1W50 and 2OF0 were taken from RCSB PDB database. Models of ligands with high similarity score to (2S) -1- (2,5-Dimethylphenoxy) -3-morpholin-4-yl propan-2-ol were obtained from the ZINC database. The analyze of structural similarity and physicochemical properties were calculated by software in the Swees drug design database. Molecular docking was performed by Molegro Virtual Docker software.

Results and Discussion: In our study with molecular docking method, High docking score between ZINC19790773 (selected from Murray CW et al study) and the active site of the enzyme was seen. The binding site was distant of aspartic acids 32 and 228 in active site of the enzyme. The docking scores of interactions of our study ligands with the aspartic acids 32 and 228 at the active site of the enzyme were lower than other binding sites on the enzyme. In our study, the binding energy of some ligands with the active site of the enzyme was greater than binding energy of ZINC19790773 for active site of enzyme

Keywords: Beta-secretase ‹Amyloid precursor protein ‹Alzheimer

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The analysis of biochemical and hematological parameters in psychiatric patients with a history of IV drug abuse, addiction and hepatitis C in Ahvaz city during 2012-2015

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Introduction: The contaminated injection equipments have pivotal role in spread of HCV infection. IV drug users are one of the populations with high risk of HCV infection. Objectives: our goal was to evaluate the role of a hazardous action (intravenous injection with contaminated equipments) in threat of public health.

Methods: In this study, we collected data on 37 psychiatric patients with a history of IV drug abuse and addiction with HCV and compared to psychiatric patients with a history of IV drug abuse without HCV. Here was measured biochemical and hematological parameters and analyzed by SPSS.

Results: We found levels of AST and ALT significantly increased, but ALP and albumin none significantly decreased in patients ($p \leq 0.05$). Moreover, PT, aPTT and ESR levels in patients were slightly higher than control group. In addition, a significant correlation between AST and ALT to serum creatinine in patients may indicate a relationship between kidney problems followed by hepatic damage. The mean value of FBS, Tg and cholesterol levels were nearly similar in both groups. The serum level of calcium and phosphate in patients were significantly lower and higher than control group respectively ($p \leq 0.05$). There was a reduction and increment in serum level of free T3 and free T4 respectively and the level of TSH in patients was nearly 3 times higher than control group. Thus, primary hypothyroidism has been seemed at patients.

Conclusion: Finally, we concluded the evaluation of IV drug abuser for prognosis of HCV widespread is very important.

Keywords: HCV ،IV drug users ،liver disease

Fe3O4@ CNT preparation as an efficient nanocomposite for loading and release an antiviral drug

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Introduction: Nanotechnology bring a lot of improvement in the engineering and biomedical field in recent years. Considering numerous applications of functionalized metal oxide nanoparticles in magnetic resonance imaging, electronics, catalysis and drug delivery; herein, in the new sciences, the nanocomposites preparation, based on nanotubes and nanoparticles, has been a noted topic in this area.

Materials and Methods: In this study, we have been tried to synthetized a benefit nanocomposite based on metal oxide nanoparticles. Metal oxide nanoparticles have been used for many applications such as magnetic resonance imaging, drug delivery, and treatment by neutron irradiation, electronics, catalysts, optics. In this study, iron oxide nanoparticles synthesis investigated by solvothermal synthesis method and by putting different functional groups such as SiO2 and NH2 on the nanoparticle surface, the properties of the particles were further improved. Furthermore, these nanoparticles prepared by green synthesis method by Bacillus sp. CKCr-7. UV-Vis spectroscopy, Scanning Electron Microscopy (SEM) and Fourier-transform infrared spectroscopy (FTIR) techniques characterized the synthesized samples.

Results and Discussion: As results shown, the obtained iron oxide nanoparticles were predominantly monodispersed and were stable for more than two months without significant agglomeration. After the nanoparticles synthesis, they were loaded upon carbon nanotubes, and then the nanocomposites were fully characterized. Afterward, the resulting nanocomposites and functionalized nanoparticles examined in biomedical fields for example in the delivery of active antiviral drug and in the engineering field to improve the lithium ion batteries quality. For this aim, the amount of drug loading/release was evaluated in different physiological pHs, including mouth and stomach pH values. Keywords: Fe3O4@ CNT nanocomposite, Bacillus sp. CKCr-7, Green synthesis, antiviral drug carriers

Keywords: Fe3O4@ CNT nanocomposite, Bacillus sp. CKCr-7, Green synthesis, antiviral drug carriers

Plant-derived Nanoparticles as A Novel Berberine Delivery System Effectively Suppresses Jurkat T-ALL Cells

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Introduction: Berberine (BBR), a natural alkaloid, has exerted significant anticancer activity in the treatment of various cancers. However, its low bioavailability, water solubility, and intestinal absorption have limited its clinical application. The present study focuses on the bioformulation of grape-derived nanovesicles (GDN) as a carrier for BBR and the investigation of whether GDNs induce anticancer activity against acute lymphoblastic leukemia.

Method: Grape nanoparticles were isolated and purified by differential ultracentrifugation steps. The structure, size, and zeta potential of nanoparticles were evaluated using scanning electron microscopy (SEM) and dynamic light scattering (DLS). Berberine was then loaded into GDNs and entrapment efficiency and in vitro release were evaluated. MTT assay was used to determine the cytotoxicity of free BBR and BBR-loaded GDNs on Jurkat cells. Following treatment with 30 and 60 μM of BBR-loaded GDNs or free BBR, the expression of apoptosis-related genes was quantified by qRT-PCR. Furthermore, flow cytometry was used to analyze apoptosis.

Results: SEM images and DLS data indicated the GDNs sphere shape with an average size of 278 nm. MTT assay showed higher cytotoxic effect of BBR-loaded GDNs compared to free BBR solution. Flow cytometry results also showed a significant higher apoptosis in BBR-loaded GDNs in leukemic cells dose- and time-dependently. Furthermore, apoptosis-related gene expression analysis revealed increased expression of caspase-3, -8, -9, and Bax genes and decreased BCL-2 expression in BBR-loaded GDNs.

Conclusion: Our findings indicate that GDNs may function as a nano-vehicle for BBR, enhancing its anticancer and cytotoxic activities in leukemic cells.

Keywords: Apoptosis, Berberine, Cancer, Drug delivery, Jurkat, Leukemia, Plant Nanoparticles

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Association of M55L and Q192R polymorphisms of paraoxonase 1 gene (PON1) with recurrent pregnancy loss risk: A case-control study

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Introduction: Recurrent pregnancy loss (RPL) refers to the incidence of two or more abortions before the first half of pregnancy. Oxidative stress has been hypothesized to play a central role in RPL. Objective: To investigate the relationship between Q192R and L55M polymorphisms of PON1 as antioxidant enzyme and the risk of RPL.

Methods: In this case-control study, 110 women with RPL (case) and 110 healthy fertile women (control) referred to the Research and Clinical Center for Infertility, Shiraz, Iran were enrolled. Genomic DNA was extracted from the peripheral blood in all participants. Polymorphisms were genotyped by polymerase chain reaction-restriction fragment length polymorphism method.

Results: Statistical analysis of Q192R polymorphism showed a significant difference for the RR genotype between the case and control group (OR = 11, CI = 1.39-86.87, p = 0.005) but none for the QR and QQ genotypes. No significant association was observed between the R and Q allelic frequency in the RPL participants compared to the control group (p = 0.53). Also, statistical analysis of the L55M polymorphism for MM genotype in the case group compared with the control group showed a significant difference (OR = 3.59, CI = 0.97-13.30, p = 0.042), but none for the LM and LL genotypes.

Conclusion: The findings showed a significant correlation between the Q192R polymorphisms and the L55M PON1 enzyme and RPL in this study population.

Keywords: Abortion, PON, Polymorphism, Recurrent pregnancy loss, Pregnancy

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Evidence for the Effect of Mutated Chondroitinase ABC I on the Motor Function of Rats with Spinal Cord Injury

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Page | 644

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Introduction: Chondroitinase ABC I (ChABC I) facilitates axonal regeneration by degrading chondroitin sulfate proteoglycans (CSPGs). Nevertheless, thermal instability of ChABC I has limited its therapeutic applications. Since we previously showed a higher thermal stability of Q140A mutant, here, we intended to study its influence on rats with spinal cord injury (SCI).
Methods: Wild-type and mutated enzymes were expressed and purified from E. coli BL21. To induce SCI, 50 male rats were subjected to T9 vertebra laminectomy and divided into: SHAM-operated, control groups, and two groups receiving wild-type and mutated enzymes. Locomotor scaling and sensory tests were used to evaluate motor function and neuropathic pain, respectively over a 28-day period. Finally, tissue samples were collected to evaluate indigested CSPGs, re-myelination, and neuroinflammation.
Results: Injection of ChABC I enzymes improved CSPGs digestion and re-myelination. Although there was no change in the sensory function, the motor function of injured animals increased after the treatments. Remarkably, there was a higher level of CSPGs digestion and locomotor scoring in animals treated with mutated enzyme compared to those receiving wild-type. Nevertheless, inflammatory factors levels did not alter in serum and spinal cord tissues after the treatments. **Conclusion:** Both wild-type and mutated enzymes improved CSPGs digestion, re-myelination, and motor function in rats with SCI. These results were more notable when mutated enzyme was used compared to wild-type suggesting higher thermal stability and catalytic efficiency of the mutant Q140A and its potential in the future clinical applications.

Keywords: SCI, ChABC I, CSPG, BBB, Tail Flick Latency, Hot plate

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Evaluation of the effect of Boswellic acids on the neutrophil-to-lymphocyte ratio and the signaling pathway of NF-κB in patients with moderate COVID-19, in a randomized double-blind placebo-controlled clinical trial

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Introduction: Although the rapid emergence and prevalence of SARS-CoV2 is a considerable universal public health threat, efforts to find an effective treatment to manage COVID-19 symptoms have not yet been met. Many studies have shown that pro-inflammatory pathways play a key role in the pathogenesis of COVID-19. There is plenty of evidence suggesting that Boswellic acids (BAs) have medicinal effects due to their immunomodulatory and anti-inflammatory effects. Owing to the properties of BAs, our study was performed to investigate the effect of BAs on the serum inflammatory biomarkers such as pro-inflammatory cytokines and also NF-κB signaling pathway in PBMC of moderate COVID-19 patients.

Methods: This study was performed as a randomized double-blind, placebo-controlled clinical trial on 47 patients with COVID-19 admitted to the hospital with 14-days follow-up. There were two groups: BAs and Placebo groups. Changes in the clinical symptoms, neutrophil and lymphocyte levels, serum concentrations of CRP, LDH, IL-1β, IL-6, TNF-α and IL-10, and activation of the NF-kB signaling pathway in PBMC were considered as outcomes.

Results: Our clinical trial revealed some improvements in the clinical symptoms were detected in the BAs group. Hematologic findings showed a significant decrease in the percentage of neutrophils ($P < 0.006$) and neutrophil-to-lymphocyte ratio (NLR) levels ($P < 0.003$), associated with a significant increase in the percentage of lymphocytes in the BAs group compared with the placebo ($P < 0.002$). Additionally, a significant decrease in LDH ($P < 0.04$), CRP ($P < 0.034$), IL-6 ($P < 0.001$), and TNF-α ($P < 0.001$) levels was detected in the BAs group. Also, our data showed that phospho-IκB protein and NF-kB p65 mRNA expression significantly decreased and IκB protein significantly increased in the BAs group compared with the placebo group.

Conclusion: Overall, the treatment with BAs resulted in alleviation of COVID-19 clinical symptoms, decline in the level of pro-inflammatory cytokines, and leads to inhibition of the NF-κB signaling pathway.

Keywords: COVID-19, Inflammation, Boswellic acids, NF-κB signaling pathway

A-10-1178-1

The effects of resveratrol on markers of Endoplasmic reticulum (ER) stress in patients with type 2 diabetes: a randomized, double-blind, placebo-controlled clinical trial

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Introduction: Endoplasmic reticulum (ER) stress plays an undeniable role in the pathogenesis process of type 2 diabetes mellitus (T2DM), leading to pancreatic beta-cell loss and insulin resistance. Recent findings from in vitro studies also demonstrate that ER stress-related factors might contribute to cytokine-induced beta-cell death and thus lead to the progression of diabetes. We previously demonstrated that resveratrol exerts several antioxidant properties. Here, we investigate the potential effect of resveratrol against the increased levels of ER stress-related factors in patients suffering from diabetes. Hence, this study aimed to determine whether resveratrol supplementation affects hyperglycemic-induced endoplasmic reticulum (ER) stress markers in a randomized, double-blind, placebo-controlled clinical trial.

Methods: A total of 48 patients with T2DM were randomly assigned to receive 800 mg/day of resveratrol or placebo during 2 months period. To evaluate the effects of resveratrol against diabetes complications, western blot analysis was used to examine the expression of certain ER stress proteins including C/EBP homologous protein 10 (CHOP) and glucose-regulated protein 78 (GRP78) in PBMCs.

Results: According to the findings obtained from our study, resveratrol consumption gives rise to the remarkable decline in the expression of mentioned ER stress proteins including, GRP78 and CHOP compared with the placebo group. Furthermore, concomitant with having no crucial side effects resveratrol was well tolerated.

Conclusions: According to our observations from this clinical trial, 8 weeks of supplementation with 800 mg/day of resveratrol has a protective effect against high glucose-induced ER stress in PBMCs of patients with T2DM. To conclude, our study helps shed more light on the protective effects of resveratrol supplementation against diabetes complications by inhibiting the expression of ER stress markers.

Keywords: Diabetes, Endoplasmic reticulum (ER) stress, Resveratrol, PBMC, Randomized clinical trial

A-10-1892-1

Fabricating Polymeric Nanoparticles Co-Loaded with Metformin and Silibinin for Targeting hTERT and ALK Genes Expression in Lung Cancer Cell line

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Introduction: Despite current therapies, lung cancer remains a global issue and requires the creation of novel treatment methods. Recent research has shown that biguanides including Metformin (MET) and Silibinin (SIL) have a potential anti-cancer effect. As a consequence, the effectiveness of MET and SIL in combination against lung cancer cells was investigated in this study to develop an effective and novel treatment method.

Methods: Niosomal nanoparticles were synthesized via the thin-film hydration method, and FE-SEM, FTIR, AFM, and DLS techniques were used to evaluate their Physico-chemical characteristics. The cytotoxic effects of free and drug-loaded NPs, as well as their combination, on A549 cells, were assessed using the MTT assay. An apoptosis test was used while under the influence of medication to identify the molecular mechanisms behind programmed cell death. Using a cell cycle test, it was determined whether pharmaceutical effects caused the cell cycle to stop progressing. Additionally, the qRT-PCR technique was used to evaluate the levels of hTERT, ALK, BAX, and BCL2 gene expression after 48-hour medication treatment.

Results: In the cytotoxicity assay, the growth of A549 lung cancer cells was inhibited by both MET and SIL. Compared to the individual therapies, the combination of MET and SIL dramatically and synergistically decreased the IC50s of MET and SIL in lung cancer cells. Furthermore, the combination of MET and SIL produced lower IC50 values and a better anti-proliferative effect on A549 lung cancer cells. Real-time PCR results showed the expression level of the hTERT, ALK, BAX, and BCL-2 were significantly reduced in lung cancer cell lines treated with MET and SIL compared to single treatments. ($P<0.001$).

Conclusion: It is anticipated that the use of Nano Niosomal formed MET and SIL would improve lung cancer treatment outcomes and improve the therapeutic efficiency of lung cancer cells.

Keywords: Niosomal Nanoparticles, Metformin, Silibinin, Lung cancer, hTERT, and ALK

Enhanced Anti-cancer effect of Curcumin loaded-niosomal Nanoparticles in combination with heat-killed Saccharomyces cerevisiae against human colon cancer cells

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Introduction: Colorectal cancer is one of the most lethal malignancies in the world. The treatment efficiency of colorectal cancer is imperative due to its high metastasis rate. Chemotherapy which is used in the treatment of cancer causes drug resistance after a period of usage. Probiotics and bioactive compounds are substances of a natural origin that have been used to treat various types of cancers. Despite the advantages of bioactive substances, their use is restricted due to low bioavailability, insufficient solubility, and low dispersion rate in aqueous media. Nano-carriers such as niosome could pave the way for the efficient treatment of colon cancer. In this study, we used curcumin-loaded niosomal nano-particles in combination with a heat-killed form of Saccharomyces cerevisiae as an anti-cancer agent against colorectal cancer cell line.

Methods: Firstly, Saccharomyces cerevisiae yeast probiotic was cultivated and heat-killed form of probiotic was obtained by heating in a water bath. Curcumin loaded niosomal nano-particles were synthesized with thin-film hydration method. The synthesized nanoparticles were characterized by DLS, FT-IR, FE-SEM, TEM, and AFM techniques. The cytotoxicity and gene expression changes of these agents were determined with MTT and real-time PCR, respectively. In order to investigate the effect of these agents on the cell cycle arrest, apoptosis, and metastasis, additional follow cytometry and wound-healing tests were performed.

Results: The results showed a higher decrease in the expression of genes involved in metastasis including COL10A1, MMP2, and MMP9 in the treatment of cancer cells with a combination of niosome encapsulated curcumin and heat-killed form of Saccharomyces cerevisiae relative to the other forms.

Conclusion: Taken together, the findings of this study suggested that encapsulation of curcumin into niosome could increase its anti-cancer effects on colon cancer cells. It was also revealed that combining curcumin-loaded noisome nano-particles with Saccharomyces cerevisiae could significantly improve the treatment efficiency of colon cancer.

Keywords: Probiotics, Bioactive compound, Colorectal cancer, Niosomal Nanoparticles, Combination therapy

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A-10-1892-3

The Enhanced Anti-Cancer Effect of Nanostructured Niosome Loaded Bioactive Curcumin via Reduced Folate Carrier (RFC) Gene Expression in Human Breast Cancer Cells

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Page | 649

Introduction: In recent years, breast cancer has been one of the most common types of cancer. Recent developments in nanotechnology and nanomedicine have generated many promising drug delivery systems. Niosomes are non-ionic surfactant vesicles with a bilayer structure that have been used to deliver various medicinal elements, including chemotherapeutic agents. Curcumin is a bioactive substance that due to its low solubility and low absorption by the digestive system, is loaded inside the Niosome and it acts as an effective and specific medicine. RFC is one of the most important transporters of folate and disruption of this carrier can cause cancer. In this study, the effect of Niosome containing curcumin on RFC protein gene expression in breast cancer cell line (MDA-MB-231) has been investigated in order to reduce abnormal folate.

Methods: Niosome NPs were synthesized by reverse phase evaporation method with Span60 and cholesterol then curcumin was loaded in Niosome and their size and nanoformulation were checked by DLS. These nanocarriers were characterized by DLS, SEM, FE-SEM, TEM, and AFM. By performing MTT, the percentage of cell viability was determined. Morphology and spectrum of drugs were measured by FT-IR. RNA extraction was performed. In order to count the cells in different stages of the cell process, cell cycle analysis and apoptosis tests were used by flow cytometry. In the end, the primers related to the RFC protein gene were designed and the expression of RFC was assessed by the RT-PCR method.

Results: The treatment of cancer cells with Nano-curcumin resulted in a larger decrease in the expression of genes associated with proliferation, including RFC, BAX, and BCL2, compared to the free forms.

Conclusion: Our results, demonstrated that Curcumin-loaded niosomal nanocarrier is an efficient method in breast cancer therapy with the possibility of high targeting, slow drug release, and low toxicity.

Keywords: Reduced Folate Carrier, Breast cancer, Niosomal Nanoparticles, Nano medicine

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A new Insight into Curcumin-Mediated MicroRNAs Regulation in Colorectal Cancer: A Systematic Review

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Page | 650

Introduction: There are several methods for the treatment of colon cancer, including surgery, chemotherapy, radiotherapy, and gene therapy, but because of their side effects and inefficiency, scientists are looking for safer and more effective methods. One of these methods is the employment of phytochemical compounds such as curcumin. Studies have identified various a mechanism by which curcumin inhibits cancer growth and metastasis. An interesting mechanism is a change in expression levels of microRNAs. In this review article, we have focused on target microRNAs of curcumin and their categorization in colorectal cancer and its application in translational medicine.

Methods: Related articles were selected from PubMed and Web of Science databases and STROB checklist was applied for selected articles. In silico analysis was performed to identify the signal pathways in which the given miRNAs are involved and also the target genes of these miRNAs using mirpath database.

Results: Based on the results of 16 related articles, 23 miRNAs were affected by curcumin. After curcumin treatment, miR-497, miR-200c, miR-200b, miR-409-3p, miR-34, miR-126, miR-145, miR-206, miR-491, miR-141, miR-429 and miR-101 were overexpressed in colorectal cancer, while downregulation of miR21, miR155, miR-221, miR-222, miR-17-5p, m iR-130a, miR27, and miR20a was reported. These molecules manage cellular behavior in three ways: 1) inhibition of cell proliferation and induction of apoptosis, 2) inhibition of EMT, migration, and invasion, and 3) sensitization to chemotherapy. The heatmaps demonstrated that these miRNAs are enriched for important signaling pathways such as PI3K-Akt, MAPK, phagocytosis, cell adhesion, jak-stat, TGF beta, and p53.

Conclusion: Curcumin as a natural compound regulates the expression of certain microRNAs which leads to the suppression of colon cancer growth and metastasis.

Keywords: colorectal cancer, curcumin, microRNAs, translational medicine

A-10-1894-3

Fabricating Antibody Conjugated Super Magnetic Oxide Nanoparticles for Early Detection of Prostate Stem Cell Antigen

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Introduction: Prostate cancer is one of the most widespread cancers in the world. Early diagnosis is the most important factor in treatment efficiency. Furthermore, new methods for early diagnosis and treatment play an important role in the treatment of prostate cancer. In this study, we designed targeted conjugation of antibodies with iron nanoparticles and evaluated the binding properties of antibodies to prostate cancers and benign tissues. This method in addition to having a lower cost has high sensitivity and specificity and therefore provides an early and accurate diagnosis method of prostate cancer.

Methods: In this study, anti- PSCA antibodies were purified and conjugated to super magnetic oxide nanoparticles (SPION). Then, iron staining on prostate adenocarcinoma tissues was performed. At the same time, immunohistochemically staining was performed on similar tissues to compare the results. In addition, benign prostatic hyperplasia (BPH) samples were used as a control sample.

Results: In adenocarcinoma tissues with iron staining, many blue spots are seen compared to benign tissues, and the number of these spots increases with increasing tumor grade.

Conclusion: These findings indicate the characteristic of iron staining as a conjugate antibody to iron can be an appropriate approach to specific staining of tumor markers in cancer tissues and can be used to diagnose prostate cancer due to its safety, low cost, sensitivity, and specificity.

Keywords: Anti-PSCA Antibody, Conjugation, SPION, Benign prostatic hyperplasia, Adenocarcinoma

Chicoric acid reduces cell death and ALT, AST, LDH enzymes in palmitate-induced fatty liver cell model.

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Introduction: Non-alcoholic fatty liver disease (NAFLD) is the abnormal accumulation of fat in liver cells. HepG2 cells show similar morphology to liver parenchymal cells. cell damage caused by palmitate, leakage (LDH) and transaminase enzymes ALT and AST increase in the culture medium of these cells. The main aim of this study is to evaluate the treatment effect of chicoric acid (CA) in palmitate (PA)-induced NAFLD HepG2 model.

Methods: The appropriate concentration of palmitate (PA) and cichoric acid (CA) was obtained by MTT assay and cell viability was investigated using flow cytometry in the studied cell groups. HepG2 cells were pre-treated with palmitate for 24h, and then were exposed to CA, for another 24h and and enzymatic biomarkers related to fatty liver (ALT, AST, LDH) were measured in the study groups.

Results: CA (100 µM and 200 µM) significantly reduced apoptosis and necrosis levels in PA-treated (0.75 mM) HepG2 cells, ALT, AST, and LDH in PA-treated HepG2 cells showed a significant increase compared to the control, and after treatment with cichoric acid, the effect of changes was significantly reduced ($p < 0.05$).

Conclusion: Reduction of cell death (apoptosis and necrosis) and reduction of biomarkers of cell damage under the influence of Chicoric acid in HepG2 cells pretreated with palmitate indicate that these compounds may be potential agents in the treatment of non-alcoholic fatty liver disease (NAFLD) in the future.

Keywords: chicoric acid, palmitate, lactate dehydrogenase, Aspartate transaminase (ALT), alanine transaminase (AST)

A-10-1711-1

Intracellular crosstalk between four main cell death pathways: necroptosis, ferroptosis and autophagy as backup death routes

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Apoptosis necroptosis, ferroptosis and autophagy are four major processes to determine cell fate. The interaction between these routes determines the balance of cell death and cell survival. The engagement of regulated cell deaths is tightly controlled by a complex network of signaling mechanisms that often exhibit cross talk between receptors, enzymes, and downstream signaling products. Networking of cell death pathways show that a cell can divert to an alternative pathway even in the presence of inhibitors of the primary pathway. These findings hold promising implications in the design of novel therapeutics for the treatment of numerous diseases, ranging from neurodegenerative disease to cancer. Here, we explore the emerging idea of cell death as a signaling network, considering connections between four main cell deaths pathways.

Keywords: Apoptosis, Necroptosis, Ferroptosis, Autophagy, Cell deaths crosstalk

A-10-1915-1

Association between vitamin D and acute kidney injury: Diagnostic & Prognostic approach

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Introduction: Activation of the immune system followed by inflammation can lead to Acute Kidney Injury (AKI). AKI is a common complication characterized by rapid deterioration of kidney function. Vitamin D is involved in inflammation prevention and cell apoptosis. However, not much is known about the effect of vitamin D on AKI.

Methods: We obtained the findings of our study by reviewing several articles in PubMed and google scholar, and examining the role of vitamin D in disease.

Result: Immune system activation and inflammation onset, followed by induction of oxidative stress reactions and the production of Reactive oxygen species (ROS) can lead to AKI. Vitamin D plays an important role in preventing inflammation, inhibiting ROS production and cell apoptosis. Increasing vitamin D with an increasing effect on inflammatory cytokines and HO1 and NrF2 pathway, as well as impaired gene signal (TGF-B) and podocyte and Angiotensin II function, inhibits inflammation and prevents AKI. Vitamin D increment also inhibits ROS production by activating WNT and inducing PPARY / HO1 expression in the MAPK pathway. Also, the presence of BSM I and FOK I polymorphisms increases Vitamin D Receptor (VDR) expression and prevents AKI. As a result, the effect of vitamin D on AKI can be understood.

Conclusion: Due to the regulatory role of vitamin D in many signaling pathways involved in inflammation, apoptosis and ROS production, it can be effective to design strategies to prevent AKI.

Keywords: Vitamin D, acute kidney injury, Reactive oxygen species

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A-10-1936-1

Biochemical Damage by Fungal Toxins (Mycotoxins)

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Fungal toxins or mycotoxins are toxic chemicals produced by many fungi (moulds) and cause various harmful effects, such as acute, chronic, carcinogenic (mutagenic) and teratogenic poisoning. Some disrupt the production of proteins and some neurotoxins. A wide range of fungi produce potential toxins that are important for human health all over the world. These mycotoxins include aflatoxins, ochratoxin A, fumonisin, trichocenes, zeralenol, etc. This research is a documentary research that has been explained by referring to the reliable scientific databases of Google Scholar, PubMed, Scopus and SID.

Results: Some of these mycotoxins have a low molecular weight, are chemically stable and resistant to thermal processes such as autoclaving, boiling, cooking and fermentation. Also, the chemical structure of some mycotoxins causes them to be placed between the double helix of DNA. This causes problems in DNA replication. Mutations in genes that control the cell cycle can lead to cancer. If the mutation occurs in the sperm and egg, it can cause birth defects or mutations in the individual's children.

Keywords: Mycotoxin, biochemical damage, fungi

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Astaxanthin improves glucose metabolism and inflammation in patients with type 2 diabetes mellitus: A randomized clinical trial

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Page | 656

Introduction: The rising incidence of type 2 diabetes mellitus (T2DM) is a major public health problem and According to research on the effects of carotenoids in the control of diabetes, On the other hand, based on research on the effects of mir-27a on glucose metabolism, we decided that during a 12-week clinical trial in patients with type 2 diabetes, to evaluate the potential effects of astaxanthin supplementation as an anti-inflammatory agent on the expression of miR-27a as an inflammatory marker and patients' plasma glucose control.

Methods: This randomized, double-blind, placebo-controlled clinical trial was conducted in 68 patients with T2DM who met our inclusion criteria, randomly receiving 10 mg/day of oral AST (n = 34) or placebo (n = 33) for 12 weeks. free MicroRNA levels and plasma glucose concentration were measured.

Results: Following the 12-week administration of AST, we observed that the relative expression level of miR-27a decreased significantly in comparison to the control group (fold change expression ~ 0.02993) (p-value ~ 0.047). The glucose concentration (FBS) levels were high across all two groups at baseline, with no significant difference between groups. After the two weeks of treatment with a 10 mg dose of Astaxanthin, FBS showed significant regulation. FBS displayed a 14% reduction in average levels (from 126.86 ±26.98 to 108.85 ± 19.74 mg/dL), which were statistically significant (p-value < 0.05).

Conclusion: We demonstrated that because participants with type 2 diabetes often have uncontrolled glucose metabolism. The findings of this study indicate that AST serves as a positive modulator of glucose metabolism that may be via reducing mir-27a and suggest it may be a promising target for the treatment of T2DM.on the other hand the anti-inflammatory properties of AST can, at least in part, be the consequence of its specific effects on the expression of miR-27a.

Keywords: Astaxanthin, diabetes mellitus, miR-27a

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Agastache foeniculum lipophilic fraction ameliorates oxidative stress in macrophage cells stimulated by lipopolysaccharide

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Introduction: Agastache foeniculum is a Lamiaceae perennial plant that has long been used traditionally as a medicinal plant for gastrointestinal, cardiovascular, and nervous treatments, as well as to treat pain, cold, and fever. Agastache leaves, and flowers were used as poultices and infusions to treat blood cough, fever, heart conditions, and burns. The essential oil of this plant is high in estragole, which has antioxidant, anti-inflammatory, antifungal, and antibacterial properties. In some pathological conditions, the NADPH oxidase (NOX) is the most critical contributor to superoxide production.

Methods: The effects of Agastache foeniculum essential oil (AFEO) and oil (AFoil) on oxidative stress stimulated by lipopolysaccharide (LPS) in the macrophage cell were examined. The effect of AFEO and AFoil on the activity and expression of NOX, catalase (CAT), superoxide dismutase (SOD), NFR2, and NF-kB in the LPS-stimulated macrophage cell was studied. The interaction patterns of AFEO and AFoil components with NOX, SOD, CAT, NRF2, and NF-kB proteins were analyzed by molecular docking.

Results: Estragole was the main ingredient in AFEO. The major chemical components of AFoil are linolenic acid, estragole, palmitic acid, linoleic acid, and oleic acid. NOX activation was stimulated in macrophage cells by LPS. AFEO and AFoil decreased NOX activity while SOD and CAT activities were increased in LPS-stimulated macrophages. AFoil, which contains estragole and omega-3 fatty acids, had a better antioxidative effect than AFEO, which contains estragole. Estragole, linoleic acid, and linolenic acid bind to different hydrophobic pockets of NOX, SOD, CAT, NFR2, and NF-kB through establishing hydrogen bonds and Van der Walls interactions with different binding energies.

Conclusion: The mechanisms involved in lowering oxidative stress markers depended on down-regulating superoxide-producing enzymes and up-regulating superoxide-removing enzymes at gene and protein levels. The AFoil emulsion can be used to reduce the detrimental impacts of oxidative stress.

Keywords: Estragole, Oxidative stress, NADH oxidase, Superoxide dismutase, catalase

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Therapeutic effect of exosomes injection from allogeneic fat mesenchymal stem cell culture in a pulmonary fibrosis model in rats

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Page | 658

Introduction: Pulmonary fibrosis is a chronic interstitial lung disease, which is caused by damage to the lung parenchyma by inflammatory factors and fibrosis. Today, research on extracellular vesicles derived from mesenchymal stem cells is one of the areas of interest in regenerative medicine. Studies show that therapeutic use of exosomes as a non-cellular treatment method has a number of advantages that can be a good justification for its replacement in conventional cell therapy methods.

Methods: in this study, we evaluate the effects of adipose-derived mesenchymal stem cells (adMSCs) originating exosomes to repair pulmonary fibrosis. Here we present a series of studies utilizing exosome by inhalation to treat models of lung injury and fibrosis. Male adult Sprague-Dawley (SD) rats were randomly divided into three groups: the control group, the exosome receiving group with a concentration of 500μg/ml, and 250 μg/ml. Tissue samples and the levels of oxidative stress and inflammatory factors in each group were compared.

Results: exosomes isolated ranged in size from 30 to 150 nm and demonstrated the characteristic cup-shaped morphology with TEM. We showed that an inhalation treatment of exosome exhibited therapeutic potential for lung regeneration in experimental models of pulmonary fibrosis. Pathologic alteration of lung tissue, levels of pro-inflammatory cytokines, were measured to evaluate the therapeutic effect of treatment with MSCs exosomes.

Conclusion: Our results demonstrate that exosomes, constitutively produced by adMSCs, have the potential to be utilized as a therapeutic tool for effective tissue-engineered lung

Keywords: exosome, fibrosis, mesenchymal stem cell, RAT model

A-10-1492-1

Suppressing colorectal cancer metastasis and angiogenesis by citrus Auraptene in a mouse model of colorectal cancer

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Introduction: CRC is a prevalent gastrointestinal cancer in the world. Auraptene, a natural flavonoid found in citrus fruits, is known to have anticarcinogenic effects on CRC. Herein, we examined the anti-metastatic and anti-angiogenesis properties of Auraptene in a mouse model of CRC.

Methods: CT-26 xenograft mice were generated and randomly divided into six groups: (i, ii, iii) Auraptene groups injected intratumorally at concentrations of 50, 100, and 200 µM, (iv) Sham control mice injected intratumorally with normal saline and dimethyl sulfoxide (DMSO) as Auraptene solvent, and (v) positive mice injected intraperitoneally with 5 mg/kg of 5-FU. After 14 days, the mice were sacrificed and the tumors were harvested for pathological and Molecular studies. The anti-metastatic and the anti-angiogenesis property of Auraptene in the tumor tissue was evaluated by Real-time PCR of MMP2, MMP9, E-cadherin, VEGF-A and its receptor genes, and the protein levels of two MMPs were measured by the western blot assay.

Results: In this study, Auraptene decreased the risk of metastasis and angiogenesis by reducing the mRNA expression of MMP2, MMP9, E-cadherin, VEGF-A and its receptor (VEGFR1). Moreover, the protein levels of MMP2 and MMP9 were decreased. Pathological findings revealed detectable necrosis in tumor cells treated with 100 and 200 µM of Auraptene and 5FU compared to the control group, whereas tumor cells in other groups did not exhibit morphological changes.

Conclusion: According to our results, Auraptene may be a good candidate for adjuvant treatment.

Keywords: colorectal cancer, Auraptene, anti-angiogenesis, anti-metastatic effect

A-10-1236-1

Delivery of Rapamycin by Liposomes Synergistically Enhances the Chemotherapy Effect of paclitaxel on ovarian Cancer cells

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Introduction: Ovarian cancer is the most lethal type of cancer among gynecologic malignancies. Paclitaxel has been considered as the first therapeutic agent in chemotherapy of ovarian cancer but induces drug resistance. Our objective in this study was to investigate the effect of Rapamycin in increasing the antitumor activity of Paclitaxel in ovarian cancer cells and from Nanoliposomes were used to deliver drugs to cells.

Methods: SKOV3 ovarian cancer cell line were cultured in RPMI 1640 medium supplemented with 10% FBS, 1% penicillin and streptomycin at 37C°, a humidified atmosphere of 5% CO_2. The liposomes were prepared by the hydration of the thin lipid film, and the morphology and size of liposomes were characterized DLS and TEM. The amount of drug-loaded in liposomes (Encapsulation Efficiency) was determined by HPLC and the cytotoxic effects were assessed by MTT assay. The type of cell death was evaluated by flow cytometry analysis. P70S6k and mTOR genes expression were measured by RT-PCR.

Results: The results of DLS and TEM analysis demonstrated that liposomes with moderately uniform and spherical in shape were less than 150 nm in size. HPLC analysis determined that the EE of Paclitaxel, and Rapamycin in liposomes are greater than 90%. Paclitaxel and Rapamycin-loaded liposomes induced cell death and reduced viability of skov-3 cells in a time and concentration-dependent manner. The blank liposomes have no toxic effects on cell growth and viability. Rapamycin Liposome synergistically enhanced the antitumor effects of Paclitaxel encapsulated into liposomes via reducing the expression of p70s6k and mTOR genes involved in the PI3K/AKT/mTOR signaling pathway (CI value <1).

Conclusion: This study revealed that combination of Paclitaxel with Rapamycin may be a useful therapeutic strategy for enhancing the anti-cancer efficacy of Paclitaxel in treatment of ovarian cancer via inhibiting the signaling pathway of PI3K/AKT/mTOR.

Keywords: Ovarian cancer, Paclitaxel, Rapamycin, liposome

A-10-1083-1

Knocking out of OPN gene using CRISPR/cas9 in combination with conventional radiotherapy inhibits the progression of MDA-MB-231 breast cancer cells

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Introduction: Although invasion and metastasis into other cells and tissues is a critical step in breast neoplasm, no biomarker reliably determines tumor prognoses and diagnosis. However, some previous studies have indicated that the OPN high expression is responsible for promoting aggressive behavior, poor prognosis in tumor cells, and reducing the survival of patients. Hence, the effects of the OPN knockout through the CRISPR/Cas9 technique alone/along with conventional radiotherapy are emphasized.

Methods: We applied the CRISPR/Cas9 system to the OPN gene knockout in the MDA-MB-231 breast cancer cell line. The cells were exposed to a single dose of 2 Gy after transfection. In the following, OPN mRNA levels, cell proliferation, apoptosis, and activation of checkpoint proteins were measured using quantitative real-time RT-PCR, MTT assay, Annexin V/PI, western blotting technique, respectively.

Results: The OPN knocking-out combined with irradiation in MBA-MB-231 cells has demonstrated morphological changes, including the communication pattern, shape, size, and cells structure. The OPN expression was meaningfully reduced alone or along with irradiation. Also, the cell viability potential was significantly decreased. While, knocking out of OPN gene combined with irradiated caused to remarkably increased apoptosis rate. Examination of activation of checkpoint proteins illustrated that the p-Chk1 and p-AKT proteins level were substantially declined after OPN knocked out combined with radiotherapy.

Conclusion: Our data indicated that after OPN knock-out alone or along with radiation, the MDA-MB-231 cells showed a significant radiosensitivity. Therefore, knocking out the OPN gene combined with conventional radiotherapy may become an impressive therapeutic purpose.

Keywords: Osteopontin, Breast cancer, Radiotherapy, CRISPR/Cas 9

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Effects of Sodium Hydrosulfide (NaHS) on Cisplatin-Induced Hepatic and Cardiac Toxicity

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Introduction: To investigate the effects of sodium hydrosulfide (NaHS) against cisplatin (CP)-induced hepatotoxicity and cardiotoxicity in rats.

Methods: Thirty-two male Sprague Dawley were divided into four groups as follows: (1) control group, which received only normal saline; (2) NaHS group, which was intraperitoneally injected with NaHS (200 µg/kg/d, dissolved in saline) for 15 days; (3) CP group, was intraperitoneally injected with a single dose of CP (5 mg/kg) and (4) CP plus NaHS group, received CP along with NaHS. Blood and tissue samples were harvested for biochemical, histopathological, and immunohistochemical investigations. One-way analysis of variance was used to test the statistical significance.

Results: CP injection significantly increased alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), lactate dehydrogenase (LDH), Creatine Phosphokinase (CK-MB), cholesterol, low-density lipoprotein (LDL), triglyceride (TG), and lipid peroxidation levels, while high-density lipoprotein (HDL), albumin, glutathione peroxidase (GPx), superoxide dismutase (SOD) and catalase (CAT) levels were significantly reduced with pathological alterations in liver and heart tissues. Co-treatment of NaHS with CP ameliorates the biochemical and histological parameters. Also, Treatment with CP alone resulted in increased tissue expression of interleukin-1β (IL-1β) in the liver and heart but co-treatment NaHS with CP reduced the expression of this inflammatory factor.

Conclusions: We conclude that NaHS operates in the liver and heart as an anti-inflammatory and powerful free radicals scavenger to inhibit the toxic effects of CP, both at the biochemical and histopathological levels.

Keywords: Cisplatin, Hepatotoxicity, Cardiotoxicity, Sodium Hydrosulfide, Stress oxidative, IL-1β

A-10-1041-1

Anti-hyperglycemic properties of Agastache foeniculum essential oil and fatty acid

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Introduction: Hyperglycemia often promotes superoxide accumulation, which may increase oxidative stress. Reducing superoxide production in hyperglycemia and the inflammatory condition is an emerging way to reduce protein and lipid oxidation and diabetes complication. The effect of Agastache foeniculum essential oil (AFEO) and oil fraction (AFoil) on Hyperglycemia-stimulated oxidative stress and the pathogenicity of AFEO and AFoil on oxidative stress was assessed.

Methods: The stimulatory effects of AFEO and AFoil on the activity and expression of NADH oxide (NOX), catalase (CAT), superoxide dismutase (SOD), and the expression of nuclear respiratory factor 2 (NRF2) and nuclear factor-kappa B (NF-kB) in the hyperglycemia-stimulated macrophage cell line, were studied. The interaction patterns of AFEO and AFoil components with NOX, SOD, CAT, NRF2, and NF-kB proteins were also deduced using molecular docking. **Results:** Estragole was the main ingredient in AFEO (97%). Linolenic acid (32.10%), estragole (16.22%), palmitic acid (12.62%), linoleic acid (12.04%), and oleic acid (8.73%) were the major chemical components of the AFoil. NOX activation was stimulated in macrophage cells by HG. AFEO and AFoil decreased NOX activity while increased SOD and CAT activities in stimulated macrophages. AFoil with estragole and omega-3 fatty acids was better than AFEO with estragole in anti-hyperglycemic activity. According to molecular docking research, estragole, linoleic acid, and linolenic acid bind to different hydrophobic pockets of NOX, SOD, CAT, NFR2, and NF-kB using hydrogen bonds, Van der Walls bonds, pi-alkyl, and pi-anion interactions, with different binding energies.

Conclusion: AFEO and AFoil showed anti-diabetic activity. The mechanisms in lowering oxidative stress markers depended on down-regulating superoxide-producing enzymes and up-regulating superoxide-removing enzymes at gene and protein levels. The AFoil emulsion can be used to reduce the detrimental impacts of hyperglycemia.

Keywords: Estragole, Anti-diabetes, NADH oxidase, Superoxide dismutase, Catalase

A-10-1266-1

Identification of overlapped genes and critical pathways associated with diabetic nephropathy and ESRD: An in-silico study

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Introduction: Diabetic nephropathy is the leading cause of morbidity and mortality in both type 1 diabetes (T1D) and type 2 diabetes (T2D). Additionally, Diabetic nephropathy is now the most typical cause of end-stage renal disease (ESRD) globally. Therefore, in silico analysis on differentially expressed genes and system biology may present some novel therapeutic approaches for this condition.

Methods: In the current study, GSE142153, including transcriptional profiling of healthy controls, patients with diabetic nephropathy, and patients with ESRD, was analyzed with the Limma package. Then, overlapped genes between diabetic nephropathy and patients with ESRD were selected through Venn Diagram. Then, we used the EnrichR package to study the system biology of selected overlapped genes. Afterward, the interaction network of identified differentially expressed genes was drawn in Cytoscape using the GeneMANIA plugin.

Results: A total of 31 overlapped differentially expressed genes were identified using microarray data analysis. According to the results of EnrichR, hemoglobin alpha binding (GO:0031721), hydrogen peroxide catabolic process (GO:0042744), and endocytic vesicle lumen (GO:0071682) were selected as the most significant Molecular Function (MF), Biological Process (BP), and Cellular Component (CC), respectively. The GeneMANIA network interaction was constructed, including 48 nodes and 576 edges, and finally, the string network with 12 nodes and 27 edges was identified.

Conclusion: This study, therefore, identified some novel overlapped genes and key pathways involved in diabetic nephropathy and ESRD, which could help define and develop novel therapeutic strategies.

Keywords: diabetic nephropathy, ESRD, overlapped genes, pathway

A-10-1275-1

The effect of hydroalcoholic extract of Securigera securidaca seed on serum levels of angiogenesis factors vascular endothelial growth factor and Fibroblast growth factor in diabetic rats

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Page | 665

Introduction: evidence indicates that in diabetic retinopathy, nephropathy and atherosclerotic plaque, there is excessive angiogenesis, whereas, in wound healing and myocardial perfusion, blood vessel growth is impaired. It is known that angiogenesis is regulated by a counter balance between endogenous Angiogenesis stimulators and angiogenesis inhibitors which directly target the vascular endothelial cells and is modulated by multiple factors, including hyperglycemia-induced oxidative stress, growth factors and inflammatory factors. This study investigates the effects of the hydroalcoholic extract of Securigera Securidaca seeds on angiogenesis factors of VEGF, sFlt, FGF 21 and TGF-β in diabetic rats.

Methods: The treatment protocol was conducted by three HESS doses of 100, 200, and 400 mg/kg bw, glibenclamide (5 mg/kg bw) alone and glibenclamide (5 mg/kg bw) in combination with two HESS doses of 200 and 400 (mg/kg bw) in streptozotocin-induced diabetic rats. Serum biochemical profile, VEGF, FGF21, sFlt-1, Flk-1, lipid peroxidation rate (Malondialdehyde), nitric oxide, TNF-α, and hs-CRP contents were evaluated in treated groups.

Results: Most effects of HESS on the parameters were dose-dependent. Glibenclamide reduced blood sugar more effectively than the highest dose of HESS ($P<0.05$), and it can synergistically increase in combination with HESS. The effects of HESS on lipid profile were weaker than GB. HESS was more effective than GB in the prevention of lipid peroxidation and reduction of MDA levels. FGF21, sFLK1 and sFLT1 as anti-angiogenesis factors and VEGF and TGF-β as angiogenesis factors were decreased and increased, respectively in control diabetic rats. Both HESS and glibenclamide and their combinations did not show statistical significant effect on changing the mentioned values in treated groups, but glibenclamide slightly improved the values.

Conclusions: Securigera Securidaca seed consumption as a supplement with the blood sugar-lowering drugs such as glibenclamide does not have side effects on inducing and also preventing from angiogenesis damages.

Keywords: Glibenclamide, Streptozotocin, Angiogenesis, Securigera securidaca, Diabetic rats, VEGF, sFlt, FGF 21, MDA, NO, hs-CRP and TGF-β.

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Hepatoprotective effect of Silymarin against 1, 2-Dimethylhydrazine-induced carcinogenic hepatic damage in mice

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Introduction: 1, 2-Dimethylhydrazine (DMH) as a toxic pollutant is a potent colon and rectum carcinogen in animal models. Due to the hepatic metabolism of DMH, it induces oxidative stress, hepatotoxicity, and in advanced stages hepatocellular carcinoma. Silymarin (SMN) has exhibited anticancer, hepatoprotective, hepatic regeneration induction, and antioxidant effects. Therefore, we aimed to evaluate the possible protective effects of SMN on hepatic changes during DMH-induced colon carcinogenesis.

Methods: Twenty-four BALB/c male mice (25-30 g) were divided into three groups with eight mice per group (control, DMH, SMN+DMH). Colorectal cancer (CRC) was induced in the DMH and SMN+DMH groups through intraperitoneal injection of DMH at the dose of 20 mg/kg b.w. once a week for ten consecutive weeks. The SMN +DMH group received a modified diet containing 2500 ppm SMN for eight weeks after CRC induction (11-18 w); while the control and DMH groups received a normal diet. At the end of the 18th week, liver tissues were dissected immediately after cardiac blood sampling and euthanasia. The serum levels of ALT, AST, and LDH were examined using a biochemistry autoanalyzer. Moreover, malondialdehyde (MDA) and NO content, and myeloperoxidase (MPO) activity were measured in hepatic homogenates preserved at -70 oC. Histopathological evaluations of the liver samples were carried out through H&E staining.

Results: DMH administration resulted in a significant elevation in the serum levels of ALT, AST, and LDH as well as the hepatic MDA, NO, and MPO levels. When compared to the DMH group, SMN supplementation could reduce the amounts of these parameters significantly ($p < 0.05$). Additionally, histopathological examination of the liver samples indicated necrosis and periportal inflammation in the DMH group. SMN could ameliorate these changes remarkably.

Conclusion: Results suggest that SMN has the potential to ameliorate the colon carcinogen (DMH)-caused hepatotoxicity in mice bearing colon cancer.

Keywords: Silymarin, 1, 2-Dimethylhydrazine, hepatotoxicity

A-10-1354-1

Plasma MicroRNAs (miR-146a, miR-103a, and miR-155) as Potential Biomarkers for Rheumatoid Arthritis (RA) and Disease Activity in Iranian Patients

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Page | 667

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Introduction: Previous studies have shown that several microRNAs (miRNAs) are dysregulated in the whole blood as well as diverse cells and tissues from rheumatoid arthritis (RA) patients. The aim of the current study was to determine if the expression of miR-146a, miR-103a, and miR-155 in whole blood of RA patients could confer potential markers in evaluating of activity-severity of the disease in RA patients with established disease.

Methods: Whole blood samples were obtained from 30 RA patients and 30 healthy subjects. The RNA content of blood samples was isolated, cDNA was synthesized, and transcript levels of miR-146a, miR-103a, and miR-155 were determined using Real-time PCR. The clinicopathological characteristics of the patients were also evaluated.

Results: It was detected that expression level of miR-146a (fold change=1.85, P=0.004), miR-103a (fold change=2.44, P=0.0018), and miR-155 (fold change=1.94, P=0.0025) were significantly upregulated in the whole blood samples of RA patients in comparison to that of healthy subjects. Expression level of miRNAs was correlated with clinicopathological characteristics of the patients, including Disease Activity Score 28 (DAS28), Simple Disease Activity Index (SDAI), 28Tender Joint Count (TJC-28), 28Swollen Joint Count (SJC-28), C-reactive protein (CRP), Rheumatoid factor (RF), and anti-cyclic citrullinated peptide (anti-CCP) antibodies.

Conclusions: Upregulated levels of miR-146a, miR-103a, and miR-155 in the whole blood samples of RA patients could confer a potential marker of activity-severity of the disease in RA patients with established disease.

Keywords: rheumatoid arthritis, microRNA, whole blood sample, disease biomarker

A-10-1349-2

PCSK9 is highly overexpressed in RAS-mutated colorectal cancer cells

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Page | 668

Introduction: Approximately 53% of colorectal cancer cases are diagnosed with RAS mutation. Oncogenic RAS induces the proliferation and metastasis of cancer cells. However, it has not yet been possible to target RAS proteins directly. Recent studies have shown that Proprotein convertase subtilisin/kexin type-9 (PCSK9) is closely associated with proliferation and migration of the various cancer cells. In this regard in the present study, we aimed to investigate the expression of PCSK9 in three RAS-mutated colorectal cancer cell lines at the basal level.

Methods: Real-time PCR was performed in order to determine the mRNA levels of PCSK9 in three RAS mutant colon cancer cell lines (HCT116, SW480, and LS180) versus SW48 cells, which is the wild type for RAS.

Result: We found that all RAS mutant colon cancer cell lines significantly over-expressed the PCSK9 mRNA compared with SW48 cells.

Conclusion: Based on our findings PCSK9 could be a potential biomarker for RAS-mutated colorectal cancer. However, further studies such as clinical studies are needed to confirm this suggestion.

Keywords: Colorectal cancer, RAS oncogene, PCSK9

A-10-1245-1

The effect of copper nanoparticles in comparison with copper sulfate on growth rate and histological changes of organs in larvae of Amur fish (Ctenopharyngodon idella)

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Introduction: Chemical compounds, including copper oxide nanoparticles, widely used in daily life, enter aquatic ecosystems and make several pathological influences aquatic organism's tissues. Amour or Grass carp fish 'ctenophargodon idella' from Cyprinidae is hydrothermal fish also is an important source of protein for human. Because of its nourishment from aquatic plants it is effective on biological control of aquatic plants.

Methods: Therefore, in this research sulfated copper $CuSO_4$, $5H_2O$ as disinfectants(1,1.5mg/l) and CuO nanoparticle(100,200mg/l) effects on growth index fingerlings Amor were studied. For this aim, 180 Pieces fingerlings Amour (4/5 ± 0.5g) for 20 days in 4 treatment groups compared with the control group were examined.

Results: In the group treated with copper sulfate 1.5 mg / L specific growth, status index, survival percentage and mean weight were lower than other groups. In microscopic studies, in gill, pathological effects contain: hyperplasia, congestion, deformity in secondary lamella and degeneration in Primary lamella, in all treatment groups and especially in copper sulfate with 1/5 mg/L concentration was observed. In all treatment groups and especially copper sulfate groups these were seen: Dilation of bowman's space, hypertrophy, tubular cells of membrane separation, degeneration of the tubules, decrease in tubular lumen, and Tubular necrosis of the kidney. In liver Special in nano treated groups, pyknotic nuclei and vacuole formation, cell swelling was observed.

Conclusion: According this result, it seems that copper sulfate with 1/5 mg/L concentration shows higher influence on growth indicator and survival and had more pathological influences on gill. Thus it is important of usage of suitable concentration of copper sulfate or CuO nanoparticle for any kind of fishes.

Keywords: Copper sulfat, CuO nanoparticle, amour fish (Grass carp), histopathology

A-10-1506-2

Thymoquinone, Protects Against Glycerol-Induced Acute Kidney Injury in Rat

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Introduction: Rhabdomyolysis is a life-threatening disease caused by releasing myoglobin from injured myocytes, which results in acute kidney injury. In this study, the effect of thymoquinone (TQ) on Rhabdomyolysis-induced kidney damage in rats was investigated.

Method: There were five groups rats (n=8): Control, rhabdomyolysis and rhabdomyolysis treated with TQ (15 mg/kg), two days before and four days after glycerol injection. Glycerol were injected intramuscularly on the third day of the experiment for induction of rhabdomyolysis. Renal function parameters on the first, fourth, and seventh days of the experiment were assessed.

Result: Glycerol injection caused a significant increase in serum level of urea, creatinine, creatine phosphokinase and urine output compared to control animals. Administration of TQ significantly decreased serum urea and creatinine on days 4 and 7, creatine phosphokinase on day four, and urine output on day 7 compared to the rhabdomyolysis group.

Conclusion: Thymoquinone, protect the kidney from rhabdomyolysis-induced kidney injury.

Keywords: Thymoquinone, Rhabdomyolysis, Kidney Failure

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A-10-1506-1

The Effect of Thymoquinone on Renal Oxidative Stress in a Rat Model of Unilateral Ureteral Obstruction

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Introduction: Oxidative stress plays a critical role in pathophysiology of ubstructive nephropathy. Unilateral Ureteral Obstruction (UUO) is an experimental animal model for evaluation of mechanisms involved in ubstructive nephropathy. Nigella sativa (NS) is a plant with many pharmacologic properties including antioxidant anti-inflammatory and anti-fibrotic actions. Thymoquinone (TQ) is the main constituent of NS. Current study is aimed to investigate the effects of TQ and renin–angiotensin system (RAS) blockade against kidney oxidative damage following UUO in rats.

Method: In this study, the rats received intraperitoneal injection of losartan (15 mg/kg), captopril (30 mg/kg), and TQ (10 mg/kg) for 18 consecutive days. At the fourth day of the experiment, laparotomy was performed, and the left ureter was ligated. Sham-operated animals received saline as vehicle, and laparotomy without ureteral ligation was done. Blood sample was collected on the first and the last days of the study for assessment of serum levels of urea and creatinine. Renal concentration of malondialdehyde (MDA) and total thiol groups were evaluated in obstructed kidneys.

Results: Two weeks after UUO, there was a significant increase in serum urea and creatinine concentration compared with day 1. Serum urea concentration in TQ treated rats showed no significant change compared with day 1. However, two weeks after UUO in TQ+UUO groups, serum creatinine concentration significantly decreased compared with day 1. In UUO group, MDA concentration showed a significant increase and total thiol content showed a significant decrease compared with sham group. Administration of TQ significantly improved these parameters compared with UUO group.

Conclusions: The current study suggests that TQ is able to improve the UUO-induced oxidative stress.

Keywords: Unilateral Ureteral Obstruction, Obstructive Nephropathy, Thymoquinone, Oxidative Stress

A-10-1538-1

Evaluation of the predictive role of MicroRNA19a as a biomarker in myocardial infarction by induction in animal samples

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Page | 672

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Introduction: Vessel diseases are a broad term for conditions that affect the structure and performance of the heart muscle and are one of the foremost vital causes of death in the world. Biomarkers are essential for the timely diagnosis of cardiovascular damage. Their detection in high-precision and reproducibility tests will provide us with data that cannot be identified through clinical examination. During this study, we tend to investigate whether or not circulating microRNAs, particularly MicroRNA19a, act as potential biomarkers for cardiovascular disease, particularly AMI (myocardial infarction).

Methods: During this case-control method, we divided twenty Wistar rats (weighing 250 to 300 g) into two groups: myocardial infarction and healthy. Standard conditions like twenty-five degrees Celsius and enough water and food are created within the animal room of Mashhad school of medicine. We also use a roc curve to diagnose and evaluate acute and healthy myocardial infarction in rats. 150 mg of isoprenaline was dissolved in 2 ml of distilled water and injected subcutaneously for two days. Weight (rat and isoprenaline) was measured with an electronic scale—twenty-four hours when the last injection of myocardial infarction(CKMB) was confirmed by troponin.

Results: serum mir19a expression in rat myocardial infarction was significantly higher than in the control group, and based on this result, this biomarker can be used to diagnose AMI.

Conclusion: These findings indicate that circulating microRNAs, especially microrna19a, are wonderful candidates for biomarkers of heart disease(AMI).

Keywords: MicroRNA, cardiovascular disease, acute myocardial infarction, microrna19a

A-10-1510-1

A Review of the Structural and Pathogenicity of the Fatal Human Coronaviruses SARS, MERS, and SARS-COV-2: Management and Development of Effective Treatment so far

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Introduction: Most Coronaviruses cause infections of the human respiratory tract, which may be mild; or its rare forms, SARS, MERS, and also the cause of the recent epidemic, SARS-COV-2, are deadly to humans. This study aims to examine the structure and pathogenicity of these three viruses and to summarize the existing knowledge to date about the achievements for prevention in combating them.

Methods: This study, according to the evidence obtained from related articles in PubMed, Nature, and a database such as Viral Zone to examine the exact structure of viruses, prove the similarities and differences in SARS, MERS, SARS-COV-2, and subsequently different pathogenicity.

Results: The entry of The three viruses, SARS, MERS, and SARS-COV-2, into host cells is done using S glycoprotein. This glycoprotein is located in the outer layer of the virus, which identifies the host cell receptors and, under a structural rearrangement, causes the virus membrane to fuse with the host cell membrane, and plays a vital role in causing viral infections. In addition to differences in the genome position of structural and lateral proteins, these three viruses also differ in the number of amino acids of the main S protein. Differences in the protein S sequence lead to disease in the host with severity and involvement of different organs and changes in cytokine levels as well as other vital markers. Host circular RNAs (circRNAs) also play an essential role in the pathogenesis of viral infections. In general, identifying and controlling the levels of these critical markers in response to these three types of viruses can also play an essential role in managing symptoms and developing specific therapies.

Conclusion: The current gap in evidence is the lack of clinical trials to accurately determine the effective drug and vaccine and the optimal and effective dosage and timing.

Keywords: Pathogenicity ‹S protein ‹Virus Structure ‹Marker ‹Treatment ‹SARS ‹MERS ‹SARS-COV-2.

A-10-1215-3

The Effects of Hormonal Activity in Ovarian Cancer

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Introduction: Ovarian cancer is the second most common gynecologic malignancy and the most common cause of gynecologic cancer death in the United States. The cellular origin and pathogenesis of ovarian cancer is not well understood and, interestingly, most tumors appear to originate from other gynecological tissues and involve the ovary secondarily. Morphological and genetic studies have given rise to several hypothesis of origination, particularly for high-grade serous tumors that lack a clear progression mode. also, a hormonal etiology has long been suspected for breast, endometrial and ovarian cancers as several risk factors for each cancer are hormonally related.

Methods: In the current study, keywords including Hormonal Activity, Ovarian Cancer, and Risk Factors were reviewed from the list of Mesh and other credible websites including PubMed, Science Direct and Google Scholar and the data was organized.

Results: Articles show normal endocrine signaling within the pre-menopausal ovary contributes to establishment of a unique and pro-tumorigenic microenvironment. Perturbation of the delicate balance of hormonal signaling factors may thus increase the risk of ovarian tumorigenesis later in life. In addition, experimental studies demonstrate the growth promoting effects of estrogen on ovarian tumors in mice and in human ovarian cancer cell lines. Evidence linking anogens to ovarian cancer includes the presence of anogen receptors on normal ovarian cells as well as benign and borderline tumors, and a doubling of anogen levels during pregnancy is associated with a 40–50% increased risk of borderline serous and invasive mucinous tumors.

Conclusion: Epidemiological research has clearly implicated hormonal and reproductive factors in the pathogenesis of ovarian cancer. The relationship between hormonal microenvironment and tumor is complicated, in no small part because the hormone receptors of many primary tumors and ovarian cancer cell lines have been inactivated either directly or indirectly.

Keywords: Hormonal Activity, Ovarian Cancer, and Risk Factors

The effect of corona virus on kidney biochemical factors

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Introduction: Sars covid 19 virus attacks the lung tissue as the target tissue, but it can involve other organs such as the liver, heart, and kidney. This virus binds to the receptors of Angiotensin_converting enzymes, which are abundantly found in the cells of the proximal tubules of the kidney, and causes failure and damage by direct attack on the kidney. Our research was carried out by measuring some biochemical factors related to the kidney and clinical symptoms of 21 people infected with the covid-19 virus who visited Valiasr Hospital in Tehran. Material and **Methods:** In order to definitively diagnose the corona virus, sputum samples were taken from the throat and end of the nose of the people and it was diagnosed with the PCR test. Then, the serum sample was checked by an autoanalyzer to evaluate biochemical factors, especially blood urea and creatinine levels. The obtained results were compared with the results of the tests before the patients were infected with Covid.

Results: 11 people (38.52 percent) had uremia, 9 people (85/42percent) had high creatinine, and 5 of them were hospitalized in the intensive care unit. 60% of patients had mild proteinuria. 85/71% had high CRP.

Conclusion: Studies have shown that if creatinine remains normal until one week after hospitalization, the kidney prognosis is very good. If creatinine is high at the beginning of hospitalization or one or two days after that, the probability of mortality due to kidney damage is 30 percent. The long-term prognosis of kidney involvement after recovery from the acute phase of Covid-19 is still unclear.

Keywords: Sars covid 19 virus,biochemical factors,kidney

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MiRNAs role in the Biology of Hepatocellular Carcinoma

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Introduction: Hepatocellular carcinoma (HCC) is the most common type of cancer among primary malignant tumors of the liver and is a leading cause of cancer-related deaths worldwide. MicroRNAs (miRNAs) are non-coding small RNAs that regulate the expression of multiple proteins in the post-translation process which exhibit oncogenic or tumor suppressive activities by directly binding to their target messenger and have been identified to play a significant role in HCC regulation. Profiling of deregulated miRNAs in HCC can associate to diagnosis, indicate optimal treatment and predict response to therapy. Furthermore, understanding the main important genes in HCC along with downstream pathways can identify possible miRNAs as therapeutic candidates.so this study aims to investigate miRNAs involvement in the biology of PC associated with their pathways.

Methods: MicroRNA specifications was accrued by using mirbase, HD and miRdSNP. The valid and predict genes obtained from miRTarBase, MIRWALK2.0, TargetScan. To identify common target genes between MiRNAs, Venn diagram used. GEPIA2 used to investigate gene expression in normal and pancreas tumor tissue. Finally, pathways archived from KEGG and David for genes with high expression difference.

Result: The result dedicated that mir-149-3p , mir-340-3p, and mir-221-3p by inhibiting Ras which actives Raf1, MEK, ERK through phosphorylation prevent proliferation of cancer cell and angiogenesis. IKK, NFkB were inhibited by blocking PI3K, which actives Ras. So MYC, BCL through inhibition cell survival, suppress cancer. Mentioned microRNAs by inhibiting Ras, PI3K, IKK, NFkB through preventing cell cycle, prevent cancer development.

Conclusion: multiple signaling pathways are involved in the pathogenesis of HCC, such as JNK, PI3K/AKT, nuclear factor kappaB (NF-κB) in which mir-149-3p mir-340-3p,mir-221-5p by effecting on Ras, IKK, NFkB1, PI3K inhibit proliferation, angiogenesis and cell survival. Mentioned microRNAs by acting as tumor suppressor prevent cancer development and tumor spread by inhibiting proliferation of cancer cell, angiogenesis and sell survival.

Keywords: Hepatocellular carcinoma, Signaling pathways, MicroRNA, Tumor suppressor

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Alantolactone; as a potent anti-metastatic sesquiterpene lactone through the STAT3 signaling pathway

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Introduction: Metastasis is one of the most important challenges in cancer treatment, and it is the reason for mortality in 90% of cancer patients. Understanding the molecular mechanisms underlying in metastasis can be very effective in tumor progression. STAT3 signaling pathway is one of the effective signaling pathways in malignancies. This signaling pathway is constitutively activated in various type of tumors and plays a very crucial role in tumor metastasis. Cancer stem cells (CSCs) and Epithelial-to-mesenchymal transition (EMT) are the two main ivers of tumor metastasis. Accumulating evidence demonstrated that the STAT3 signaling pathway plays a key role in inducing EMT and regulating CSCs. Therefore, it can be a promising therapeutic target in the treatment of metastatic tumors. Recent research has revealed that alantolactone (ALT), a sesquiterpene lactone isolated from the roots of Inula helenium, is one of the STAT3 signaling pathway inhibitors. Several studies show that this compound inhibits several of the processes involved in tumor progression and, more importantly, metastasis by inhibiting STAT3 signaling pathway. As a result, ALT can be evaluated further as an anti-metastatic compound in the treatment of various types of metastatic tumors.

Methods: We performed a comprehensive search of the scientific data published on molecular mechanism of ALT on STAT3 signaling pathway from various databases, including Google scholar PubMed, Web of Science , and Scopus.

Results: The results indicated that ALT inhibits STAT3 activation by suppressing STAT3 phosphorylation at tyrosine 705. Furthermore, ALT inhibits the translocation of STAT3 into the nucleus, DNA-binding activity, and ultimately inhibits its target gene expression. Studies reported that ALT can suppress the expression of EMT markers, CSCs markers, and ECM degradation enzymes in tumors.

Conclusion: Given the role of the STAT3 signalling pathway in metastasis, inhibiting this with ALT could be an efficient treatment strategy in metastatic tumours.

Keywords: Metastasis, STAT3 signaling pathway, Sesquiterpene lactone, Alantolactone

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Fabricating ZSM-5 Zeolite/ Polycaprolactone Nano-fibers Co-loaded with Dexamethasone and Ascorbic Acid: Potential Application in Osteogenic Differentiation of Human Adipose-Derived Stem Cells

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Introduction: Bone is a complex, elastic, and perfused tissue that can only regenerate in a limited region over life. As a result, the most suited and preferable therapies for this issue are bone grafts or bone. However, their application has been restricted due to donor-site morbidity, host immunological responses, graft scarcity, and disease transmission risk. The ZSM-5 zeolites with nanopores structure as a drug delivery system provide an appropriate drug loading process, cellular absorption, and the potential to administer several pharmacological compounds at variable release rates simultaneously. Besides, surface modification of zeolite structure using different surfactants and polymers can be improved their performance as efficient drug delivery systems. In this study, we introduced a novel scaffold where the organized release of two bioactive agents (DEX and ASC) was succeeded by using a composite ZSM-5/PCL-PEG NF through electrospinning.

Methods: The fabricated NF was characterized by FTIR, BET/BJH, and FE-SEM analyses. In vitro, drug release studies were followed to evaluate the efficiency of NF scaffolds as drug delivery systems. Osteogenic differentiation and osteogenesis of this scaffold were determined by the evaluation of the adhesion, proliferation, and osteogenic differentiation of human adipose-derived stem cells (hADSCs) counting ALP activity and extracellular matrix calcium content.

Results: After 14 and 28 days of incubation of hADSCs with DEX/ASC@ZSM-5/PCL-PEG NFs and other NFs, the results of MTT, PicoGreen, qPCR, and alkaline phosphatase (ALP) experiments revealed that hADSCs cultured on the DEX/ASC@ZSM-5/PCL-PEG NFs had superior cell adhesion, metabolic activity, and proliferation percentage compared to other forms of NFs. Furthermore, DEX/ASC@ZSM-5/PCL-PEG NFs displayed high osteogenic differentiation capability on hADSCs.

Conclusion: These results indicated that ZSM-5/PCL-PEG NFs could be used to develop a novel platform for bone tissue regeneration and engineering by facilitating the sustained/controlled release of therapeutic compounds.

Keywords: Dexamethasone, Ascorbic acid, ZSM-5 zeolite, Osteoblastic differentiation, Electrospun nanofibers.

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Therapeutic Potentials and Pharmacological Effects of Luteolin

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Luteolin belongs to a group of naturally occurring compounds called flavonoids that are found widely in the plant kingdom. It is often found in combination with glycosides in many fruits, vegetables and plants. Preclinical studies have shown that this flavone possesses a variety of pharmacological activities, including antioxidant, anti-inflammatory, antiviral, anticancer, anti-atherosclerotic, anti-diabetic and neuroprotective effects. Many researchers have revealed that the above mentioned pharmacological actions are mainly due to its antioxidant property. But, luteolin has a very limited bioavailability, which consequentl affects its biolofical properties and efficacy. To overcome this issue, different strategies are needed like implication of the novel lipid based nanocarriers and nanomaterials. The present review is focused on the therapeutic potential of luteolin in different diseases. This study suggested that oral supplementation of luteolin might be a potential therapeutic strategy for the teatment and/or prevention of disease.

Keywords: Luteolin, Antioxdant, Cancer, Atherosclerotic

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MicroRNA regulation of leukemia in WNT pathway

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Introduction: leukemia is a clonal disorder that results from genetic and epigenetic changes in a hematopoietic stem or progenitor cells that disrupt main processes such as self-renewal, proliferation, and differentiation which has several critical signaling pathways regulating stem or progenitor cell proliferation, hematopoiesis, self-renewal, tissue repair, and apoptosis A novel group of gene expression regulators is a class of small non-coding RNAs of 18-24 nucleotides in length, function to post transcriptionally regulate protein expression termed microRNAs (miRNAs). MiRNAs can cause gene silencing through degradation of target mRNAs or blocking of translation. Dysregulated expression of miRNAs has been shown in various human diseases, such leukemia. So this study aims to investigate the relationship between leukemia and miRNAs in associated pathways.

Method: By using mirbase, HMDD and miRdSNP, miRNA properties were obtained. The miRTarBase, MIRWALK2.0, TargetScan, DIANA Tools target genes were identified. Venn diagram used to identify common target genes between MiRNAs. Using DAVID and KEGG, signal paths were obtained and the pathways associated with leukemia were interpreted. The gene network was obtained through GENE MANIA.

Result: The result demonstrated that has- mir198, has-mir-148b, has-mir-222 and has-mir-199a inhibit RAS by blocking Raf-1, MEK1/2 which active ERK, SRF and CFOS through phosphorylation in MAPK and Gap junction pathways. Mentioned microRNAs prevent allergic asthma by inhibiting (IL1b-IL6-IL15-lif-tnf) and by blocking MKK4/7, JUNK1/2 in TNF pathway. WNT signaling is critical for maintaining homeostasis that fusion protein BCR-ABL may actively adjust β-catenin levels in cells and FoxM1/ β-catenin interaction is essential for controlling canonical WNT signaling, cancer proliferation, and tumorigenesis.

Conclusion: The stimulation of WNT signaling is a frequent, varied feature of all leukemia types in which mir198, mir-148b, mir-222 and mir-199a act as tumor suppressor through the WNT signaling pathway in leukemia.so miRNAs can act as potential biomarkers in WNT pathway by inhibiting leukemia progression.

Keywords: Leukemia, MAPK pathway, MicroRNA, WNT pathway

Genetic Cassettes Profiling of Class I Integron and Antimicrobial Susceptibility Profiles Among Pseudomonas Aeruginosa Isolates Collected from Patients in North of Iran

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Introduction: Pseudomonas aeruginosa is an opportunistic nosocomial bacterium, especially in infection wards andamongpatients with burns. The present study adessed the molecular investigation of the gene cassettes of Class I integrin (intI) and its relationship with multiple ug resistance in clinical samples of P. aeruginosa isolated from Babol hospitals in north of Iran.

Introduction: This study aimed to detect the frequency of intI and gene cassettes in the clinical isolates of P. aeruginosa.

Methods: In this study, from 75 clinical samples, 30 strains were identified using specific biochemical methods. After determining antibiotic susceptibility using disk diffusion and agar dilution, the frequency of the intI gene and its gene cassettes were determined using the polymerase chain reaction (PCR) method.

Results: The highest resistance rate was observed for cefotaxime, ampicillin, and nitrofurantoin using disk diffusion and agar dilution methods. The molecular analyses revealed that 60% of the isolates had the intI genes. The frequency of the aadB, dfrA1, and bla-OXA30 genes were 61, 66, and 33%, respectively.

Conclusions: The high resistance of Pseudomonas isolates is due to the presence of intI and its gene cassettes. Considering their high resistance to cefotaxime, gentamicin, ampicillin, and imipenem in hospitals, selecting appropriate ugs or generally changing the treatment course for patients is possible to prevent the spread of resistance inducing genes and the development of nosocomial infections.

Keywords: Pseudomonas aeruginosa, Class 1 Integron, Gene Cassette, Antibiotic Resistance

Recombinant production of E. coli Asparginase in E. coli BL21DE3

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Introduction: L-asparaginase is a drug enzyme derived from E. coli and is one of the drugs used to treat acute lymphoblastic leukemia. Asparaginase is an enzyme that catalyzes the amino acid hydrolysis of asparagine. Many tissues are able to synthesize asparagine from glutamine, but leukemia cells are unable to synthesize asparagine. Decreased blood asparagine after the use of the asparaginase can lead to death for these cells.

Methods: The asparaginase gene of E. coli was amplified using PCR technique. After purification, the gene was cloned into pET28a vector and transformed into a bacterial host. After transformation, different protein expression conditions were investigated for optimization. Recombinant enzyme expression was confirmed by SDS-PAGE and Western blotting. The asparaginase enzyme was then purified by affinity chromatography using a column containing Ni-NTA resin and hybrid method and finally its enzymatic activity was investigated.

Results: The best production of asparaginase enzyme in E. coli was at 37 ° C, 1 mM concentration of IPTG and incubation 20 hours after induction. Insoluble asparaginase enzyme was purified using a Ni-NTA column and the refolding process was performed on the column. The results showed that the refolded enzyme is active and its activity is concentration-dependent.

Conclusion: Due to the great importance of asparaginase production in Iran and the need of a group of patients to use this enzyme, in this project, by optimizing the expression and purification process, L-asparaginase enzyme was produced on a laboratory scale.

Keywords: Acute lymphoblastic leukemia, Asparaginase, recombinant protein

rs11895168 C allele and the increased risk of breast cancer in Isfahan population

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Introduction: Cancer of the breast is the most common malignancy among women, as well as cancers of the ovary. About 5 -10% of breast cancer incidences are caused by these elements, which are inherited through variants in breast cancer-risk enhancing genes, with ErbB4 being one of them. To date, some of the single nucleotide polymorphisms in the EebB4 gene have been studied for their possible association with breast cancer risk. There has been no study on the importance of rs11895168, a microRNA-related SNP located in ErbB4 30UTR, in breast tumors. Our study investigated the frequency and association of rs11895168 with breast cancer. Materials and **Methods:** With Tetra-primer ARMS PCR, 364 breast cancer samples and 192 healthy samples were genotyped for rs11895168. Using genotype frequencies, rs11895168 was associated with risk of breast cancer and also clinicopathological characteristics of patients.

Results: Different alleles at rs11895168 affect the binding strength of miR-1276, a potential tumor suppressor, according to our in silico studies. In a statistical analysis, genotypes harboring the rs11895168 C allele were significantly associated with increased breast cancer risk.

Conclusion: In addition to the elevated risk of breast cancer, the rs11895168 C allele is significantly associated with ER/PR tumor cell positivity.

Keywords: Breast cancer- ErbB4- microRNA-related single nucleotide- polymorphism- rs11895168- Tetra-primer ARMS-PCR

Effects of palmitate and chicoric acid on Smad2/3 and p-Smad2/3 protein levels in the PBMCs of newly diagnosed patients with type 2 diabetes

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Introduction: Transforming growth factor β (TGF-β)/Smad signaling pathway has an important role in the etiology of type 2 diabetes (T2D). Binding of TGF-β1 to the receptors (TβRI and TβRII) leads to phosphorylation and activation of Smads. So, targeting this pathway is a new therapeutic approach in the improvement of T2D. Chicoric acid (CA) is a polyphenol component with a variety of functions such as anti-oxidant, anti-inflammatory and anti-diabetic. Although the molecular mechanisms by which CA improves diabetes has not been determined exactly. This study was aimed to evaluate the effects of palmitate and CA on Smad2/3 and p-Smad2/3 protein levels in peripheral blood mononuclear cells (PBMCs) of newly diagnosed patients with T2D.

Methods: 20 patients with T2D, aged between 40 and 60 years, were recruited in this study. PBMCs were isolated from whole blood samples immediately and then treated with palmitate and CA as follows: control group (untreated, treated with bovine serum albumin (BSA) 1 % for 12 h), CA group (treated with 50 µM CA for 6 h), palmitate group (treated with 500 µM palmitate for 12 h), palmitate + CA group (pretreated with 500 µM palmitate for 12 h and then treated with 50 µM CA for 6 h). Then, Smad2/3 and p-Smad2/3 protein levels were measured by western blotting. **Results:** p-Smad2/3 protein levels were significantly increased in palmitate group compared to control group (p < 0.001). Unlike palmitate, p-Smad2/3 protein levels significantly were decreased by CA (p < 0.05). Also, CA attenuated palmitate-increased p-Smad2/3 protein level however it was not significant. Furthermore, the results failed to indicate significant difference in Smad2/3 protein levels between groups.

Conclusions: These findings reveal that CA could be as a novel TGF-β/Smad signaling inhibitor. Therefore, CA would be suggested as a novel agent for the T2D therapy.

Keywords: Type 2 diabetes (T2D), Palmitate, Chicoric acid (CA), Smad2/3, p-Smad2/3

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Alteration of ATP7b gene expression and histological changes during copper toxicity in the testes of rates under vitamin C treatment

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Page | 685

Introduction: Copper is essential trace nutrients playing important role in general health and fertility. Copper in large quantities can be a reason for fertility diseases. ATP7b is a metal transporting protein that controls the cellular disposition of copper. This study aims to analyze the histological changes and expression profile of ATP7b in rat testes following copper toxicity and treatment with vitamin C.

Methods: Twenty-four male rats were randomly assigned into four groups (n=6). Control, copper sulfate (10 mg/kg; i.p), vitamin C (100 mg/kg; i.p), copper sulfate +vitamin C (100mg/kg; i.p) doses for 10 days. After receiving treatments, the animals were decapitated, their testes were removed, the right testis was put in formalin (15%) for histological studies, and the other was frozen at -80°c temperature for analyzing the gene expression of ATP7b assayed using RT- PCR.

Results: there is no significant difference between the control group and the other groups which have received copper sulfate, vitamin C and copper sulfate+ vitamin C while, there is small changes in gene expression rate during this period. Also, there were histological changes in the level of blood vessels and cell morphology compared to the control group.

Conclusion: During copper toxicity, the copper transporter (ATP7b) level is stable, also vitamin C treatment is modulated and approaches the control group level. Copper toxicity induces significant pathophysiological changes in the testes of rats.

Keywords: copper transporter gene, histopathology, ascorbic acid, genital system

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in silico approach for the epitope-based peptide vaccine against COVID-19

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Introduction: COVID-19 is still a deadly disease that remains yet a major challenge for humans. Vaccination is currently the only effective method to prevent COVID-19, and structural proteins are critical targets for vaccine development. The CoV envelope (E) protein is a small, integral membrane protein involved in several aspects of the virus' life cycle, such as assembly, budding, envelope formation, and pathogenesis. This study aimed to predict the protective peptide with bioinformatics methods and resources for vaccine development.

Methods: molecular docking has been widely utilized to predict the binding structures of protein–peptide complexes. In order to investigate the model of interaction of the peptide with HLA-A*0201, the PEP-FOLD server at: https://bioserv.rpbs.univ-paris-diderot.fr/services/PEP-FOLD3 generates three-dimensional structure of peptide. Crystal Structure of HLA-A*0201 with 7KGO code and Xray diffraction at 2.15 Å resolution was received from the https://www.rcsb.org. HADDOCK 2.2 (http://haddock.science.uu.nl/services/HADDOCK2.2) was used to execute the docking simulations program then analyzed in DS Visualizer 3.5 software.

Results: The binding energy of the best bound conformation of peptide was -223.07 kcal/mol. The Ligand RMSD was 78.93 Å. Binding model and the best docked pose of peptide showed 2 hydrogen bonds by GLN155, and GLU166 and hydrophobic interactions with Thr163, His114, Tyr99, Arg97, Gln155, Leu156, His70, Ala69, Tyr159, Glu63, Trp167 and Arg170.

Conclusion: The in silico molecular docking study revealed that studied peptide, have good affinity toward HLA-A*0201 as receptor. Therefore, this peptide can be used in vaccine design.

Keywords: COVID-19, vaccine, molecular Docking, in silico

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Expression and purification of recombinant isocitrate dehydrogenase in E. coli BL21(DE3)

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Introduction: The tricarboxylic acid (TCA) cycle is for the aerobic oxidation of fuel molecules. Isocitrate dehydrogenase (IDH) is one of the important enzymes of this cycle. IDH catalyzes a fundamental biological reaction which is necessary for producing molecules that are responsible for providing cellular energy. During the oxidative decarboxylation, IDH enzyme catalyzes isocitrate and NAD+/NADP+ to alpha-glutarate and NADH/NADPH. Isocitric acid as a substrate for IDH is found in a large number of natural and processed foods, beverages, candies and dairy products due to its flavoring and preserving properties. Therefore, over the past two decades, IDH has been considered as an important compound for measuring isocitric acid in the food industry. **Methods:** In this study, we performed codon optimization of IDH from Yarrowia lipolytica yeast. The gene was synthesized and cloned in PET28a vector and transformed to a BL21 strain of E. coli. Expression conditions were tested at various temperatures and concentrations of IPTG and Lactose as inducers. The gene was purified by Ni-Sepharose column using different buffers. Expression and purification analysis was determined by SDS-PAGE. The activity was monitored as a change in absorbance at 340 nm due to the isocitrate-dependent rate of NADP+ reduction. **Results:** The best expression condition was at 22 °C for 16 h using 0.3 mM IPTG as inducer. Recombinant protein was expressed as soluble in supernatant. The best activity of enzyme was seen at room temperature and in pH=10 (optimum PH). **Conclusion:** The results showed that IDH gene was successfully expressed in E. coli BL21 as soluble form. The purified IDH by the Ni-Sepharose column showed suitable activity.

Keywords: Isocitrate dehydrogenase, Yarrowia lipolytica, TCA cycle, Cloning, Expression

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Combination of 5-azaytidine and hanging drop culture convert fat cell into cardiac cell

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Introduction: Despite considerable advances in the treatment of cardiovascular disease, it remains to be a leading cause of death with an ever-increasing incidence in the global population. One of the promising approaches for the treatment of cardiac disease is stem cell therapy.

Methods: In this study, we compared the cardiomyogenic differentiation rate, from human adipose-derived stem cells (hADSCs) in a three-dimensional (3D) hanging drop (HD) spheroid culture system, versus a two-dimensional (2D) culture condition at different concentrations of 5-azacytidine (5-Aza). 5-Azaytidine (5-Aza) is a pyrimidine nucleoside analogue of cytidine that initiates cell differentiation programs through DNA demethylation. The hADSCs were isolated and cultured both in 2D and 3D HD conditions, with either 10 or 50 µM concentrations of 5-Aza. Then DNA content, gene expression, and protein content were analyzed.

Results: 3D HD culture resulted in a higher percentage of cells in G0/G1 and S phase in the cell division cycle, whereas 2D culture led to a greater percentage of cells in the G2/M phase. A significantly higher gene expression rate of HAND1, HAND2, cTnI, Cx43, βMHC, GATA4, NKX2.5, and MLC2V was observed in HD treated with 50 µM 5-Aza. This was confirmed by immunocytochemistry.

Conclusions: These findings suggest that 50 µM concentration of 5-Aza can induce hADSCs to differentiate into cardiomyocytes. The differentiation rate was significantly higher when accompanied by the 3D HD culture system. This work provides a new culture system for cell differentiation for cardiovascular tissue engineering.

Keywords: 3D culture, 5-Azaytidine, cardiac, cardiac cells, cardiac disease, hanging drop culture, human adipose derived stem cells, human adipose stem cells, myocardium, regeneration, scaffold, stem cells

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Deliberation the predictive role of microRNA 21 as a biomarker in animal model induced myocardial infarction

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Introduction: Cardiovascular disease is a group of diseases that occur in the heart or arteries. CVD is one of the most important life threatening factors in human societies and leads to many deaths every year. Various factors increase the risk of developing the disease, including heredity, age, and sex, which are not available to individuals and cannot be changed. Also, factors such as high blood pressure, obesity, and smoking are available to individuals and can change. To diagnose cardiovascular disease, various indicators such as troponin and CKMB can be used, and even an electrocardiogram can be used. In recent years, a series of biomarkers called microRNAs have been used. In this study, we tried to use a special type of these biomarkers called miR- 21-3P for accurate and timely diagnosis of acute myocardial infarction.

Methods: Blood samples were taken from two groups, one of which was a healthy group and the other group included rats treated for acute myocardial infarction. After confirming the stroke in the treatment group, we used a real-time PCR device to measure miR-21-3p. We also used a ROC curve to diagnose and evaluate acute and healthy myocardial infarction in rats.

Result: In the treatment group, the expression level of CKMB and troponin levels was significantly higher than the healthy group ($P<0.001$). Similarly, the serum level of Mir-21 expression in sick mice was significantly higher compared to the healthy group ($P<0.05$).

Conclusion: The expression of this selective biomarker of Mir21-3P was excessive and this indicates the special importance of this microRNA in the diagnosis of acute myocardial infarction.

Keywords: Key words: Cardiovascular disease, miR-21, Acute heart attack, MicroRNA, AMI

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Evaluation of anti-diabetic activity of chitosan-encapsulated cinnamon extract on streptozotocin-induced diabetic rats

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Page | 690

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Introduction: Evaluation of anti-diabetic activity of chitosan-encapsulated cinnamon extract on streptozotocin-induced diabetic rats Background: Cinnamon has powerful anti-diabetic properties. Encapsulation is a technology in which target compounds are coated by wall compounds to form capsule particles. Chitosan is a natural polymer that has been extensively researched due to its enormous potential in the fabrication of nanocarrier systems.

Methods: Cinnamon encapsulation based on chitosan ionic gelation by tripolyphosphate anions (TPP) and study of physicochemical properties of nanoparticles with DLS and TEM and determine the release characteristics of the drug in the buffer. Animals were fasted overnight and diabetes was induced by a single intraperitoneal injection of a freshly prepared solution of streptozotocin (55 mg/kg b.w) in citrate buffer (pH 4.5). After 72 hours, animals with fasting blood glucose levels greater than 250 mg / dL were considered diabetic. The control groups included healthy and diabetic, and the treatment group received chitosan-encapsulated cinnamon daily by gavage for 4 weeks.

Results: Encapsulated cinnamon had a positive effect on biochemical parameters such as FBS, insulin, HA1C compared to the diabetic control group. TEM results showed that encapsulation was performed and DLS test confirmed the presence of particles in the nanoparticle. In the release profile, a significant amount of cinnamon was released within 24 hours.

Conclusion: Chitosan-encapsulated cinnamon nanoparticles were successfully prepared by ionic gelation method. The level of blood glucose content was significantly reduced and showed anti-diabetic activity in nanocapsule-treated diabetic rats. Therefore, nanoparticles with high encapsulation efficiency and continuous release were introduced as a potential anti-diabetic drug.

Keywords: Cinnamon, Chitosan, Diabetes, Encapsulation, Drug release

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Effects of carfilzomib alone and in combination with cisplatin on the cell death in cisplatin-sensitive and cisplatin-resistant ovarian carcinoma cell lines

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Introduction: Previous studies on the ef ficacy of platinum-based drugs and selective inhibitors of protea- some have revealed promising outcomes. This study is aimed to evaluate the effects of the combination of cis- platin and car filzomib on the cell death induction and drug ef flux transporters expression in cisplatin-sensitive (A2780s) and cisplatin-resistant (A2780cp) ovarian cancer cells lines.

Methods: MTT cytotoxic assay was conducted to determine the cytotoxicity. Drug interactions were analyzed based on Chou-Talalay's principles and real-time PCR analysis was performed to determine possible alterations in mRNA levels of MRP1 and BCRP.

Results: A2780s cells were more susceptible to both cisplatin and car filzomib while analyses of drug inter- actions between the two agents showed synergistic effects in all affected fractions of drug-treated A2780s and A2780cp cells (CI<0.9) with the combination indices being significantly lower in A2780cp cells (p < 0.01). We also found that although mRNA levels of BCRP and MRP1 were significantly altered in both cells exposed to each drug alone, only the combination regimen was able to significantly reduce the mRNA levels of these genes in A2780cp cells (p<0.001).

Conclusion: This combination might be a potential strategy for suppressing cell growth via downregulating the drug ef flux transporters expression, especially in cisplatin-resistant ovarian cancer cells.

Keywords: cisplatin, carfilzomib, drug combination, ovarian neoplasms

The value of mRNA expression of S100A8 and S100A9 as blood-based biomarkers of inflammatory bowel disease

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Introduction: and study aims Non-invasive biomarkers of inflammatory bowel diseases (IBD) are of critical importance. Here, we evaluated the S100A8 and S100A9 mRNA expression, as the heterodimers of calprotectin, in the blood leucocytes of IBD patients to find how their expression associates with the disease characteristics.

Methods: In this cross-sectional study, 59 IBD patients and 30 healthy subjects were included. The flare and remission phases of disease were identified in 46 and 13 patients, respectively. Blood leucocytes were isolated, and the S100A8 and S100A9 mRNA expression were evaluated in the isolated leucocytes using relative quantification real-time PCR.

Results: The mean S100A8 and S100A9 mRNA expression were significantly higher in IBD patients than in the controls ($p = 0.03$ and $p = 0.02$, respectively). The mean S100A8 and S100A9 mRNA expression were significantly higher in the flare phase of the disease compared with the remission phase ($p = 0.01$ and $p = 0.007$, respectively). S100A8 distinguished IBD patients from controls with the sensitivity and specificity of 73% and 64%, and flare phase of disease from remission with the sensitivity and specificity of 67% and 62%. On the other hand, S100A9 distinguished IBD patients from controls with the sensitivity and specificity of 81% and 70%, and flare phase of disease from remission with the sensitivity and specificity of 68% and 64%.

Conclusion: The S100A8 and S100A9 mRNA are differentially expressed in blood leucocytes of IBD patients compared to healthy controls as well as active versus quiescent disease. Thus, they can be potentially used as a blood-based biomarker in the monitoring of IBD.

Keywords: IBD.S100A8 mRNA, S100A9 mRNA, Non-invasive biomarker

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Investigating The Role of hsa-miR-190 as Therapeutic target in JAK/STAT pathway in Autoimmune diseases

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Introduction: Autoimmune diseases are increasingly recognized as disease entities in which dysregulated cytokines contribute to tissue-specific inflammation. In organ-specific and multi organ autoimmune diseases, the cytokine profiles show some similarities. MicroRNAs are small non-coding RNAs that regulate post-transcriptional gene expressions that play an important role in fibrogenic process in multiple organs.so this study aims to investigate the relationship between autoimmune diseases and microRNAs in JAK/STAT pathway.

Method: By using mirbase, HMDD and miRdSNP, miRNA properties were obtained. The miRTarBase and MIRWALK2.0 target genes were identified. Venn diagram used to identify common target genes between MiRNAs. Using DAVID and KEGG, signal paths were obtained and the pathways associated with diabetes were interpreted.

Result: We identified hsa-miR-190-5p as the best miRNA, its target genome and associated cell signaling pathways. This results that hsa-miR-190 phosphorylates JAK1, JAK2, and Tyk2, which phosphorylate intracellular tyrosine residues that serve as docking sites for STAT3 in Autoimmune diseases. JAK and STAT are expressed by hsa-miR-190 and directly coupled to this receptor-binding of the cytokine (IL-6 or IL-11) to its receptor (IL-6R or IL-11R) triggers the homo dimerization of GP130.The binding of ETI/Ang II which is activated by hsa-miR-190, induces the phosphorylation of tyrosine in the JAK2 kinases, which in turn activates STAT1 and STAT3.

Conclusion: Autoimmune diseases is caused by overexpression of the IL-6 receptor α (IL6Rα) on the CD4+ T cells surface. That increases phosphorylation of pSTAT3 in response to IL-6. Blockade of STAT3 phosphorylation can reverse the resistance of the effector T cells. The JAK/STAT pathway is crucial in transmitting signals from many cytokines and growth regulating gene expression and functions. In this study we found that factors into the nucleus the role of hsa-miR-190 in autoimmune diseases is associated with the JAK/STAT pathway in which hsa-miR-190 might be a novel bio-marker in autoimmune diseases.

Oxidative balance and its role in health and disease

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Oxidative balance and its role in health and disease Summary Oxidative stress is a phenomenon caused by an imbalance between the production and accumulation of reactive oxygen species (ROS) in cells and tissues and the ability of a biological system to detoxify these reactive products. ROS can and do play several physiological roles (i.e. cell signaling) and are usually produced as byproducts of oxygen metabolism. However, environmental stressors (eg, UV, ionizing radiation, pollutants, and heavy metals) and xenobiotics (ie, antiblastic drugs) contribute to increased ROS production, thus causing an imbalance that leads to cellular damage and becomes tissue (oxidative stress). Several antioxidants have been used in recent years due to their actual or potential beneficial effects against oxidative stress, such as vitamin E, flavonoids, and polyphenols. While we tend to describe oxidative balance as equally harmful to the human body, it is true that it is used as a therapeutic approach to treat clinical conditions such as cancer with a certain degree of clinical success. In this review, we describe the latest findings in the field of oxidative balance and highlight its good and bad aspects for human health.

Keywords: review; Oxidative stress; healthy diet; antioxidants; healthy lifestyle

Keywords: Oxidative stress ،healthy diet ،antioxidants ،healthy lifestyle

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Comparison of IgG against COVID-19 between postmenopausal and non-menopausal women vaccinated with Sinopharm vaccine

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Introduction: Since December 2019, the coronavirus disease (COVID) has spread among the people of the world. Past studies have shown that viral diseases are more common and the immune response is stronger among menopausal women than non-menopausal women. Therefore, in this study, we aimed to compare the amount of IgG against COVID-19 between postmenopausal and non-menopausal women vaccinated with Sinopharm vaccine.

Methods: In this case-control study, 90 females vaccinated with the Sinopharm vaccine were randomly selected during February to April 2022 that including 45 menopausal participants as case group and 45 non-menopausal controls. Then, the demographic characteristics were obtained and blood samples were taken from all subjects. A complete blood count (CBC) were carried out and finally the levels of IgG against COVID-19 were measured by using the enzyme-linked immunosorbent assay (ELISA) method.

Results: The mean age was 33.3±7.3 and 60.2±7.02 for control and menopause women. A significant difference was found between two groups for the levels of IgG antibodies against COVID-19 (P=0.002, 17.2±9.83 for case group and 10.2±9.80 for control subjects). After adjusting, IgG against COVID-19 was significantly correlated to the menopausal state (OR [CI] = 1. 08 [1.03–1. 15]; P= 0.003).

Conclusions: The results of this study showed that menopausal women had higher levels of IgG against COVID-19 in comparison with non-menopausal females. However, more complementary studies are needed in this regard.

Keywords: COVID-19, Menopause, Women, IgG against COVID-19

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Effects of arbutin on glucose uptake by glucose transporter 4 (GLUT4) and its cytoprotective properties in L6 skeletal muscle cell line

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Page | 696

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Introduction: It has been well known that oxidative stress and increased intracellular reactive oxygen species (ROS) have a pivotal role in disrupting the insulin signaling pathways leading to cellular insulin resistance. In this study, we evaluated arbutin effects on glucose uptake by GLUT4 and cytoprotective properties in the L6 skeletal muscle cell line.

Methods: The effect of arbutin and t-BHP on glucose uptake in cultured L6 cells was investigated by monitoring the fluorescence of 2-NBDG in the L6 cells using flow cytometry. We also evaluated gene expression levels of GLUT1 and GLUT4 in the L6 cells by q-RT-PCR analysis.

Results: The results from the study demonstrated that the optimum ROS generation occurred 3 hours after 100 µM t-BHP treatment and pretreatment with arbutin (500 and 1000 µM) significantly inhibited the t-BHP induced ROS generation ($P<0.05$). Our result indicated that 3 hours pretreatment of L6 cells with 1000 µM of arbutin prior to 50 µM t-BHP significantly increased glucose uptake than the 50 µM t-BHP alone group ($P<0.05$). The results demonstrated that pretreatment with 1000 µM arbutin saves glucose uptake in the arbutin + t-BHP group than the t-BHP group. An increase in the uptake of 2-NBDG by L6 cells can be associate with increased expression of GLUT4 and GLUT1.

Conclusion: These findings may suggest that arbutin promotes glucose uptake in t-BHP-treated L6, probably through inducing GLUT1 and GLUT4 expression.

Keywords: ROS, Arbutin, t-BHP, GLUT4, Glucose uptake