The 15th Iranian National Congress of Biochemistry & 6th International Congress of Biochemistry and Molecular Biology

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President of Congress

Professor. Tahereh Changiz

In the name of God

Dear Distinguished Guests

It is a blessing to have the honor to inform you that the 15th Biochemistry Congress and the 6th **International Congress of Biochemistry and Molecular Biology** will be held in the beautiful and historical City of Isfahan. My colleagues and I are grateful to the almighty for the opportunity of hosting distinguished professors, colleagues and students from 25th to 28th August. This scientific event provides an opportunity for the scientists and researchers from Iran and all over the world to provide information updates, exchange of views and to get acquainted with the recent advances in biochemistry, molecular biology and related sciences.

Therefore, we invite all the professors and experts of biochemistry, molecular biochemistry and other related fields to make the congress more fruitful and magnificent with their own effective presence and constructive partnership. Exchange of information on the recent advances in biochemistry and molecular biology can lay the basis for more specialized lab services, broader research activities and growth of the country. It is hoped that the presence of a large number of researches and students in a scientific and intimate atmosphere, combined with the valuable presence of the health and treatment authorities of our country, with help meeting the goals and improve the health policies of our beloved country.

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ID:5

The effect of intraperitoneal injection of lead in different doses on liver function in male Wistar rats

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Objective: The aim of the present study is to examine the effects of lead on serum levels of liver-related parameters in Wistar rats.

Material and Methods: In this study, the effect of intraperitoneal injection of lead in different doses of 4 and 6 mg per kilogram of body weight on liver function in 24 male Wistar rats was studied after a short period (15 days) and long period (60 day) of treatment time. Serum concentration of liver-related parameters was measured at the end of the period. Data were compared using spss18. To examine the results, $P<0.05$ was considered as the level of significance of the differences.

Results: According to the results, it seems that in short term lead has not created significant changes in the average activity of SGOT, SGPT, LDH, and ALP enzymes, total protein, and direct bilirubin between the control and the treatment groups. This is while with the increase in duration of injection in long-term period, these changes are significant. During the test, no deaths were observed in animals.

Conclusion: The results suggest that the changes made by lead on the activity of the enzyme measured depend on the duration.

Keywords: Lead, aspartate aminotransferase, alanine aminotransferase, lactate dehydrogenase, alkaline phosphatase

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ID:14

Palmitate-induced impairment of autophagy turnover leads to increased inflammation in skeletal muscle cells by regulating the oxidative stress process

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Objective: Autophagy is a cellular process activated in response to various stresses such as starvation, hypoxia, and oxidative stress. Autophagy was reported to modulate the inflammatory pathways. However, the role of autophagy in regulation of palmitate-induced inflammation of skeletal muscle C2C12 cells is not known.

Material and Methods: In the present study, we investigated the autophagic pathway in C2C12 cells treated with 0.5mM palmitate. We showed that the protein levels of LC3B and P62 increased after 12h palmitate treatment in C2C12 cells. Besides, inhibition of autophagy by chloroquine (CQ) and activation by rapamycin was associated with elevated mRNA and protein levels of IL-6 and TNF-α inflammatory cytokines in the C2C12 cells. To study the mechanism by which autophagy impairment leads to the activation of inflammatory responses, we measured Reactive oxygen species (ROS) levels in palmitate-treated cells.

Results: It was found that palmitate induces ROS production in C2C12 cells. In the further experiment, we showed that pretreatment of the cells with N-acetyl cysteine (NAC), a ROS scavenger, resulted in reduction of inflammatory responses along with the amelioration of LC3-B and P62 protein in the C2C12 cells treated with palmitate.

Conclusion: These findings suggest that palmitate-induced impairment of autophagy turnover leads to increased inflammation in skeletal muscle cells by regulating the oxidative stress process.

Keywords: autophagy, IL-6, TNF, LC3-B, Oxidative stress

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ID: 17

Evaluation of antiproliferative effect of a new exopolysaccharide produced by Halorubrum sp. TBZ112

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Objective: Microbial exopolysaccharides (EPSs) have several applications in pharmaceutical, nutraceutical and cosmetic industries. In the present study we aimed towards extraction, purification, monosaccharide composition and antiproliferative effect of exopolysaccharides produced by Halorubrum sp. TBZ112.

Material and Methods: The EPS production by Halorubrum sp. TBZ112 was performed in modified marine broth at optimized conditions. The precipitated exopolysaccharides by cold absolute ethanol were dialyzed against distilled water and was finally freeze-dried and weighted. The FT-IR, SEM, high-performance anion exchange chromatography (HPAEC) and high-performance size exclusion chromatography (HPSEC) coupled with multiangle light

scattering (MALS) were performed. Antiproliferative effect of the EPS was done using MTT assay with concentration range of 100-1000 µg/ml in MKN45 and HDF cells for 24 and 48 h.

Results: Halorubrum sp. TBZ112 excreted 480 mg. L-1 of EPS under optimal growth conditions. Analyses by HPAEC indicated that the extracted EPS is a heteropolysaccharide containing ten moieties. The molecular weight of Halorubrum sp. TBZ112'EPS was estimated to be 5.052 kDa. All the EPS sample concentrations had no significant effect on the proliferation of human dermal fibroblast (HDF) and MKN-45 cells (p.value>0.05).

Conclusion: The EPS from TBZ112 is relatively low molecular weight in comparison with other described EPSs isolated from extreme marine habitats and it is the first EPS produced by an extremely halophilic archaeon related to Halorubrum genus. This EPS can be applied as a biocompatible compound and requires more investigations in terms of their biological activities and further chemical structure details.

Keywords: Exopolysaccharide, Halorubrum, Biocompatible, Antiproliferative effect

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ID:23

The effects of vitamin E supplementation on endometrial thickness, and gene expression of vascular endothelial growth factor and inflammatory cytokines among women with implantation failure

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Objective: This research was performed to determine the effects of vitamin E supplementation on endometrial thickness, and gene expression of VEGF and inflammatory cytokines among women with implantation failure.

Material and Methods: A randomized clinical trial was done among 40 women with implantation failure aged 18-37 years old. Participants were randomly divided into two groups: group A (n=20) received 400 IU vitamin E supplements and group B (n=20) received placebo for 12 weeks. Fasting blood samples were taken at baseline and after the 12-week treatment to determine biomarkers of oxidative stress, and gene expression of VEGF and inflammatory cytokines.

Results: After the 12-week intervention, compared with the placebo, women with implantation failure who consumed vitamin E supplements had significantly increased serum vitamin E levels (+18.6±15.0 vs. -1.5±1.0 nmol/mL, P<0.001) and endometrial thickness (+1.1±0.9 vs. -0.5±0.3 mm, P=0.01), and significantly decreased plasma malondialdehyde (MDA) concentrations (-0.4±0.3 vs. +0.4±0.3 µmol/L, P<0.004). In addition, results of RT-PCR demonstrated that compared with the placebo, vitamin E intake downregulated gene expression of oxidized low-density lipoprotein (Ox-LDL) (P=0.008), interleukin-1 (IL-1) (P=0.02) and tumor necrosis factor alpha (TNF-α) (P=0.007) in peripheral blood mononuclear cells of women with implantation failure.

Conclusion: Overall, vitamin E supplementation for 12 weeks among women with implantation failure had beneficial effects on endometrial thickness, MDA values, and gene expression of Ox-LDL, IL-1 and TNF-α.

Keywords: Vitamin E, supplementation, implantation failure, gene expression

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ID:25

Sodium valproate ameliorates Aluminum - induced cell death and oxidative stress in PC12 cells

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Objective: Previous studies have implicated the role oxidative stress in Aluminum (Al)-induced neurotoxicity. Furthermore, recent studies have indicated that sodium valproate (SVP) had neuroprotective effects against oxidative stress. In the current study we aimed to explore whether SVP can exert protective effects against Al-induced cell death, apoptosis and oxidative stress in PC12 cells.

Material and Methods: In this in vitro study PC12 cells were treated with various concentration of Aluminum maltolate (Almal) (100-1500 µM) in the presence and absence of SVP (50-400µM). MTT assay was used to explore the effects of SVP on Almal-induced PC12 cell death. Flow cytometry using 7AAD/annexin-V and 2',7'-Dichlorofluorescin diacetate (DCFDA) were applied to quantify the effects of SVP on Al-induced apoptosis and oxidative stress, respectively. Mitochondrial membrane potential (MMP) was evaluated with a fluorescence microplate reader using rhodamine 123.

Results: A 48 h exposure of PC12 cells to Almal (100-1500 μM) dose dependently reduced cell viability; increased the percentage of apoptotic cells, enhanced oxidative stress and MMP. The effects of Almal at IC50 concentration (1000 μM) on cell death, apoptosis, oxidative stress, and MMP were significantly ($P<0.05$) blunted by SVP in a dose dependent manner.

Conclusion: The findings suggest that SVP can inhibit Al-induced cell death and apoptosis of PC12 cells via ameliorating oxidative stress.

Keywords: Aluminum, Sodium valproate, Oxidative stress, Apoptosis, PC12 cells

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Hyaluronic acid algorithm-based models for assessment of liver fibrosis: translation from basic science to clinical application

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Objective: The estimation of liver fibrosis is usually dependent on liver biopsy evaluation. Because of its disadvantages and side effects, researchers try to find non-invasive methods for the assessment of liver injuries. Hyaluronic acid has been proposed as an index for scoring the severity of fibrosis, alone or in algorithm models. The algorithm model in which hyaluronic acid was used as a major constituent was more reliable and accurate in diagnosis than hyaluronic acid alone. This review described various hyaluronic acid algorithm-based models for assessing liver fibrosis.

Material and Methods: A PubMed database search was performed to identify the articles relevant to hyaluronic acid algorithm-based models for estimating liver fibrosis.

Results: The use of hyaluronic acid in an algorithm model is an extra and valuable tool for assessing liver fibrosis.

Conclusion: Although hyaluronic acid algorithm-based models have good diagnostic power in liver fibrosis assessment, they cannot render the need for liver biopsy obsolete and it is better to use them in parallel with liver biopsy. They can be used when frequent liver biopsy is not possible, in situations such as highlighting the efficacy of treatment protocol for liver fibrosis.

Keywords: Algorithm, hyaluronic acid, liver disease, liver fibrosis

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ID:32

The study of urinary biopyrrin levels and its correlation with blood oxidative stress in patients with liver cirrhosis

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Objective: Reported that urine biopirin is one of the most valuable biomarkers for assessment of oxidative stress. On the other hand, liver cirrhosis is one of the hepatic disorders that significantly affects the antioxidant defense system and increases oxidative stress. Therefore, the main aim of this study was to investigate the amount of biopyrrin in urine and its relationship with the level of oxidative stress in patients with liver cirrhosis.

Material and Methods: In this study, a total of 136 subjects were selected in four groups: control group (group A), healthy subjects, and the patients were divided into three groups; the cirrhotic patients without ascite flouid (group B), the cirrhotic patients with ascite flouid and Infected (group C) and cirrhotic patients with ascitic fluid without infection (group D). In subjects with the aim of this study, and by obtaining informed written consent of the urine samples for measuring the biopyrrin using Costebio ELISA kit and serum for measuring malondialdehyde using calorimetric thiobarbituric acid method and total antioxidant capacity using Randox kit was taken from them. SPSS software version 16 was used to analyze the results.

Results: The mean levels of urinary biopyrrin and lipid peroxidation increased significantly in the three case groups compared to the control group (in both cases, $p<0.0001$). The mean levels of total antioxidant capacity in the three case groups showed a significant decrease compared to the control group ($p<0.0001$). There was an inverse and signiicant correlation between urine biopyrrin levels and total antioxidant capacity of serum ($r= -0.814$, $p=0.001$), and a direct and significant correlation between urinary biopyrrin and levels of malondialdehyde in serum was observed ($r= 0.819$, $p=0.004$).

Conclusion: The results of this study show that oxidative stress increases in patients with liver cirrhosis and the other hand, there is a strong and significant correlation with the amount of urinary biopyrrin and oxidative stress in patients with liver cirrhosis.

Keywords: Urinary Biopyrrin, Oxidative Stress, Liver Cirrhosis

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Evaluation of oxidative stress markers in male favic patients

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Objective: Favism is caused by the intolerance of fava bean or inhalation of Vicia faba pollen. Patients have deficiency in glucose-6-phosphate dehydrogenase, enzyme which play a role in maintaining the balance of active oxygen species and its deficiency causes oxidative damage. The purpose of this study was to measure the serum levels of some oxidative stress markers in favic patients and compare them with healthy subjects.

Material and Methods: In this case-control study, blood samples were collected from male favic patients (n=100) and healthy subjects (n=100) with 2-6 years old. Measurements of oxidative stress parameters were performed using appropriate kits. Data analysis was performed using SPSS software.

Results: There was no significant difference between the serum levels of paraoxonase (140.82 ± 0.5 for patients and 112.50 ± 23.42 for healthy cases) and carbonyl (0.62 ± 0.12 for patients and 0.58 ± 0.11 for healthy cases) in two groups ($P<0.05$) while the level of catalase (3.7 ± 0.8 for patients and 11.2 ± 1.1 for healthy cases) and thiol (0.15 ± 0.05 for patients and 0.24 ± 0.04 for healthy cases) showed a significant difference in patients and control group ($P<0.05$).

Conclusion: Based on the results, it can be concluded that deficiency in G6PD enzyme can lead to oxidative damage by altering the serum levels of some oxidative stress parameters.

Keywords: G6PD, favism, oxidative stress

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Different Application of Aptamers for Cancer Diagnosis and Therapy (Research review)

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Objective: Nucleic acid aptamers are short single-stranded oligonucleotides that fold into unique three-dimensional structures and bind to a wide range of targets, including proteins, small molecules, metal ion, viruses, bacteria, and whole cells, with high specificity and binding affinities (from the low nanomolar to picomolar range) similar to those of antibodies. Aptamers also have advantages compared to antibodies, such as rapid in vitro selection, cell-free chemical synthesis, low immunogenicity and superior tissue penetration because of their smaller size. SELEX Technology: The selection cycle starts by mixing an initial DNA or RNA library with the target of interest. A library generally consists of up to 1015 random sequences of 20–60-nucleotides flanked by fixed primer regions at the 5′ and 3′ ends. After incubation, target-bound sequences are separated from unbound sequences through various partition strategies. A nucleic acid aptamer-based platform is superior to current antibody-based strategies, as aptamers allow: better tissue penetration; lack of immunogenicity; faster target accumulation and shortened body clearance, enabling the use of shorter-lived radioisotopes; simpler, better controlled, and thus less expensive chemical production; lack of aggregation issues amenability to a variety of chemical modifications that are needed for production and storage, such as pH changes or elevated temperature.

Keywords: Cell-specific aptamer, SELEX, cancer diagnosis, cancer therapy, targeted delivery

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Detection of PHA in Escherichia coli contains of Genes Encoding Poly (3-hydroxyalkanoate) Synthase from Pseudomonas aeruginosa PTCC 1310

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Objective: The aim of this study was to express these genes and optimize the conditions for their expression in E.coli. The optimization of conditions for phaC genes expression can serve as an important stage for establishing PHA production in E.coli.

Material and Methods and Results: To confirm the expression of functional PHA synthase enzymes by E.coli BL21 (DE3) cells carrying the phaC genes, the accumulation of PHA in bacteria was detected with Nile red. The E.coli BL21 (DE3) cells carrying the phaC gene, E.coli BL21 (DE3) without the phaC gene (as the negative control) and P.citranolleise (as the positive control) were investigated for PHA production. E.coli BL21 (DE3) cells were streaked on an LB plate supplemented with sodium-gluconate (0.5%w/v), Nile red (0.05 µg/ml), IPTG (0.1 mM) and ampicillin (100 µg/ml).

Conclusion: Using a Nile red plate assay, the accumulation of PHA in bacteria was detected which confirmed the expression of functional PHA synthase enzymes enzymes in E.coli BL21(DE3) cells. To increase the yield of PHA

production, using mutant strains of E.coli that could block the oxidation of fatty acids and accumulate greater level of PHA is also recommended.

Keywords: PhaC1, PhaC2, Polyhydroxyalkanoate, Protein expression, PHA detection

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Lead Contents in Ca Dietary Supplements

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Objective: Calcium is one of the most important nutritional elements for optimal bone and dental health, and prevention or treatment of osteoporosis. Studies suggest that calcium, along with vitamin D, may have benefits beyond bone health, and it is generally accepted that the heart, muscles, and nerves also need calcium to function properly. However, the safety and efficacy of some calcium supplements have been questioned and it is important for individuals to know what types of supplements are the most appropriate.

Material and Methods: An academic search was conducted in EMBASE and PubMed databases for investigating lead content in calcium supplements between years 2000 to 2017. Different forms of calcium supplements are available in the markets; bonemeal, dolomite, refined, natural source calcium carbonate salts, and other chelates such as calcium citrate.

Results: Studies indicated that increased Pb concentration in the supplements ($p<0.001$) may pose a health risk particularly to children with milk intolerance who rely on these products to meet their calcium requirement. Investigations showed only 10% of commonly manufactured Ca supplements analyzed by Graphite Furnace and Flame Atomic Spectrometry met the criteria of acceptable Pb levels (1.5 g/daily dose). It was also found that lead intake was highest in chelated calcium supplements whereas lowest through calcium supplements with vitamin D formulation. Another study indicated that the chelated calcium such as calcium gluconate, calcium lactate and calcium citrate were free of lead.

Conclusion: It is important manufacturers to improve their quality control procedures and to label their products with possible lead level accordingly so that consumers can make informed choices.

Keywords: Calcium Supplements and, Lead, Atomic Graphite Furnace Spectrometry, Flame Atomic Absorption Spectrometry

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ID:40

Comparative study of Oleracein E and Oleracein L effects on antioxidant enzyme activities, diabetic factors and damage oxidative biomarker levels in β-TC6 pancreatic cell line

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Objective: Oleracein E and Oleracein L are two active components in Purslane. The object of this research is use these alkaloids that are effective in metabolism and have herbal origin. We select indicators including anti-oxidant enzyme, oxidative damage biomarker, glucose releasing enzymes and anti-diabetic factors to examine the role of both alkaloids on effective factors in diabetic pathway.

Material and Methods: β-TC6 cells were cultured for 24 hours. Then glucose uptake, insulin secretion, Super Oxide Dismutase (SOD), Catalase (CAT), Glutathione Peroxidase (GPX), malondialdehyde (MDA), dityrosine (DTY), alpha amylase and alpha glucosidase of pancreatic cell line were evaluated in the range of 0 to 400 µM of two alkaloids. Two alkaloids were purchased from Sigma Company.

Results: Data showed that both alkaloids able to increase antioxidant enzyme activities and decrease of oxidative biomarkers significantly. α-amylase and α-Glucosidase showed similar enzymatic properties, since two alkaloids exhibited hypoglycemic effect by inhibition of these enzymes. These essential components induced relatively high glucose uptake and insulin secretion in pancreatic β-TC6 cell line.

Conclusion: Increase in inter cellular glucose levels by diabetes causes increased free radicals and oxidative stress in pancreatic cell. Treatment with both alkaloids cause inhibiting the production of free radicals and prevents the oxidative stress. Since two alkaloids have significant stimulator antioxidant properties and anti-diabetic on the pancreatic cell line, they can be used to as a vegetable in the food, protect pancreas to oxidative stress and can suggest that these have the hypoglycemic potential and could be useful on the diabetes therapy.

Keywords: anti-diabetic factors, antioxidant enzymes, oleracein E; oleracein L, glucose releasing enzymes, pancreatic β-TC6 cell line

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ID:42

A Dual-function Liposome-based Probe Made of Microalgae in Cancer Therapy

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Objective: Undoubtedly, the biochemical characteristics of liposomes have been well known. Thereby they can be employed as suitable carriers in research and clinical field. On the other hand, microalgae contain some pigments possessing unique properties such as cytotoxicity, antiproliferation and pro-apoptotic. Furthermore due to physicochemical features of a pigment called Phycobilin, it can be used as fluorescent material. In this paper, a kind of novel probe will be introduced.

Material and Methods: The hydrophobic pigment Fucoxanthin (Fuco) is incorporated in among tails of phospholipid bilayer of targeted liposome coated by polyethylene glycol. Fuco possesses potent anticancer as well as antiangiogenic properties. Thus it implicates therapeutic role in liposome structure. Moreover phycobilin-coupled antibodies or conjugation of phycobilins with protein A on the surfacee of liposome can act as a tracer in monitoring and imaging tumoral tissue.

Results: Natural pigments in this probe as both diagnostic and therapeutic may cause low side effects. Besides the payload of liposome is higher than other drug delivery systems.

Conclusion: By using this probe, imaging and treatment can be done simultaneously. Targeted therapy and lack of radiolabeled materials for monitoring are considered as extraordinary traits of these probes.

Keywords: Liposome, microalgae, probe, phycobilin, cancer

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Fatty Acid Metabolism in cancer cells

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Objective: Cancer has attracted more and more attention in recent years owing to its high morbidity and mortality rate. Cancer cells often have characteristic changes in metabolism, including glucose and fatty acid metabolism. Fatty acids are required for the synthesis of membranes and signaling molecules and are mainly used for the production and storage of energy. In this article, we review and summarize some of the important enzymes of lipid metabolism pathway in the genesis and progression of cancers.

Material and Methods: The literature review and recent investigations were studied. Data were analyzed and the consistent and controversial results were compared.

Results: According to studies, upregulation of lipogenesis is a hallmark of cancer and blocking the lipogenic pathway is known to cause tumor cell death by apoptosis. In addition, fatty acid oxidation also is highly required for survival and growth in some tumors. Changes in lipid metabolism can affect numerous cellular processes, including cell growth, proliferation, differentiation and motility.

Conclusion: Although, dysregulation of fatty acid metabolism is well known as a part of malignant transmutation in many different cancers, identification and targeting of the enzymes involved in order to prevent and/or treat cancer needs more research.

Keywords: Cancer, fatty acid, metabolism

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Investigating the expression of microRNAs involved in acute myeloid leukemia molecular pathways

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Objective: Acute myeloid leukemia is the most lethal leukemia among blood cancers. Its prevalence is 3 to 4 per 100,000 people, and the number of people infected increases annually. Understanding its molecular mechanism can play an important role in the diagnosis and treatment of this disease. Considering this issue, in the present study, we have tried to study the current paths with further investigation. The expression of miR-181a and miR-155 in patients and cell lines have been analyzed.

Material and Methods: In this study, 4 NB-4, U-937, KG-1 and HL-60 cells were classified as AML (acute myeloid leukemia) and 15 AML patients and 15 samples as controls for this study were used. One-way ANOVA and t-test were used to analyze the data and also to evaluate the expression of Real-Time PCR.

Results: Our studies showed that the expression of miR-181a, that is a tumor suppressor, is increased in patients with the more progressive disease, which in the subsequent studies indicates a prognostic role of this miRNA. Expression of the cells in the form of acute forms was also high. In the case of miR-155, which was also an oncogenic membrane, expression in both cell and human cells increased in comparison to the control sample.

Conclusion: The present study showed that the highest the severity of the disease, the increased expression of miR-181a, which was raised in those who were treated and declined, the survival rate was highest. While the expression of miR-155 reduced the amount of cell proliferation with effect on cyclin factors. Possibly by controlling some of these miRNAs, one can expect better treatments.

Keywords: Acute myelogenous leukemia, miR-155, miR-181a, cancer

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Evaluation of the effect of sulforaphane isothiocyanate antioxidant on acute myeloid leukemia cell lines

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Objective: Acute myeloid leukemia has the highest mortality among leukemias and the factors cause this leukemia, is miRNAs. Generally, disrupted of the expression of miRNAs can play a role in changing the regulation of proteins in vital and important cell pathways. On the other hand, components that affect the miRNA expression have a high importance therapeutic effect. Therefore, we study the effect of sulforaphane on acute myeloid leukemia cell lines and the expression pattern of miR-155 and miR-181a.

Material and Methods: In this study, 4 classes of HL-60, U937, KG1 and NB4 were used for the treatment. The doses used for the treatment of the cells were 15, 30, 45 and 60 µM of sulforaphane in 24 and 48 hours. After treatment, miR-155 and miR-181a expression were evaluated. In order to determine the apoptosis of the cells, a flow cytometry was used at that time.

Results: Our findings suggest that sulforaphane reduces the number of live cells and increases the mortality rate of myeloid rats. ($P<0.05$). The use of this substance caused a significant reduction in the expression of both miRNA in the cells of patients group ($P<0.05$). Reduced expression of miR-155 can be positively related to the factors and proteins involved in the cellular circulation. The reduced level of miR-181a will probably affect the regulatory genes in the process of differentiation and proliferation of myeloid. Apoptosis assays also showed that the highest apoptosis has occurred in 60 µM of sulforaphane in KG1 cells with 46.60% rate of apoptosis.

Conclusion: The results indicate that sulforaphane increases the death rate of AML cells and decreases the expression of miR-155 and miR-181a. In this study, the number of live cells decreased. Anyway, in future studies, it is better to performance intervention inhuman in order to determine the clinical effects of sulforaphane.

Keywords: Myeloid leukemia, miR-155, miR-181a, sulforaphane

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ID:51

An electrochemical Aptasensor for detection of PDGF-BB in human plasma sample and MCF-7 breast cancer cell lysates

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Objective: Platelet-derived growth factor BB, an important cytokine in serum, is a protein marker for cancer diagnosis and directly involved in tumor growth and progression. Therefore, accurate and rapid detection of PDGF-BB is significant in biomedical fields. Electrochemical techniques have recently been utilized for low cost, accurate and sensitive detection of PDGF-BB. In present study, a novel electrochemical aptasensor using cubic gold nanoparticles based on the specificity of aptamer-target recognition for quantification of PDGF-BB was constructed.

Material and Methods: Novel structure of gold nanoparticles containing alpha-cyclodextrin and specific DNA aptamer used for construction of GNPs-alpha-CD-Apt-Au biosensors. The fabricated aptasensors were employed for the detection of PDGF-BB in standard, human plasma samples and MCF-7 cells using an electrochemical AUTOLAB system, cyclic voltammetry (CV) and square wave voltammetry (SWV) techniques.

Results: Under optimized condition the calibration curve for PDGF-BB was linear in 0.52-1.04 nM with lower limit of quantification

of 0.52 nM. Also the fabricated aptasensor exhibited excellent analytical performance for MCF-7 cells determination, ranging from 328-593 cells mL-1, with lower limit of quantification of 328 cells mL-1.

Conclusion: The results indicated that the use of GNPs-alpha-CD can improve the affinity of the PDGF-BB binding and accurate detection of PDGF-BB. Therefore, the GNPs-cubic-alpha-CD-Apt-Au aptasensor showed high sensitivity, selectivity, stability and applicability for the detection of PDGF-BB.

Keywords: Electrochemical Aptasensor, Platelet-derived Growth factor BB, Cancer biomarker, Gold nanoparticles

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ID:60

Association of Plasminogen Activator Inhibitor-1, Oxide-LDL and MDA serum levels with Coronary Artery Disease and it Extent

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Objective: Coronary Artery Disease (CAD) is consequences of atherosclerosis. Studies have suggested that there were various factors which involved in CAD developing and extension. These factors include Plasminogen Activator Inhibitor-1 (PAI-1), Lipid Peroxidation and Oxidative Stress. The aim of this study is evaluation of PAI-1, Oxide-LDL and MDA (Malondialdehyde) serum level in patients with CAD and also association of this biomedical parameter with CAD extension. The evaluation of these factors can be useful for inhibition of the disease progression.

Material and Methods: 200 subject including 160 with CAD and 40 healthy individuals. Patients were divided into 4 subgroups: 40 subjects with no (NVD), 40 single (1VD), 40 double (2VD) and 40 triple vessel disease (3VD) according to angiography results. ELISA procedure was used to determine the serum of PAI-1 and Oxide-LDL levels. Serum MDA level was measured based on reaction with Thiobarbituric Acid (TBA).

Results: Serum PAI-1, Oxide-LDL and MDA levels in patient with CAD were found to be significantly higher than control group (p=0.001). In addition, in patients with 2VD serum PAI-1 levels were significantly higher than NVD and control group, 3VD significantly higher as compare with 1VD and control group (p=0.001). In patients with 2VD serum Oxide-LDL levels were significantly higher than NVD and control group (p=0.001), 3VD significantly higher as compare with 1VD and control group (p=0.001). In patients with 2VD serum MDA levels were significantly higher than NVD and control group, 3VD significantly higher as compare with 1VD and control group (p=0.001).

Conclusion: These findings suggested that PAI-1, Oxide-LDL and MDA are markers of CAD, because serum levels of the above parameters in patients with CAD were higher than control group and also statically were association with CAD extension and it possible that this parameter are involved in developing CAD. Therefore the evaluation of this parameter can be useful for inhibition of the CAD progression.

Keywords: Plasminogen Activator Inhibitor-1, Oxide-LDL, MDA, Coronary Artery Disease, Extent

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ID:62

Induction of apoptosis and G2/M cell cycle arrest by epirubicin in human MDA-MB231 breast cancer cells

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Objective: Epirubicin (EPI) is an anticancer drug, structurally related to anthracyclines and widely used as a potent chemotherapeutic agent in the treatment of various cancers. EPI acts to stabilize topoisomerase-DNA complex and producing double strand breaks (DSBs), which is one of the most important hallmark of apoptosis.

Material and Methods: The cells were exposed to EPI for 24h and genomic DNA was extracted from drug treated and the controls, run on agaros gel electrophoresis. Also DNA fragmentation was analyzed with diphenylamine reaction method. The cell cycle distribution was determined by staining DNA with PI and after staining with PI solution, the cells were subjected to FACS analysis of their DNA contents. Apoptosis was also quantified using an annexinV/PI detection kit and analyzed immediately by flow cytometry. The HMGB1 protein was extracted from media of drug treated and the controls, run on SDS-PAGE, and then detected by western blot.

Results: Both agarose gel electrophoresis and diphenylamine reaction represented a significant increase ($p<0.001$) in DNA fragmentation especially at high concentration (≥80 µg/ml) of epirubicin treatment. The cells show increased number of the cells in G2/M phase after epirubicin treatment. The population of apoptotic and necrotic cells was significantly increased at high concentration of drug. The results also revealed that HMGB1

appear in the media of late apoptotic and necrotic MDA-MB 231 cells.

Conclusion: The present study demonstrate that epirubicin as chemotherapy agent cause cell shrinkage, DNA fragmentation, G2/M cell cycle arrest and also leads MDA-MB231 cells to HMGB1 release and apoptosis.

Keywords: Epirubicin, FACS, Apoptosis, HMGB1, Topoisomerase

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ID:63

Analysis of the effect of ginger on reducing cox-2 gene expression in ht-29 colon cancer stem cells

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Objective: Colon cancer is the second reason of mortality caused by cancer in the world, after lung cancer. Ginger has anti-inflammatory properties due to its content of [6]-gingerol and, hence, can play a role in the prevention of colon cancer. COX-2 gene expression is increased in colon cancer. The effect of ginger extract on reducing COX-2 gene expression in colon cancer HT-29 cells was investigated in this study.

Material and Methods: In this laboratory research, HT-29 cells of colon cancer were cultured in a 75 ml flask. Ginger extract at four concentrations (10, 20, 30, and 40 mg/mL) was added to the cells, which were cultured in the 96-well plates and the plates were incubated t 37˚C for 24, 48, and 72 hours in a 5% Co2 atmosphere. the MTT test was performed on HT-29 cells and the densities of the plates were read using an ELISA instrument. Total cellular RNA was extracted and expression of the COX-2 gene was investigated using the RT-PCR method. A sample not treated with the ginger extract was used as the positive control and GAPDH as the internal control.

Results: Determination of the expression of the COX-2 gene using the RT-PCR method indicated that the ginger extract at 20 mg/ml reduced expression of the COX-2 gene compared to using Aspirin as the positive control.

Conclusion: Results of this research indicated use of ginger extract at 20 mg/ml could play an important role in decreasing of colon cancer cell and in reducing the expression of the COX-2 gene.

Keywords: ht-29, ginger, colon cancer, COX-2

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ID:65

Correlation analysis of vitamin D and IL-35 serum level in coronary artery disease patients

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Objective: Accumulating evidences show that the novel anti-inflammatory cytokine IL-35 is secreted from regulatory T cells and can alter the progression of inflammatory and autoimmune diseases. The role of inflammatory and anti-inflammatory cytokines in the pathogenesis of atherosclerosis is increasingly evident. On the other hand, recent studies revealed that vitamin D has several roles in control of human immune system function. A low vitamin D status may be an important factor of cardiovascular disease. Here, we investigated the relation between vitamin D status and regulatory T cells (Tregs) inhibitory cytokine, IL-35, in patients suffering from coronary artery disease (CAD).

Material and Methods: 40 patients suffering from 1 vessel disease (n=20) or 2 vessel disease (n=20) enrolled in this study and compared to the control group (n=20). Vitamin D serum level was measured using Electrochemiluminescence assay. IL-35 was measured using ELISA. Coronary artery stenosis was confirmed by angiography.

Results: Vitamin D and IL-35 concentrations in control group (25.4±9.2, 8.1±3.9 respectively) were significantly higher than patients with 1 or 2 vessel disease (11.1±5.8, 3.2±1.1 respectively, $p<0.05$). Subgroup analysis revealed that IL-35 (but not vitamin D) was significantly higher in one vessel disease patients (10.2±7.3) compared to those with 2 vessel disease (3.5±2.1, $p<0.05$). IL-35 was positively correlated to vitamin D serum levels ($r=0.46$, $p=0.028$).

Conclusion: The positive correlation between IL-35 and vitamin D suggests that vitamin D may affect the coronary artery status through anti-inflammatory effect of IL-35 and regulatory T-cell function.

Keywords: IL-35, vitamin D, coronary artery disease

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ID:66

STAT3 SNP rs1053004 affects susceptibility to acute kidney injury

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Objective: Twenty to thirty percent of patients undergoing cardiopulmonary bypass (CPB) develop AKI (acute kidney injury) which is defined by the increase in serum creatinine>0.3 mg/dl in 48 h. STAT3 is one of the main transcription factors in development of inflammation and inflammation is the main cause of AKI after CPB. Hence the aim of this study was the elucidation of the influence of STAT3 gene polymorphism on development of AKI after CPB.

Material and Methods: STAT3 SNP rs1053004 were investigated in 90 patients undergoing coronary artery bypass, in Bandar Abbas, Iran. Patients categorized to AKI (n=33) and Non-AKI (n=57) groups according to the changes in creatinine serum level during the first 48 hour after surgery and compared. Single nucleotide polymorphism was investigated using sequence-specific primers.

Results: Chi-square analysis revealed that the SNP rs1053004 distribution was in Hardy-Weinberg equilibrium (HWE). There were 40% men and 42% women in AKI group and 51% men and 50% women in the non-AKI group (p>0.05). Comparison of the genotypes frequency in AKI and Non-AKI group showed that the frequency of GG (8% versus 20.7%) and AG (47% versus 29.1%) genotypes were significantly different. Rs1053004 GG genotype was significantly associated with a decreased risk (OR=0.2, 95% CI=0.08-0.56, P=0.01) while AG genotype increased the risk (OR=1.76, 95% CI=0.9-3.5) of CPB-AKI. The distribution of AA genotype was not significantly different between AKI and non-AKI groups.

Conclusion: The results showed that rs1053004 polymorphism was significantly associated with a decreased risk of AKI after CPB.

Keywords: Acute kidney injury, cardiopulmonary bypass, polymorphism

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ID:78

Subclinical hypothyroidism increases serum triglyceride levels via PCSK9

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Objective: It has been proven that serum triglyceride (TG) levels increase in overt hypothyroidism (OH). But this issue with subclinical hypothyroidism (SH) is still controversial. In SH, thyroid hormones include FT3 and FT4 are in normal values, while serum levels of thyroid stimulating hormone (TSH) increase. Some studies suggest that SH cannot increase the lipid profile, including TG, but some results suggest that it can be effective in increasing the levels of TG by regulation of Proprotein convertase subtilisin/kexin type 9 (PCSK9). PCSK9 is a serine protease and a secreted protein which increases cholesterol levels in plasma via inducing degradation of low-density lipoprotein receptor (LDLR).

Material and Methods: Anthropometric data and laboratory characteristics including serum TSH, FT4, TG and PCSK9 levels were evaluated from 20 newly diagnosed patients with SH and 20 healthy subjects in a cross-sectional study. Then statistical analysis and the correlation between the obtained data were examined.

Results: TSH levels were significantly higher in SH patients compared controls and FT4 levels was significantly lower in patients than healthy subjects. Serum levels of TG and PCSK9 were significantly higher in the patient group compared to controls, and they have a significant negative correlation with FT4.

Conclusion: Some new studies suggest that PCSK9, like its effect on LDLR, can reduce the number of VLDLR in the surface of hepatocytes. Thus the removal of TG from the serum decreases by the liver. The present study suggests that in SH patient's thyroid function can increase serum TG levels via PCSK9 regulation.

Keywords: Subclinical hypothyroidism, Triglyceride, Proprotein convertase subtilisin kexin 9

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ID:79

The effect of 24-hydroxy cholesterol on ROS produced by beta-amyloid in astrocyte isolated from C57BL/6 mice

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Objective: Alzheimer's disease is a neurodegenerative disorder that characterized by the accumulation of beta-amyloid plaques outside the cells and intercellular hyper phosphorylation of tau protein. Amyloid beta is involved in both the pathogenesis of

Alzheimer's disease and induction of reactive oxygen species. Since 24-hydroxy cholesterol (24-OHCho) as a polar metabolite can eliminate excess cholesterol in the brain, we investigated the regulatory role of 24-OHCho on reactive oxygen species level induced by exogenous cholesterol or amyloid beta.

Material and Methods: Astrocytes were isolated from the brain of newborn C57BL/6 mice and cultured in DMEM + 10% FBS. Cells were incubated with various amounts of cholesterol and generated ROS was evaluated by fluorimeter. Also intracellular ROS was measured in the presence of beta amyloid with or without of 24-OHCho and results were analyzed by using ANOVA and SPSS software.

Results: The findings showed that production of ROS was significantly increased when astrocytes were treated with exogenous cholesterol or amyloid beta compare to control. However, treating with 24-hydroxy cholesterol significantly inversed increased ROS level in beta-amyloid group.

Conclusion: Beta-amyloid is reported to increase cholesterol levels in Alzheimer's patients. On the other hand, 24-hydroxy cholesterol is the one of the important factors in regulating cholesterol in the central nervous system that by the reduction of cholesterol can play an effective role in reducing ROS.

Keywords: Alzheimer, Amyloid beta, 24-hydroxy cholesterol, Cholesterol, Reactive oxygen species

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ID:80

Association of MTHFR Gene Polymorphisms and Male Infertility in Iranian Azoospermic Men

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Objective: Male infertility is a multifactorial disorder influenced by several genetic and environmental factors. Methylenetetrahydrofolate reductase (MTHFR) is an important enzyme contributing to metabolic pathway of folate in spermatogenesis and male fertility. Variations in the MTHFR gene polymorphisms would mainly lead to amino acid exchanges, affecting the enzymatic activity of the gene. Two of the well-known single nucleotide polymorphisms of this gene are 677(C/T) and 1298(A/C) positions, which are predisposition factors to male infertility in some populations. This study aims to evaluate the MTHFR gene polymorphisms at 677 and 1298 positions in patients with azoospermia as compared to healthy men in Fars, Iran.

Material and Methods: A total number of 248 azoospermic patients and 197 healthy men from Fars, Iran participated in this study. The PCR-RFLP technique was used to investigate the polymorphism of the MTHFR gene at 677(C/T) and 1298(A/C) polymorphisms followed by enzymatic digestion with HinfI and MboII enzymes, respectively.

Results: This study has shown an association between azoospermia and A1298C and 677(C/T) polymorphisms. 677(C/T) and 1298(A/C) genetic polymorphisms conveyed an increase in azoospermia risk (OR=1.9, 95% CI= 1.3–2.9, p=0.000 and OR= 1.7, 95% CI =1.1–2.5, p=0.01 respectively). Combined MTHFR gene polymorphisms revealed higher azoospermia risk in 677(C/T)/CT-1298(A/C)/AC combined form (OR= 3.8, 95% CI= 1.9–7.6, p=0.000).

Conclusion: Our findings suggest that MTHFR 677(C/T) and 1298(A/C) polymorphisms are risk factor for azoospermia in Iranian patients from Fars Province. Furthermore, these two gene polymorphisms may act synergistically to increase the risk of azoospermia.

Keywords: Male infertility, Azoospermia, MTHFR gene

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ID:81

Investigating anti-diabetic effects of Melilotous officinalis on prevention of glycation and fructation of hemoglobin protein

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Objective: Many important biochemical mechanisms are activated in the presence of high levels of glucose, which occur in diabetes. Elevated levels of glucose accelerate the formation of advanced glycation end-products (AGEs). Formation of endogenous AGEs can lead to further protein modifications and activation of several inflammatory signaling pathways. AGEs inhibition has been shown to prevent diabetes complications, and therapeutic advances have resulted in several agents that prevent their adverse effects. The aim of this study was to investigate the effects of the Melilotous officinalis extract on preventing hemoglobin glycation in the presence of glucose and fructose.

Material and Methods: Hemoglobin was extracted from healthy donors and incubated in the absence and presence of glucose,

fructose and Melilotous officinalis extract. Protective effects of this extrac against glycation and fructation of hemoglobin were investigated by different fluorometry methods.
Results: Our results showed that fructose and glucose glycated the hemoglobin protein and alter its structure. Ethanolic and aqueous extract of Melilotous officinalis can prevent glycation and fructation of hemoglobin glycation in a dose dependent manner.
Conclusion: It can be concluded that the Melilotous officinalis extract has significant effects against diabetes complications.
Keywords: Diabetes complications, glycation, fructation, Melilotous officinalis
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Terminal extensions of mouse IMPDH1 isoforms modulate physiological function of the enzyme

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Objective: Inosine monophosphate dehydrogenase (IMPDH), the rate-limiting enzyme of the de novo pathway of guanine nucleotide biosynthesis, catalyzes the oxidation of IMP to XMP with the continuous reduction of NAD to NADH. Mammalian IMPDH has two homologues, IMPDH1 and IMPDH2, which are 84% identical in amino acid sequence and enzymatic activity. Human IMPDH1, propounds three isoforms, 514(canonical isoform), 546 and 595(retinal isoforms), which are named according to their amino acid length. In comparison to canonical isoform, both 546 and 595 IMPDH1 isoforms have a 32 residues C-terminal extension while 595 isoform has an additional 49 residues on its N-terminus. In this report, we will show the influence of the terminal extensions on the kinetic behavior of the enzymes relative to that of the canonical form.
Material and Methods: After extraction of mouse recombinant IMPDH1 isoforms from E.coli and their purification by affinity chromatography (Ni-NTA spin kit), enzyme kinetic assay was performed at the saturated concentration of NAD and variation concentrations of IMP in 10 mM Tris-HCl (PH=8), 1mM DTT, 5mM EDTA and 50mM KCl, and the reduced NADH production was monitored at 340 nm by a UV-visible spectrometer.
Results: Kinetic parameters (Km, Vmax) of mouse canonical and retinal IMPDH1 isoforms, determined by Michaelis-Menten and LineWeaver-Burk approaches, were significantly different. Although Vmax of retinal isoforms was lower than that of the canonical form, however their Km (affinity) values were higher.
Conclusion: Based on our data, it might be concluded that the N and C-terminal extensions have impaired some degree of rigidity on the enzyme active site with subsequent lower substrate affinity.
Keywords: IMPDH1, rate limiting enzyme, UV-visible spectrometery
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ID:95

Anti-cancer and antioxidant effects of Spirulina platensis derived C-Phycocyanin in colon carcinoma cells in vitro and in vivo

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Objective: The Phycobiliprotein C-Phycocyanin(C-PC), the main light harvesting biliprotein, extracted from Spirulina platensis, has been demonstrated to have a series of physiological and pharmacological attributes without leading to harm and toxicity. In this research, attempted to evaluate potential of anti-cancer and antioxidant C-PC on mice colon carcinoma cells (CT-26) and human colorectal cancer cell lines (HT-29) in vitro and in vivo.
Material and Methods: The CT26 and HT29 carcinoma cells were treated with various concentrations of C-PC extract (1-100µg/ml) in 48hr.Then its anti-proliferative effect was measured by morphological observations, DAPI and AO/PI Staining, MTT assay, fluorescence microscope and Flow cytometry assays. Antioxidant effects of C-PC on CT26 tumor cells transplanted in Balb/c mice was also checked out in vivo. 21 male Balb/c mice were randomly divided into three equal groups. Group1 was used as control. Group 2 and 3 received Phycocyanin (1 mg/kg and 2 mg/kg) respectively, daily for 4 week via Gavages. Finally, levels of Malondialdehyde, Glutathione peroxidase, Superoxide dismutase and Catalase enzymes and Total antioxidant capacity were assessed in liver homogenate and serum.
Results: C-PC showed considerable anti-proliferative effect on CT26 and HT29 tumor cell lines with IC50=47.4 µg/ml and IC50=49.4µg/ml respectively. Further studies involving fluorescence microscope and Flow cytometry revealed characteristic apoptotic features like cell shrinkage, membrane blebbing and nuclear condensation into dense granules. In addition, C-PC, because of its antioxidant potential, significantly (P<0/001),

decreased Malondialdehyde (lipid peroxidation index) and increased levels of liver antioxidant enzymes.

Conclusion: Our results confirmed this idea that C-PC can be used supplementary material in preclinical experiments and further investigation are recommended for finding C-PC molecular mechanism and medical applications.

Keywords: C-Phycocyanin, Anti-cancer, Antioxidant, Colorectal cancer, Apoptosis

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ID:119

The regulation of cancer cell energy: Crosstalk and network between the various types of cells

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Objective: In recent years, researchers have cited the relationship between tumor cells and normal cells around them. Researchers have also recognized that tumor cell control is critical to human health and survival. One of the methods of controlling tumor cellular metabolism is through regulation of the growth and energy of the tumor cell. The level of glycolysis is high in tumor cells. Also, tumor cells, by building up a network with neighboring cells, provide energy in addition to performing glycolysis through the protein degradation and the use of certain amino acids.

Material and Methods: Many methods have been used to control the metabolism of damaged or tumor cells and inhibit energy production by researchers. To determine the association of damaged or tumor cells with neighbor and adjacent cells, a co-culturing technique was used. Esophageal erosive and non-erosive cells, diabetic and non-diabetic pancreatic cells, liver cells, parotid cells and damaged cells were co-cultured with duplicated form. To compare the results of the control group and the case study, student t-test statistical method was used and $P<0.05$ was significant.

Results: Our findings indicated that damaged and tumor cell microenvironment or media is very important in energy supply sources of injured and tumor cells. The combined results of various damaged and healthy cells showed that adjacent cells could play an important role in the metabolism and energy supply of the damaged or tumor cells.

Conclusion: It is very important to regulate the metabolism of an injured and tumor cell by controlling the amount of production and ways of providing cellular energy to maintain health. In the future, control of energy supply sources of tumor cells could be one of the treatments strategy for cancer cells treatment. Control of metabolic interactions, signaling and crosstalk between tumor cells and their non-malignant neighbor's cells will be important in cancer cells treatment.

Keywords: Cross-talk, signaling, metabolic interaction, tumor cells, damaged cells

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ID:122

Stem cell therapy for diabetes mellitus

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Objective: Diabetes is one of the chronic diseases associated with increased blood glucose, which can be due to insulin secretion or insulin resistance. Diabetes resulting from defects in both insulin secretion and insulin activity. Finding new sources for tissue reconstruction or necrosis is one of the issues that researchers have taken in recent years. In this regard, in recent years attention has been paid by researchers with regard to the potential application of stem cells in repairing and restoring the damaged tissue.

Material and Methods: Stem cells were isolated from the umbilical cord blood by using a different centrifuge, using a Max column method. Alloxan was used to create diabetic rats and two rat groups were examined by stem cell injection and without stem cell injection. The level of insulin and glucose in the serum were determined. To compare the results of the control group and the case study, student t-test statistical method was used and $P<0.05$ was significant.

Results: Our results demonstrated that the stem cell has the potential for the reconstruction and repair of the damaged tissue, so that the amount of insulin secretion increased in the group injected with stem cells compared with the control group. Blood glucose was also decreased in the injected stem cell group compared to the control group.

Conclusion: Our results indicated that stem cells have the potential to regenerate pancreatic cells, so that the amount of insulin secretion increases after injection. Therefore, stem cells can be one of the sources of tissue repair and should be used in the treatment of diabetic patients.

Keywords: diabetes mellitus, stem cell, glucose, insulin

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ID:123

Novel and non-invasive biomarkers for early detection of cancers: Breast, esophageal, glioma, glioblastoma and prostate cancer

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Objective: Novel and non-invasive biomarkers are urgently needed for early detection of cancer. Nowadays, prognosis and diagnosis of many types of cancers is frequently late, time-consuming and expensive. New approaches for diagnosis and treatment of cancers is needed. In recent years cancer diagnosis is improving. In this regard, biochemical compound can be utilized as novel cancer biomarkers. Biomarker could be readily accessible in the biological fluid and the altered production and secretion of biomarkers in biological fluid and aberrant expression of biomarker contents in the tumor cells could reflect the status of cancer. The aims of our study is to introduce the basic properties of biomarkers, the function roles of biomarkers in breast, esophageal, glioma, glioblastoma and prostate cancer, and the methods of detecting markers. We highlight the clinical values of biomarkers in breast, esophageal, glioma, glioblastoma and prostate cancer diagnosis and prognosis.

Material and Methods: Over the recent years, various bio-markers in cancer patients were evaluated by our research team on biological samples of different cancers in the form of theses and research designs. We investigate the role of biomarkers including, sarcosine, glyoxalase, fructose amine 3 kinase, nitrite, nitrate, GFAP, IGFBB-2, YKL-40, alpha-fucosidase, fucosyl transferase, GDP-fucose transferase, phospholipids carrier protein, riboflavin carrier protein and survivin, in breast, esophageal, glioma, glioblastoma and prostate cancer patients. The content of these biomarkers were measured with standard biochemical kits by using spectrophotometer or Elisa methods. To compare the means of the healthy control group and the patient group, student t-test statistical method was used and p value statistical significance; $P<0.05$.

Results: Our results demonstrate that the concentration of sarcosine, glyoxalase, fructose amine 3-kinase, nitrite, nitrate, GFAP, IGFBB-2, YKL-40, alpha-fucosidase, fucosyl transferase, GDP-fucose transferase, phospholipids carrier protein, riboflavin carrier protein and survivin biomarkers in the in breast, esophageal, glioma, glioblastoma and prostate cancer patient samples varies in comparison with healthy control samples. These changes are associated with clinical, grade parameters and cancer progression.

Conclusion: The association of changes in biomarkers measured with the progression, staging and clinical signs of breast, esophageal, glioma, glioblastoma and prostate cancer samples can help in addition to early detection of these cancer at the design of the drug and ultimately cancer treatment. Current results have several implications that motivate promising future research in the fields of drug target therapy and cancer biomarkers.

Keywords: Cancer, breast, glioma, prostate, esophageal

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ID:127

The Aurone derivatives assessment serves as proprietary probes of β amyloid aggregates in comparison with amorphous aggregates

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Objective: In 1854, the term “amyloid” was used for the first time by Virchow. To describe an aggregated substance found in the liver of a deceased patient. Despite the misleading association to starch, the term is still used an currently 27 diseases are associated with amyloid fibril deposits of normally soluble proteins. Early detection of amyloid deposit could be effective in the diagnosis and treatment of disorders such as Alzheimer’s disease (AD), Parkinson’s disease (PD) and systemic amyloidosis. In this study, we tried to synthesize the aurone derivatives as an amyloid detection probe to compare with a standard probe called Thioflavin T in the different protein conditions.

Material and Methods: β-Lactogluboline was purified via fractionation method (As an all β secondary structure) and bovine serum albumin (As a α/β secondary structure) was purchased from Sigma Aldrich. For more

precision, their qualities were evaluated by SDS-PAGE and Bradford protein assay. Furthermore, the spectrophotometric analysis of synthetic compounds such as UV-visible and fluorescence spectroscopies were considered in their individual and special wavelengths. Each synthetic compounds were excited and the emission spectra were recorded immediately at their own exclusive wavelengths, while, they were bound to the amyloid fibrils in comparison with native protein and also amorphous aggregates.

Results: The results of synthetic compounds were obtained in three different conditions, Native, Amorphous and Amyloid aggregations. We have shown that the synthetic compounds could selectively and specifically bind to amyloid fibrils almost as much as the ThT probe. Additionally, our synthetic compounds due to its neutral charge and high lipophilicity essence might cross the blood-brain barrier as an effective probe.

Conclusion: According to our result, the synthetic compounds could be accounted as remarkable probes to detect in vitro β-amyloid plaques, but it should be investigated further as potential probes for detecting β-amyloid plaques in the AD brain.

Keywords: Amyloid, Amorphous, Compounds, Probe, Synthetic

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ID:128

Protein-related cognition by the brain and the heart: Muscarinic receptor M2 variations in the physical and psychological stress

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Objective: Chronic adolescent stresses are associated with various cognitive impairments at older ages. Different chronic stressors through activating diverse biochemical pathways lead to explicit health problems. Differentiating effects of chronic physical and psychological stresses on M2 muscarinic receptors (M2MR) of the brain and the intrinsic cardiac nervous system (ICNS) allows us to find their different potency leading to cognitive damages.

Material and Methods: 21 female Wistar rats were divided into three groups (n=7, 3 weeks old); control, physical stress (electric shocks: 0.25 mA, 50 Hz, 2 sec duration, 10 min: 10 shocks), and psychological stress (witnessing electric shocks). After stress exposure in 5 consecutive days, serum corticosterone was measured for stress induction verification. Rats were then returned to their home cage for 1.5 months. In their adulthood, Y-maze and Object Recognition Task (ORT) were performed to evaluate cognitive performances of each group. Then, M2MR variation in brains and ICNSs were compared in physically and psychologically stressed rats by western blot.

Results: Both experimental groups exhibited a significant reduction in cognitive performance 1.5 months post-stress. Western blot analysis for M2MR expression level represented a significant reduction in brain and increase in ICNS of both stress groups compared to control. Comparative evaluation of cognitive impairment in stressed rats showed a major disturbance in psychologically stressed animals.

Conclusion: The reversed M2MR expression changes in brain and ICNS illustrated a kind of compensatory effect between brain and heart for cognition. Considering major cognitive impairment in psychologically stressed rats, adolescent psychological healthcare would be an effective strategy for cognitive damages prevention at older ages.

Keywords: Psychological Stress, Physical Stress, M2 Muscarinic Receptors, Cognitive Impairment, Intrinsic Cardiac Nervous System

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ID:131

Effect of aqueous and acetone extracts of Cynara scolymus flowering shoot on liver enzymes (Alanine aminotransferase, Aspartate aminotransferase, Alkaline phosphatase and γ-glutamyl transferase) in streptozotocin-induced diabetic male rats

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Objective: Due to the increasing progress of diabetes mellitus and use of alternative and low risk Herbal Medicines, this experimental study investigated the effect of aqueous and acetone extracts of flowering shoot of Artichoke (Cynara scolymus) on liver enzymes in streptozotocin-induced diabetic male rats.

Material and Methods: 42 adult male Wistar rats were used. Blood glucose levels of 36 rats were measured at first and then, 24 rats became diabetic by receiving 65 mg/Kg STZ and classified in diabetic groups. The rats were divided into 7 groups. All of them were fed regularly. They were received 500 mg/Kg of artichoke flowering shoot extract by gavage. Gavage, was done for 10 times, every other day. At the end of the 20th day, blood was taken from the heart of animals and serum

concentrations of glucose and liver enzymes were measured and obtained data were compared together.

Results: Aqueous extract, significantly reduced the levels of blood glucose, AST, ALT and ALP compared to diabetic group and ones treated with acetone extract. The activity of GGT was significantly increased in diabetic groups which treated with aqueous and acetone extracts, and normal group which treated with acetone extract, compared with normal control group (p-value<0.05).

Conclusion: According to the results of present study, the extract of this herb, especially aqueous extract, is effective in control of blood glucose and reducing liver enzymes activities.

Keywords: Alanine aminotransferase; Alkaline phosphatase; Aspartate aminotransferase; Cynara scolymus; γ-glutamyl transferase

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ID:135

Interleukin-6 Promoter SNP is Associated with its Serum Levels, Susceptibility to the Prostate Adenocarcinoma, and Bone metastasis in Iranian Population

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Objective: Interleukin-6 (IL-6) is an inflammatory cytokine shown to be a strong factor for growth, proliferation and metastasis of many malignancies. The promoter single nucleotide polymorphisms (SNPs) of -174G>C (rs1800795) can alter the transcriptional pattern of this gene. This study aims at assessing the effect of IL-6 (rs1800795) SNPs on serum levels and susceptibility to benign prostate hyperplasia (BPH) and the prostatic adenocarcinoma (PCa).

Material and Methods: The project was performed on 112 men with PCa, 118 men with BPH and 250 healthful men as control group. After DNA extraction, Genotyping of IL-6 (rs1800795) was performed using PCR TaqMan Allelic Discrimination (ABI MGB) based on. Serum IL-6 levels were measured by ELISA.

Results: As results, the G allele frequency for rs1800795 in IL-6 gene was 74.1%, 68.6% and 67% in PCa patients, BPH patients and healthy men, respectively. G showed significant differences in PCa and healthy groups (P =0.030, OR= 1.73, 95% CI: 1.05-2.21). The GG genotype indicated more frequency in PCa group, whereas the GC genotype was more common in BPH group in comparison to other groups. In addition, individuals with G allele were found to have higher levels of serum IL-6.

Conclusion: Current study identified that IL-6 -174G>C (rs1800795) is associated with serum IL-6 levels, and statistically disease-susceptible SNP in prostate cancer and its bone metastasis in a northwest Iranian population.

Keywords: TL1 cytokine [Supplementary Concept], prostate, adenocarcinoma, hyperplasia, BPH

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ID:140

Synergistic anticancer effect of ZnO nanoparticle and 5FU on the growth of MCF7 cell line

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Objective: Breast cancer is a malignant disease which is common in women. 5-Fluorouracil (5FU) is one of the most common chemotherapeutic drugs which is used for treating breast cancer. However, it is limited to use due to its side effects. On the other hand, ZnO nanoparticles as inorganic compound have shown the anticancer ability. Therefore, the aim of this study was to evaluate the cytotoxic effects of 5-FU and ZnO nanoparticles as a single or in combination on human breast cancer (MCF7) cell line.

Methods: MCF7 cell line was treated with different concentrations of ZnO nanoparticles (0-100 µg/ml) and 5-FU (0-10µm) for 48 h. The cytotoxic effects of ZnO and 5-FU were evaluated by 3-(4,5-dimethylthiaztol-2-yl)-2, 5-diphenyltetrazolium bromide (MTT) assay on MCF7 cell line. Kruskal-Wallis and Dunn's tests were used to evaluate the statistical

significance of the differences between different treated culture cells.

Results: 5-FU or ZnO as a single treatment decreased significantly the growth of MCF7 cells at 48 h. Nevertheless, combination of 5-FU and ZnO was more effective on the reduction of MCF7cell viability than each compound in vitro.

Conclusions: This study showed the synergistic anticancer effect of ZnO nanoparticles and 5-FU on MCF7 human breast cancer cell line.

Keywords: ZnO nanoparticles, 5-fluorouracil, MCF7, cell viability

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ID:156

The evaluation of the effect of morphine on the expression of cannabinoid receptors 1and 2 in two cell lines: MCF-7 and MDA-MB-231 in Breast Cancer

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Objective: Studies illustrate Opioids, specially Morphine, that are used to relieve pain in cancer patients, can increase the risk of metastasis by suppressing the immune system and in this way promote tumor growth. Morphine mechanism of action is done through Opioid receptors that are distributed in the central nervous system (CNS). On the other hand, studies in the field of cancer treatment show Cannabinoids (the active ingredient in cannabis) are applied for cancer treatment and cannabinoids exert their effects by cannabinoid receptor type 1 and 2 which are expressed on the surface of cancer cells and normal cells. As mention earlier, the effects of Morphine is done through Opioid receptors that are distributed in the central nervous system (CNS), however recent studies demonstrate that there is a functional interference in central nervous system (CNS) between Opioid receptors and endocannabinoid system.

Material and Methods: MCF-7 and MDA-MB-231 breast cancer cell lines were treated with various doses of Morphine (1.6, 0.16, 0.016, 0.0016 µM) for 24 and 48 hours, Then the gene expression of cannabinoid receptor type 1 and 2 were measured by Real time PCR methods and then CTΔΔ obtained from that were applied for statistical analysis to determine relative gene expression of cannabinoid receptor type 1 and 2.

Results: The results showed reduced gene expression of cannabinoid receptor type 1 and 2 in two breast cancer cell lines that were treated with morphine for 24 and 48 hours. This means that different doses of morphine have significant effect on the expression of both receptors in MCF-7 and MDA-MB-231 breast cancer cell lines.

Conclusion: Morphine has effect on gene expression of cannabinoid receptors in breast cancer cell lines.

Keywords: Morphine, breast cancer, cannabinoid receptor type 1 and2

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ID:158

Heterologous prime-boost strategy is an effective approach to develop a therapeutic HIV-1 vaccine

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Objective: Human immunodeficiency virus (HIV) is a major global health problem. There is an urgent need to develop an effective vaccine against HIV-1 infection, thus the vaccine must be able to induce protective immune responses, which can elicit and maintain both humoral and cellular immunity. Although, the recombinant subunit vaccines are safer than traditional ones but these vaccines are poor immunogens which need to use some effective approaches including adjuvants, delivery systems or prime/boosting. Recently, it has been shown that the heterologous prime-boost regimens are more efficient to produce a potent immunity as compared to homologous prime-boost regimens. Numerous heterologous prime-boost vaccine strategies have been tested in preclinical and clinical trials with promising results. After years of developing a potent vaccine, only six HIV-1 vaccines were almost efficient in clinical trials including a heterologous prime-boost strategy-based vaccine so-called as RV144 with 31% efficacy. Generally, the heterologous prime-boost immunizations have been generated as DNA prime/protein boost (e.g., oligomeric Env DNA prime/protein boost), DNA prime/peptide boost (e.g., MPER-V3 DNA/MPER-V3 peptide), DNA prime/viral vector boost (e.g., HIV-1 subtype C mosaic Gag DNA/ Gag MVA) and protein prime/viral vector boost (e.g., RV144: ALVAC prime [ALVAC-HIV(vCP1521)]. Future studies should be focused on developing a safe, affordable, effective heterologous prime-boost vaccine to reduce HIV-1 infections.

Keywords: HIV-1, Vaccination, Heterologous prime-boost, Subunit vaccines
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ID:159

Psychological Stress Effects on Demyelination in the Cuprizone-Induced Model of Multiple Sclerosis

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Objective: Multiple sclerosis is the most common demyelinating disease worldwide in which stress is marked as an important risk factor. Considering the increasing stressful life events and the rise of emotional disturbance in modern societies, the impact of repetitive psychological stress seriousness on demyelination extremity in a cuprizone-induced model of multiple sclerosis on female rats was investigated.
Material and Methods: Wistar rats were randomly divided into 4 groups, (n=4, age 6w, 100-120 g) as follows: (1) the control group, (2) the physical stress group (electric shocks: 0.25 mA, 50 Hz, 2 sec duration, 10 min: 10 shocks), (3) the psychological stress group (witnessing electric shocks) and (4) the demyelination group (without any exposure to special stress, just fed cuprizone). After 5 days exposure to stress (group 2 and 3), the experimental groups (i.e.2, 3 and 4) were treated with 0.6% (w/w) cuprizone for 6 weeks in order to induce demyelination. The demyelination degree was compared in groups of animals by transmission electron microscopy.
Results: According to the TEM quantified results, both stress groups illustrated fewer myelinated axons when compared to the demyelination group ($P<0.05$ for physical stress group and $P<0.001$ for psychological stress one). Notably, data showed 73% reduction of myelinated axons in physical stress group ($p<0.001$) while the reduction in psychological ones was 81% ($p<0.001$) compared to control.
Conclusion: As psychological distress has severe effects on demyelination, it seems that psychological healthcare would be an effective approach for demyelinating disease prevention.
Keywords: Psychological Stress, Demyelination, Multiple Sclerosis
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ID:170

Expression, purification and characterization of phospholipase from Natrialba asiatica

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Objective: Phospholipases (EC 3.1.1 Carboxylesterase) are interfacial enzymes that hydrolyze hydrophobic ester linkages of triacylglycerols and phospholipids.
Material and Methods: In the present investigation, phospholipase gene from halophilic archaeon Natrialba asiatica was cloned inpET-28a as cloning and expression vector and transformed into E.coli DH5α cells. Screening carried out using LB-agar plates containing kanamycin. The confirmed gene was transferred into E.coli BL21 and cultured up to OD600-nm ~2.5 in LB medium. Then, phospholipase production was induced by IPTG (0.5mM) and incubation at 37 °C for 45 min. Recombinant His-tagged protein purified using Ni-sepharose affinity chromatography. Purified phospholipase from Natialba asiatica had a molecular weight of 35 kDa on SDS-PAGE. Addition of detergents make potentially useful for industrial purposes, especially for the detergent and laundry industry. The effects of Tween 20 on enzyme was performed by the measuring the phospholipase activity on soy lecithin as substrates in the presence and absence of Tween 20.
Results and Conclusion: The enzyme activity profile showed that purified phospholipase was optimally active at pH 8.5 and 45 degrees C as optimum values. Also, study have shown that phospholipase enzyme activity has increased up to 1.5 times in the presence of 1% concentration of Tween 20 (volumetric) as a non-ionic detergent.
Keywords: Natrialba asiatica, Phospholipase, Purification, Characterization, Tween 20
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ID:174

Antagonistic effect of colony stimulating factor on cell death and HMGB1 release

induced by anticancer drug 5-Azacitidine in hematopoietic stem cells of bone marrow

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Objective: The cytosine analogue with antineoplastic activity, 5-azacitidine, is a DNA methyltransferase inhibitor which is currently considered an effective chemotherapeutic agent for epigenetic cancer therapy. Bone marrow is the most important tissue that hematopoiesis process occurs in it. High mobility group box1 (HMGB1), a chromatin associated nuclear, is a critical key of cell death and survival by regulating multiple signaling pathways, including inflammation, immunity, proliferation, metastasis and apoptosis. Colony stimulating factor (CSF) is necessary for proliferation and differentiation of hematopoietic stem cells to blood cells. The major toxicity of 5-azacitidine is myelosuppression but the precise mechanism of action remains unknown.

Material and Methods: In this study, the toxic effects of 5-azacitidine on non-adherent bone marrow cells, in the presence and absence of CSF was investigated using MTT assay, flow cytometry, diphenylamine assay, hoechst staining and intracellular HMGB1 expression and HMGB1 release by western blot analysis.

Results: The results obtained from MTT assay, showed that cell survival in the presence of CSFs possessed an 8-fold greater IC50 with respect to the absence of CSFs. Flow cytometry and diphenylamine assays revealed that 5-azacytidine in the absence of CSF increased the apoptosis/necrosis and DNA fragmentation of hematopoietic stem cells in a dose dependent manner. The apoptotic/necrotic property of 5-azacytidine was significantly decreased in the presence of CSF. The content of non-histone protein HMGB1 decreased and HMGB1 release increased as drug concentration increased but in the presence of the CSF the content of HMGB1 increased and HMGB1 release was not detected. Hoechst staining of cells treated with 5-azacytidine revealed remarkable morphological changes such as nuclear condensation suggesting occurrence of apoptosis.

Conclusion: In conclusion, 5-Azacitidine exhibits cytotoxic effect on hematopoietic bone marrow stem cells but in the presence of CSF its cytotoxicity is significantly decreased. It is suggesting its usage in combination therapy with CSF for cancer treatment.

Keywords: Hematopoietic stem cells, 5-Azacitidine, HMGB1, colony stimulating factor, apoptosis

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ID:176

A Mutation Study of Anti-Thrombin Aptamers for Designing Biosensors

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Objective: Anti-thrombin aptamers are G-quadruplex nucleic acids which bind to specific sites on thrombin molecule. Anti-thrombin aptamers are used as the recognition element in thrombin biosensors. Study of binding affinity between aptamer and protein is of great immense. There are two aptamers with high affinity and specificity for thrombin. The 15-mer aptamer is an anti-parallel G-quadruplex. Contrasting the 15-mer, 27-mer have a duplex/G-quadruplex structure. This aptamer interacts with a positively charged motif of thrombin. The positive charge of the motif leads to electrostatic bonding particularly in the duplex domain, and there are hydrophobic interactions in the G-quadruplex region. In this study, aptamer sequences were mutated based on increasing the number of purine in aptamer sequences and the binding affinity of aptamer-protein were investigated. Theses mutant aptamers help to improve designing biosensor.

Material and Methods: 27-mer structure of Anti-thrombin aptamer (PDB ID: 4I7Y) which has high affinity with thrombin was selected. A mutation in aptamer was made by Swiss-PdbViewer software. The binding affinity of aptamer-protein with H-dock and path-dock were investigated.

Results: 27-mer Anti-thrombin without any mutation had the best score in path-dock server. Point mutations in the positions of C14, T18 and T19 showed the best score in H-dock sever. According to both servers, there were not significant differences in scores of docking between 27-mer Anti-thrombin and mutant sequences.

Conclusion: Considering the results of docking, it was concluded that the point mutations in the aptamer have as much binding affinity as aptamer without mutation, but it reduces with increasing number of mutations. Hence, aptamers with point mutations can be used to detect thrombin depending on the design of biosensors.

Keywords: Anti-thrombin aptamers, thrombin, point mutation
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ID:183

A Mathematical Model to Predict the Biochemical Factors of Blood via Zinc Level in Type 2 Diabetic Patients and Normal Individual

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Objective: Diabetes is one of the most common endocrine diseases in the world that has an ever-increasing trend. It is a metabolic disorder that causes insufficient metabolism of carbohydrates, lipids and proteins. The aim of this study was to propose a model to predict the serum level of different biochemical factors of blood, based on the Zinc level.

Material and Methods: A total number of 150 people with type 2 diabetes, and 150 normal subjects as control samples were recruited in this study. Under appropriate conditions including diet and calming environment, different biochemical parameters of blood profiling including FBS, TG, Cholesterol, HDL, LDL, BUN, Creatinine and Zinc were measured. Thereafter, linear regression modeling was used to assess simultaneous effect of blood biochemical factors on Zinc level in each group. All the statistical analysis was performed in SPSS 18.0 software and $P<0.05$ was considered significant.

Results: Mean of Zinc level in diabetes patients was 72.4±25.5 and in control group was 74.7±25.5, which was not statistically significant (P=0.44). Linear regression analysis showed that HDL (coefficient= -0.37, P=0.04) was the most effective factor of Zinc level followed by HbA1c (coefficient= -2.03, P=0.18), Plt (coefficient= 0.04, P=0.16) and FBS (coefficient= 0.01, P=0.89) among diabetic patients. Moreover, the most effective factor of Zinc level among normal subjects were age (coefficient= -0.98, P<0.001), creatinine (coefficient= 24.95, P=0.02) and Plt (coefficient= -0.06, P=0.06).

Conclusion: Proposed models were successful in explaining 27.4% and 34.6% of zinc level variation among diabetes and normal subjects, respectively.

Keywords: Type 2 diabetes; Zinc; HbA1c; Modeling

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ID:185

Evaluation of the anti-tumorigenic effects of bilirubin on LS180 (with wild type p53) and SW480 (with mutant p53) colorectal cancer cell lines

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Objective: Colorectal cancer (CRC) is the third most common cancer worldwide and its development involves various genetic and molecular changes. p53 is a key tumor suppressor gene and is one of the most important elements of our body's anticancer defense. CRC patients with mutant p53 appear more chemo-resistance and have poorer prognosis than those with wild-type p53. The present study investigated the effect of bilirubin as a natural antioxidant on the cell viability and the expression level of both wild and mutant types of p53 protein in two colorectal cancer cell line, LS180 (with wild type p53) and SW480 (with mutant p53).

Material and Methods: Nontoxic concentrations of bilirubin were determined by using MTT assay. LS180 and SW480 cell lines were treated with bilirubin and DMSO (as vehicle control) for 24 and 48 hours' time intervals. Western blot analysis was employed to evaluate the expression level of p53 before and after treatment.

Results: In both cell lines bilirubin at the concentrations of 50 and 100 µM showed the best anti-cancer effects according to the cell viability analysis. The results also revealed that the level of p53 protein was higher in LS180 treated cells as compared with control. However, in the case of SW480 cell line, no considerable changes of the p53 protein was shown in treated cells compared with control ones.

Conclusion: Based on the observed changes in the cell viability and the expression level of p53 protein in these cell lines, bilirubin has a beneficial role in the prevention of CRC.

Keywords: Bilirubin, Colorectal cancer, p53

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ID:186

The study of affinity of some NSAID compounds and cox 2 selective inhibitors to cox-2 enzyme by In-silico techniques

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Objective: There are two form of cox enzyme: cox-1 and cox-2. Cox-1 is expressed in most cells and tissues. However, cox-2 is selectively induced by proinflammatory cytokines in

inflammatory sites. Non-steroidal anti-inflammatory drugs (NSAIDs) are potent anti-inflammatory agents that stop production of prostaglandins by inhibit cox enzymes. These drugs inhibit both cox enzymes, while the cox-2 enzyme should be inhibited as an inducible form of inflammation. For this reason, the use of these drugs is limited. Our goal in this study is to compare the binding power of NSAIDs and cox-2 selective inhibitor to the cox-2 enzyme.

Material and Methods: The chemical structures of cox-2 (PDBID: 5KIR) enzyme were obtained from PDB (www.RCSB.org/pdb). The chemical structures of the synthetic compounds were obtained from the data base PubChem (https://pubchem.ncbi.nlm.nih.gov) in sdf format. The graphic program ADT version 4.2.6 was used to prepare ligands and proteins. At last, we used Autodock vina version 1.1.2 to estimate their affinity to enzymes.

Results: In the present study, the affinity of study ligands to the cox-2 enzyme was investigated by using docking analysis. celecoxib, indomethacin, ibuprofen, aspirin, rofecoxib and valdecoxib ligands had the affinity rating ΔG= -8, ΔG= -7, ΔG= -6.7, ΔG= -6.6, ΔG= -6.5 and ΔG= -6.5 respectively.

Conclusion: According to the results, it is observed that the cox-2 selective inhibitors include celecoxib, rofecoxib and valdecoxib, have close binding power and in some cases more than NSAIDs. So, by making changes to the structure of selective inhibitors, used them as cox-2 selective inhibitors.

Keywords: Cyclooxygenase 1, Cyclooxygenase 2, Non-Steroidal Anti-Inflammatory Agents (NSAIDs), celecoxib, valdecoxib

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ID:187

Investigation of EMSY expression in cancerous compared to normal tissue in Iranian women with sporadic breast cancer by Real Time RT PCR

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Objective: Regarding the high prevalence of breast cancer among women and the importance of early diagnosis of disease in early stages using advanced molecular techniques and the importance of EMSY gene as a prognostic factor in breast cancer, The EMSY protein reacts with exon number 3 BRCA2 which suppresses the DNA repair function of BRCA2 in non-hereditary breast cancer, thereby EMSY introduces as a strong oncogene normal functions of EMSY involve repairing damaged DNA, genomic instability and chromatin remolding, expression of EMSY gene in the cancerous tissue compared to normal tissue of women with sporadic breast cancer was investigated by Real Time RT PCR.

Material and Methods: Extracting of tissue samples (normal and cancerous tissue) with Thrysol, Total RNA, and after synthesis of CDNA, by Real Time RT PCR technique, examined EMSY gene expression in women with sporadic breast cancer.

Results: Relative expression of EMSY gene by Real Time RT PCR technique in cancerous tissues compared with normal tissue increased by 61.6. Showed equality and a statistically significant difference in this case with P-value=0/001.

Conclusion: Our study showed that there is a possible relationship between the high expression of EMSY gene and breast cancer and could be considered as a potential target for breast cancer treatment.

Keywords: Sporadic breast cancer, EMSY, Specimen, Real Time RT PCR

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ID:190

In Silico Evaluation of novel agent for anaerobic glycolysis inhibitors in cancer treatment

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Objective: Chemotherapy based on peptides are a novel approach for cancer therapy which is related to several advantages of peptide such as: low toxicity, easy to synthesis, high target specificity and others. Current research focuses on design of peptide inhibitor for lactate dehydrogenase enzyme in breast cancer cell. Lactate dehydrogenase (LDH) is an enzyme of anaerobic glycolysis and inhibition of LDH lead to decrease tumor cells growth and progression.

Material and Methods: In this study Peptiderive Server was used for design of peptide. The best modeled peptide was selected using molecular docking software (CABS-dock) and then pharmacology properties of peptides was analysis by FAF Drugs3. Finally, the anti-proliferative activity of these compounds was confirmed on a MCF7 cell lines via MTT assay and flow-cytometric techniques.

Results: The peptide ability to disrupt protein–protein interfaces are several

attractive features when compared to small molecule. Therefore, in this study we attempted to synthesize a peptide that could interference with the interaction of enzyme subunits and inhibited lactate dehydrogenase activity because the tetrameric form of enzyme plays an important role in maintaining the active site geometry. Cytotoxic assay showed that the peptide could inhibit MCF-7 cancer cell growth, with an IC50 value of 60 µM. Our results indicated that, Inhibition of LDH case to inhibition of cell proliferation and induced cell death though the accumulation of reactive oxygen species (ROS) in the cancer cell line.

Conclusion: Inhibition of LDHA by these peptide led to impaired cell survival in cancer cells and so, making it a compelling strategy for treating cancer.

Keywords: Anaerobic glycolysis, Lactate dehydrogenase, peptide inhibitor, cancer

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ID:192

Effect of Metformin on liver Hexokinase and Glucokinase specific activity in PCOS rats

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Objective: Polycystic ovary syndrome (PCOS) is an endocrine disorder affects women in reproductive age and Insulin resistance (IR) is a critical factor in the pathogenesis of it which eventually can lead to diabetes. Considering the effects of Metformin on the reduction of glucose levels, recently it has been introduced as a curative option for PCOS patient. In the present study we assessed for the first time, the effects of Metformin on the liver Hexokinase (HK) and Glucokinase (GK) specific activities as two important enzymes in glucose metabolism in PCOS induced rat.

Material and Methods: The female rats were grouped based on PCOS condition and Metformin consumption. The morphology of ovaries was observed to confirm PCOS induction. Fasting blood glucose (FBG) and fasting serum insulin level were analyzed using glucose oxidase and ELISA methods. The HOMA-IR was used for IR levels determining. Liver HK and GK specific activity were determined using spectrophotometry.

Results: Calculating the HOMA-IR showed a sever IR in the PCOS rats (H-IR>2.5), and treatment with Metformin, significantly reduced IR amount. GK activity reduced in PCOS rats and Metformin returned it to the normal state. We also observed an increase in HK activity in PCOS; however Metformin intensified the elevation of this enzyme compared to both normal and PCOS group.

Conclusion: PCOS is usually associated with IR and this explains the prevalence of diabetes and disturbed liver enzymes activities in PCOS. Treatment with Metformin has ameliorating effects on insulin sensitivity in PCOS, and this effect might be due to improving HK and GK enzyme activities.

Keywords: PCOS, Insulin resistance, Hexokinase, Glucokinase, Metfromin

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ID:195

Cytotoxic effect of vincristine on human liver carcinoma HepG2 cells

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Objective: Vincristine is the most effective anticancer drug, widely used as a potent chemotherapeutic agent in the treatment of various cancers. Vincristine belongs to vinca alkaloid anticancer drugs. It is composed of two multi rings: vindoline and catherantine and exerts its activity by depolymerization of mitotic microtubules. In this study we have investigated the effect of vincristine on HepG2 cells.

Material and Methods: The cells were cultured in the absence and presence of various concentration of vincristine. The programmed cell death (apoptosis) was characterized by cleavage of poly ADP ribose polymerase (PARP), flow cytometry and DNA fragmentation.

Results: After exposure of the cells to vincristine, DNA fragmentation was increased in a dose dependent manner. As the concentration of vincristine was increased the content of cleaved PARP (89 KD) was increased. This data showed that apoptosis in HepG2 cells by vincristine is PARP dependent. Flow cytometry using Annexin-V-PI demonstrated that vincristine induced apoptosis. Thus at 25 µg/ml percentages apoptosis and necrosis were 5.50% and 0.48 %, but when the cells exposure to 100 µg/ml of the drug the percentages were 14.42% and 0.68 respectively.

Conclusion: The results showed that vincristine induced apoptosis in HepG2 cells and the process is PARP dependent.

Keywords: Vincristine, HepG2, PARP, Flow cytometry, DNA fragmentation

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ID: 200

Relationship between some serum trace elements (Zn, Cu, Se) levels and antioxidant status in Hashimoto's thyroiditis patients

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Objective: Hashimoto's thyroiditis (HT) is the most prevalent autoimmune thyroid disorder. Thyroid hormones have a crucial physiological role to maintain balance of metabolism of body. Also oxidative stress has been implicated in the pathogenesis of several inflammatory and immune mediated disorders including Hashimoto's thyroiditis. Therefore, present study was aimed to find the changes in serum Zinc (Zn), Copper and Selenium levels and also evaluate effect of HT on body antioxidant status.

M***aterial and Methods:*** The study people consisted of 86 subjects divided into two groups: 43 people with Hashimoto's thyroiditis (HT) and 43 age-matched healthy individuals. This study checked the amounts of total triiodothyronine (T3), total thyroxine (T4), thyroid stimulating hormone, (TSH), trace elements status and some antioxidant status parameters.

R***esults:*** The mean TSH and SOD levels was significantly increased in HT patients (1.56±0.73) compared to control group (1.09±0.62). The levels of T4 and Se were significantly lower in HT patients compared to control group ($P<0.05$). However, there was no significant difference in the mean of T3, Zn, Cu and PON-1 between hypothyroidism and control ($P<0.05$).

C***onclusion:*** These outcomes establish the hypothesis that people with HT have elevated oxidative stress and decreased trace elements levels, therefore the importance of monitoring the levels of those antioxidant capabilities and trace elements status in HT patients before treatment.

Keywords: Hashimoto's thyroiditis, Zn, Se, Cu, PON-1, SOD

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ID:205

The effect of essential oil of cultivated Satureja khuzestanica Jamzad on activity and genes expression of liver phosphoenolpyruvate carboxykinase in diabetic rats

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Objective: Researchers have been reported that Satureja khuzestanica essential oil (SKEO) has a wide range of effects such as: anti-inflammatory, antioxidant, hypolipidemic, hypoglycemic activities. Studies in diabetic animals have shown that gluconeogenesis is a major factor in the increase plasma glucose that appears in fasting and post-absorptive state. The aim of the present study is to evaluate the effect of cultivated SKEO on activity and gene expression of hepatic phosphoenolpyruvate carboxykinase (PEPCK) in normal and diabetic rats.

Material and Methods: Thirty-two wistar male rats were divided into four groups randomly; group one as control, group two as diabetic untreated, group three as sham treated with cultivated SKEO (100 mg/kg/d) in aqueous solution orally for 21 days, and group four as diabetic treated with cultivated SKEO (100 mg/kg/d) in aqueous solution orally for 21 days. After 21 days, animals were anaesthetized, liver were then removed immediately and used fresh or kept frozen until analysis of activity and gene expression of PEPCK by using the quantitative real-time RT-PCR technique.

Results: Activity of the hepatic PEPCK and its mRNA levels of diabetic rats was significantly increased compared with those of normal control rats ($p<0.001$). Hepatic activity and gene expression of PEPCK in diabetic treated groups compared with diabetic untreated groups were significantly decreased ($p>0.05$). Also, hepatic activity of PEPCK activity correlated positively with its gene expression.

C***onclusion:*** This study showed that SKEO might be an exert beneficial effects on activity and gene expression of PEPCK in diabetic rats. Therefore, SKEO may contribute to reduction of serum glucose, which seems to be related to its antioxidant properties.

Keywords: Antihyperglycemic, Gene expression, Phosphoenolpyruvate carboxykinase, Satureja khuzestanica essential oil

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ID:213

Salusins and cytokines expression in HUVECs

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Objective: Salusin-α and salusin-β are novel peptides, which have opposite role in atherosclerosis. Pro inflammatory cytokines have major role in atherosclerosis. We compared the effect of salusins on the expression of IL-6, IL-8, IL-18 in Human umbilical vein endothelial cells (HUVECs).

Material and Methods: HUVECs were cultured in completed medium and treated with salusin-β and salusin-α (3, 10, 30, 90 nM), for 6, 12h. The possible cytotoxic effect of these proteins in HUVECs was assessed using MTT assay. The mRNA expression of IL-6, IL-8, and IL-18 was assessed by real-time PCR system. The primers were confirmed by sequencing. GAPDH housekeeping gene was used as internal control.

Results: Salusins had no cytotoxic effect in HUVECs. Salusin-α (90 nM) for 6h, reduced IL-6 mRNA expression, salusin-β increased IL-6 mRNA expression at 30 nM and 90 nM for 6h treatment and 90 nM for 12h treatment. Salusin-α decreased IL-8 mRNA expression at 10 nM, 30nM, 90nM for 6h treatment, salusin-β enhanced IL-8 mRNA expression at 30 nM ,90 nM for 6h treatment, and at 90 nM for 12h treatment. IL-18 mRNA expression was decreased at 90 nM of salusin-α for 6h treatment, salusin-β increased IL-18 mRNA expression at 30 nM and 90 nM for 6h treatment, and at 90 nM for 12h treatment.

Conclusion: Salusin-β accelerated and salusin-α attenuated inflammatory responses in endothelial cells. These novel finding indicated new properties of salusins which may help to understand atherosclerosis pathogenesis.

Keywords: Atherosclerosis, cytokines, salusin-alpha, human, salusin-beta

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ID:214

Protective role of Adiponectin in preventing hyperglycemia-mediated kidney cell damage through altering Sirtuin-1 level

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Objective: Adiponectin (APN) is an adipocytokine, secreted from adipose tissue and has anti-inflammatory, anti-aging and anti-diabetic properties. Hyperglycemia can damage the renal cells and Sirtuin 1 (SIRT1) has an important role in kidney cell response to hyperglycemia. In this regard, the protective role of the APN in preventing hyperglycemia-mediated cell damage is important. Therefore, understanding the relationship between adiponectin, and SIRT1 protein is helpful in deciphering the mechanism of adiponectin function.

Material and Methods: In this study, Human Embryonic Kidney -293 (HEK-293) cells were cultured under normal and high glucose, without and with APN (1, 10 and100 ng/mL) for 48 hours. To evaluate hyperglycemia-mediated cytotoxicity, cell viability was determined, using MTT assay and SIRT1 protein was assayed, using ELISA method.

Results: Data showed that APN in high dose (100 ng/mL) significantly increased SIRT1 protein, compared with the control high glucose ($P \leq 0.05$). The cytotoxicity assay showed a significant decrease in cell viability in high glucose, compared to the normal glucose condition ($P \leq 0.05$) and APN increased the cell survival, in a dose-dependent manner.

Conclusion: According to the results, APN can be useful in preventing renal cell damage in hyperglycemia condition. It seems APN enhancement strategy can be beneficial in diabetics to reduce kidney cell damage.

Keywords: Hyperglycemia, HEK-293 cells, Sirtuin1, Cytotoxicity, Adiponectin

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ID:216

Synergic antiproliferative effect of 5-Azacytidine, a DNA methyltransferase inhibitor, in combination with Alimta anticancer drug against A549 cells

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Objective: Lung cancer is the leading cause of cancer-related deaths worldwide. Besides genetic mutations, epigenetic alterations have widely been reported to play a major role in the genesis of lung cancer. 5-azacytidine is a nucleoside analogue that inhibits DNA methyltransferases (DNMT) and leads to DNA hypomethylation. As the effects of epigenetic single agent treatment of solid tumors have been limited, the investigative focus now lies on combination therapies of epigenetically active agents with conventional chemotherapy. Therefore, the aim of this study was to evaluate the combination of 5-azacytidine, as chemosensitizing agent, with Alimta, a new-generation antifolate drug, in lung cancer A549 cell lines.

Material and Methods: A 549 cells were exposed to low doses of 5-azacytidine and varying doses of Alimta for 72 h. Cell proliferation was assayed by MTT and potential synergism was calculated according to the method of Chou and Talalay. Also, colony formation assays, acridine orange/ethidium bromide staining, Annexin

V/Propidium iodide assay and cell cycle analysis were performed.

Results: The results showed that pre-treatment of A549 cells with 5-azacytidine resulted in the increase of their sensitivity to Alimta thus the IC50 value of Alimta (13μM) reduced to 3μM. Combination treatment indicated synergistic reduction of colony formation. Treatment of A549 cells with Alimta and 5-azacytidine resulted in an increase in early and late apoptosis; upon combination treatment there was increase in early apoptosis by 30.34%, late apoptosis by 25.12 %, and no change in necrotic fraction of cells. In addition, cell cycle analyses showed an increase in S phase population by Alimta, which was gradually replaced by Sub-G1 cell population by 5-azacytidine combined with Alimta.

Conclusion: In conclusion, 5-azacytidine increases the chemosensitivity of Alimta in lung cancer cells in apoptotic signaling and provides a rationale for combination chemotherapy of DNMT inhibitors with traditional anticancer drugs in lung cancer.

Keywords: A549 lung cancer cell, 5-azacytidine, Alimta, apoptosis, DNA methyltransferases

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ID:220

Curcumin as a Potent Osteoinductive Agent Promotes Matrix Mineralization and Osteogenic Activity of human Mesenchymal Stem Cells

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Objective: Human bone marrow mesenchymal stem cells (hBMSCs) are novel therapeutic tool in regenerative medicine. Despite years of research, efficient differentiation of MSCs into osteoblastic lineage still demands further investigations. Use of osteoinductive agents would be an appealing strategy to deal with this challenge. The current study aims to examine osteoinductive potential of curcumin as a natural polyphenol on osteogenic differentiation of hBMSCs.

Material and Methods: MSCs were isolated from bone marrow and characterized. The cytotoxicity of curcumin on hBMSCs was assessed by MTT assay. Alkaline phosphatase (ALP) activity and calcium deposition were evaluated in hBMSCs cultures after 7 and 14 days. qRT-PCR was used to assess the expression levels of osteoblastic markers.

Results: There was no cytotoxicity associated with the concentrations of 10 and 15 μM of curcumin. ALP activity and calcium assay showed higher level of matrix mineralization in the presence of curcumin compared to control group. Gene expression level of osteoblastic markers that include Runx2, osterix, collagen typeI, osteopontin and osteocalcin significantly up-regulated in culture that contained curcumin in a time/dose-dependent manner.

Conclusion: It is confirmed that curcumin as a natural compound with the ability to stimulate osteogenic differentiation and accelerate matrix mineralization have the potential to be utilized in bone regeneration.

Keywords: Curcumin, MSCs, Osteogenesis

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ID:221

Hypolipidemic activity of Dracocephalum kotschyi extract via AKT-mediated induction of PPARγ expression in adipose tissue

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Objective: Dracocephalum kotschyi, a well-known Iranian traditional medicine, was evaluated in terms of hypolipidemic properties. Enhanced PPARγ-mediated lipogenesis with subsequent accumulation of triglycerides droplets in adipocytes is considered as a therapeutic strategy for treatment of diabetic patients with hyperlipidemia. Here, we compared serum lipid profile of DKE (Dracocephalum kotschyi extract)-treated diabetic rats with negative and positive controls. Furthermore, adipose tissue expression levels of p-JNK, p-AKT, p-FOXO1, t-FOXO1 and PPARγ, as the main regulators of lipogenesis, were determined using western blot technique.

Material and Methods: Streptozotocin-induced diabetic rats were orally treated with DKE at two different doses (0.25 and 0.5 ml/rat.day) and serum biochemical factors were evaluated during the 28 treatment days.

Results: Treatment with DKE (0.25 ml/rat) decreased the sera levels of TG, TC and LDL by 48, 31 and 43%, respectively, compared to the untreated diabetic group, whereas the dose of 0.5 ml/rat resulted in a decrease of TG, TC and LDL by 54, 40 and 54%, respectively. The

serum level of HDL was 45% higher in DKE-treated group (0.5 ml/rat) than that of the untreated diabetic group. Western blot analyses demonstrated decrements of p-JNK (0.25 ml/rat, 31% and 0.5 ml/rat, 40%) and t-FOXO1 (0.5 ml/rat, 36%) expression levels in addition to the increased levels of p-AKT (0.25 ml/rat, 52% and 0.5 ml/rat, 97%), p-FOXO1 (0.25 ml/rat, 48% and 0.5 ml/rat, 51%) and PPARγ (0.25 ml/rat, 33% and 0.5 ml/rat, 79%) in DKE-treated rats compared to diabetic control group.

Conclusion: This study demonstrated that DKE reverses hyperlipidemia symptoms in streptozotocin-induced diabetic rats via rebalancing the PPARγ and FOXO1 adipose expressions.

Keywords: Adipose tissue, Dracocephalum kotschyi, hyperlipidemia, PPARγ

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ID:224

Rosmarinic acid inhibits lipogenesis despite induced activity of AKT in 3T3-L1 cells

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Objective: Rosmarinic acid, a bioactive natural antioxidant, is believed to possess ERK-mediated anti-lipogenesis activity in 3T3-L1 cells. However, antioxidants are known as JNK inhibitors that subsequently induce lipogenesis in adipocytes. Relevant emerging data propose that inhibition of JNK results in an augmented insulin-signaling pathway and increased level of p-AKT which ultimately leads to induced lipogenesis. In this study, we investigated both mentioned pathways in rosmarinic acid-treated 3T3-L1 adipocytes.

Material and Methods: 3T3-L1 cells were treated with DMI medium (DMEM containing 1 µM dexamethasone, 0.5 mM 3-isobutyl-1-methylxanthine, and 1.5 µg/ml insulin). After 48 hours the DMI medium was replaced by 10 µg/ml insulin-supplemented DMEM. Determination of lipogenic effects was proceeded via evaluating the triglycerides content of the treated cells. The expression levels of p-AKT, p-ERK and tubulin were determined by western blot technique.

Results: The cells were treated with 50 µM rosmarinic acid for 48 hours and the TG content was measured using the relevant kit (Pars Azmun, Iran). Our data indicated that rosmarinic acid reduces the TG content in 3T3-L1 cells by about 33% compared to that of untreated cells ($P<0.05$, n=15). In this study, rosmarinic acid treated 3T3-L1 cells (50 µM) demonstrated a 37% increased expression of p-ERK compared to the untreated cells ($P<0.01$, n=3) that is in accordance with other studies. On the other hand, the expression of p-AKT demonstrated a 17% increase ($P<0.5$, n=3) relative to control samples.

Conclusion: This study demonstrated that in rosmarinic acid treated 3T3-L1 cells, the activation of AKT loses its impact on lipogenesis with a mechanism that still remained unknown.

Keywords: Lipogenesis, Rosmarinic acid, p-AKT, p-ERK

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ID:228

Study the effects of bilirubin on the expression of BECN1 and LC3 genes in LS180 and SW480 colorectal cancer cell lines

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Objective: Colorectal cancer (CRC) is one of the most prevalent and deadly cancers worldwide. Among the factors and mechanisms that are involved in the multifactorial etiology of CRC, autophagy is an important transformational switch that occurs when a cell shifts from normal to malignant. ROS have been copiously reported as early inducers of autophagy upon nutrient deprivation. Bilirubin is recognized as the most potent endogenous antioxidant. The anti-oxidant property of bilirubin has given us the initiative to assess its effect on autophagy. The present study investigated the effect of bilirubin on the expression levels of autophagy markers, BECN1 and LC3 genes in two colorectal cancer cell lines, LS180 and SW480.

Material and Methods: Nontoxic concentrations of bilirubin were determined by using MTT assay. LS180 and SW480 cell lines were treated with bilirubin and DMSO (as vehicle control) for 24 and 48 hours' time intervals. Quantitative Real-Time PCR was used to assay the mRNA expression levels of BECN1 and LC3 genes.

Results: By using MTT assay, concentrations of 50 and 100 µM bilirubin were determined as nontoxic concentrations for the studied cell lines. Based on the results of Quantitative Real-Time PCR, BECN1and LC3 expression level decreased in both cell lines.

Conclusion: Based on the observed changes in the expression levels of BECN1 and LC3 genes which are involved in autophagy process, bilirubin has an antitumor defense role in the studied cell lines, probably through the control of autophagy as a key step in survival and drug resistance of tumor cells.

Keywords: Colorectal cancer, Bilirubin, Autophagy, BECN1, LC3

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ID:229

Metformin attenuates oxidative stress and liver damage after bile-duct ligation in rats

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Objective: The aim of current study was to investigate the effects of metformin (Met) on oxidative stress markers in bile duct ligation (BDL)-induced liver fibrosis in rats.

Material and Methods: The male Wistar rats divided into four groups including SC (sham control), BDL (Bile duct ligation surgery), Met1 (BDL surgery and administration of 250 mg/kg of metformin) and Met2 (BDL surgery and administration of 500 mg/kg of metformin). After BDL, the animals treated with Met by gavage for 10 days and the hematoxylin and eosin staining, biochemical analysis and oxidative stress markers were assayed.

Results: Hepatotoxicity was verified by remarkable increase in plasma levels of AST, ALT, ALP, GGT and liver histology 10 days after the BDL surgery. The results showed that treatment with Met significantly reduced plasma ALP and alleviated liver injury indexes ($P \leq .05$). Furthermore, BDL caused a considerable increase in hepatic lipid peroxidation, protein oxidation and NO metabolites production, as well as a significant decrease in plasma GSH and FRAP levels ($P \leq .05$), interestingly, all of the changes were reversed by Met administration.

Conclusion: Metformin exerts antioxidative effects in the liver fibrosis and may represent a protective effect when administered to rats with BDL-induced hepatic injury.

Keywords: Oxidative stress, Cholestasis, Metformin, Antioxidant

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ID:233

Evaluation of the association between serum testosterone levels and severity of 6-hydroxydopamine- induced Parkinsonism in rat

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Objective: Parkinson's disease is a neurodegenerative disease, which is the most common age dependent neurodegenerative disorder after Alzheimer's disease. The disease is caused by the destruction of dopaminergic neurons in the substantia nigra. Parkinson's disease symptoms appear when about 60-80% of these neurons are destroyed and dopamine do not produce enough. Oxidative stress, mitochondrial dysfunction, protein aggregation and autophagic stress has been implicated in Parkinson's. Early diagnosis of Parkinson's disease can result in more effective treatment and preventing the exacerbation of the disease. Identifying the biomarkers can help in the diagnosis. Testosterone levels is reduced in patients with Parkinson's disease. Regarding the controversy about the relationship between serum testosterone and prolactin and Parkinson's disease, this study was designed to evaluate the serum levels of testosterone in Parkinson's disease in the animal model.

Materials and Methods: Male wistar rats, weighing 200-300gr were divided into control, sham and Parkinsonism groups. Parkinson's disease was induced by injecting 6-hydroxy dopamine in the MFB by Hamilton syringe. The development and severity of Parkinsonism was measured by apomorphine-induced rotational tests. In the third and sixth weeks after stereotaxic surgery, and after the behavioral tests, blood samples were collected from the animals' tail and heart, and the serum levels of testosterone were evaluated by ELISA.

Results: Control and sham group did not show rotation but the Parkinson's group showed significant rotation that sixth week was more than the third week. Parkinson's rats were divided into two groups, mild and severe, based on severity of symptoms. In both groups, testosterone level was increased, but it was significant only for the severe group.

Conclusion: The results of study showed that 6-hydroxy dopamine-induced Parkinsonism is associated with increased serum levels of testosterone.

Keywords: Parkinson Disease, 6-Hydroxydopamine, Testosterone, Substantia Nigra, Behavioral Test

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ID:241

Role of regulatory miRNAs of PI3K/AKT signaling axis in the pathogenesis of colorectal cancer

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Objective: Colorectal cancer (CRC) is a malignant disease with high mortality in the world. In a large number of CRC patients, up-regulation of PI3K/AKT signaling pathway is reported. MicroRNAs, small noncoding 18-25 nucleotides RNAs, regulate wide range of biological processes in several cancers including CRC. In this review, we summarize the role of PI3K/AKT signaling regulatory miRNAs in the pathogenesis of CRC.

Material and Methods: Comprehensive search was performed via PubMed, Scopus, Web of Science and Google scholar database using the following keywords: [colorectal cancer OR colon cancer] and [microRNA OR miRNA OR mir] and [PI3K OR AKT OR mTOR OR PTEN]. Search strategy was limited to English language studies.

Results: Results show that oncogenic or tumor suppressor microRNAs are correlated with tumorigenesis behavior including proliferation, progression, migration, invasion, differentiation as well as resistance to chemo/radiotherapy in colorectal cancer. MiRNAs can affect PI3K upstream and downstream mediators in post-transcriptional levels and change function of PI3K, AKT, mTOR and transcription factors trough up-regulation or down-regulation of these molecules.

Conclusion: These findings clearly support the role of PI3K/AKT regulatory miRNAs as potential novel diagnostic and prognostic biomarkers in CRC patients. Taken together, restoration of tumor suppressor miRNAs or targeting oncogenic miRNAs with biological and pharmacological inhibitors could be a potent therapeutic strategy for CRC patients.

Keywords: PI3K/AKT signaling, MicroRNA, Colorectal cancer

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Simvastatin and Temozolomide Co-treatment induce cell death in Glioblastoma cell lines

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Objective: Glioblastoma multiforme (GBM) is the common, invasive, and incurable malignant tumor of the central nervous system. Nowadays, surgery, radiotherapy, and chemotherapy using Temozolomide (TMZ) are the gold standard protocol for treatment of patients. The main problem is resistance to TMZ and survival chance is too low. Recently, several studies showed that statins especially simvastatin have beneficial effects not only inhibits mevalonate cascade and reducing cholesterol, but also influences the expression of many proteins to involve in cells growth including Ras/Raf/Mapk, and Rho GTPase. In this study, we attempted to evaluate the combined effect of Simvastatin+TMZ in Glioblastoma cell lines.

Material and Methods: The concentration (0–20 μM) of simvastatin (0–1000 μM) of TMZ, also the combination of Simvastatin 1, 2.5 μM with (100 μM) TMZ during 24–96 hours on cell viability of Glioblastoma cell lines (U87, U251) were examined with MTT assay.

Results: Our data indicate that Simvastatin induces significant cell death in U251 and U87 for concentrations greater than 5 μM in 48 h and greater than 1,2.5 μM in 72,96 h. According to our data, the combination of TMZ 100 μM with simvastatin (1, 2.5 μM) increase the ability of TMZ in cell death in 48, 72,96 hours. The results were evaluated by one-way or two-way ANOVA followed by Tukey's, using Graph Pad Prism 7.0. P-value<0.05 was considered statistically significant.

Conclusion: These results indicate that co-treatment of Simvastatin and TMZ has a major impact on the lethal ability of TMZ in glioblastoma cancer.

Keywords: Cancer, Simvastatin, Temozolomide

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Thymus vulgaris as cholesterol reducing blood-contact adsorbent

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Objective: In hyperlipidemia i.e., high levels of cholesterol, when there is no potential alternative to drug therapy, the extracorporeal column adsorption is the most effective tool to immediately reduce the blood lipid content. In current study, Thymus powder performance as a biocompatible serum-contact adsorbent was investigated according to isothermal and kinetic batch adsorption experiments using the actual human pooled serum as adsorbing medium.

Material and Methods: To measure the isothermal data, 0.1 g of adsorbent was equilibrated with 0.1 dl pooled serum at different concentrations (150 to 200 mg/dl), and the final concentration of the cholesterol was measured after 24 h. For gathering the kinetic data, 0.5 g adsorbent was poured in 0.5 dl pooled serum solution with the initial

concentration of 175 mg/dl, and the concentration of the solution was monitored at different time intervals. X-Ray Diffraction technique, Scanning Electron Microscopy, and Fourier Transform Infrared spectroscopy were also used to characterize the Thymus powder before and after adsorption.

Results: Cholesterol removal was increased from 30% to 50% with increasing adsorbent dose from 0.01 to 0.1 g; meanwhile, further increase had negligible effect on the blood cholesterol level. Cholesterol adsorption capacity of the powder was around 85 mg/g. The adsorption mechanism could be explained as "chemical adsorption" through "H-bonding" on the surface of the fluffy fibers and inside the Thymus powder pores. These results were also confirmed bay FTIR and SEM analyses results.

Conclusion: Cholesterol adsorption from human blood serum was studied using Thymus as a biocompatible and effective herbal biosorbent for possible application in extracorporeal blood perfusion therapy.

Keywords: Serum, Thymus, Cholesterol, Biosorption, Extracorporeal perfusion

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Serum levels of calcium, zinc and vitamin D, but not magnesium, are correlated with inflammatory and atherogenesis indices in polycystic ovary syndrome patients

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Objective: Polycystic ovarian syndrome (PCOS) is associated with an increased number of cardiovascular risk factors and atherogenesis. A possible correlation between serum level of magnesium, calcium, 25 (OH)D and zinc with cardiovascular disease was recorded. But the correlation of these minerals with inflammatory and atherogenic indices was not assessed in the PCOS patients, controlled by dietary intake. We aimed to explore the potential relationships between serum zinc, magnesium, calcium and vitamin D with inflammatory and atherogenic indices in PCOS patients controlled by dietary intake.

Material and Methods: A case-control study with 103 PCOS patients and 206 healthy controls matched by age and BMI was conducted.

Results: There was a significant increase in serum TG/HDL-C (p=0.001), LDL-C/HDL-C (p=0.01), TNF-α, IL-6 and hs-CRP (p<0.001), as well as a significant decrease in adiponectin to leptin ratio (p<0.001) in the PCOS compared to healthy control group. Serum levels of calcium, zinc and 25 (OH)D had significant effect on adiponectin to leptin ratio (p=0.004, p=0.03 and p<0.001), adjusting for other variables. Serum zinc had significant effect on IL-6 and TNF-α levels (p=0.004 and p=0.01, respectively). Higher serum zinc level decreases IL-6 and TNF-α by 88% and 89%, respectively. Serum calcium had significant effect on TG/HDL-C ratio (p=0.02). Calcium decrease this ratio by 63%, adjusted for other variables. No significant correlation was seen between serum magnesium level and athrogenic indices and/or inflammatory markers in the PCOS group.

Conclusion: Results provide clues to element treatments in the PCOS patients. Calcium, zinc and vitamin D supplementation may decrease inflammation and risk of atherogenesis in this group.

Keywords: polycysticovary syndrome, inflammation, atherogenesis, zinc, magesium

ID:254

The effect of vinorelbine on High-Mobility Group protein N2 and induction of apoptosis in lung cancer A549 cells

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Objective: Vinorelbine is a Vinca alkaloid antitumor drug, widely used in the treatment of cancers such as advanced non-small cell lung cancer. The main mechanisms of vinorelbine cytotoxicity is due to its interactions with tubulin and chromatin components. High-Mobility Group protein N2 participate in the processes such as transcription and DNA repair. Therefore, this study focuses on the effect of vinorelbine on non-histone chromatin proteins such as HMGN2 protein.

Material and Methods: The cells were exposed to various concentrations of vinorelbine and the viability determined by MTT assay. HMGN2 proteins were extracted from the control and drug-treated cells and analyzed by immunoblot. HMGN2 gene expression was studied by Real-time PCR. For morphological study, cells were stained with Acridine orange/ethidium bromide. To determine the percentage of apoptotic cells flow cytometry with annexin V/PI was performed.

Results: The results obtained from MTT assays showed that viability of A549 cells decreased

in a dose- and time- dependent manner with IC50 value of 0.5 µm after 48 hours of exposure. The content of HMGN2 decreased on SDS-gel upon increasing drug concentration and western blots confirmed it but HMGN2 release into extracellular space was not detected. Moreover, Real-time PCR showed that the expression of this gene was decreased by increasing vinorelbine concentration. Acridine orange/ethidium bromide staining of cells revealed morphological changes such as chromatin condensation and nuclear fragmentation indicating occurrence of apoptosis and necrosis. The flow cytometry results showed increased in the percent of apoptotic cells and necrotic cells as the drug concentration increased.

Conclusion: In conclusion, vinorelbine affects HMGN2 of A549 cells preceding the cells into apoptosis and necrosis. The mechanism of action is possibly through the direct interaction of vinorelbine with HMGN2.The other possibility is compaction of chromatin under exposure to vinorelbine which inhibits chromatin transcription and replication.

Keywords: HMGN2, apoptosis, vinorelbine, A549

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ID:256

The Study of DNA methylation patterns of prodynorphin gene (PDYN) promoter in morphine tolerant rats

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Objective: The repeated administration of morphine may result in the development of morphine tolerance, which involves the altered expression of numerous genes, including PDYN in the lumbar spinal cord. In the light of this fact, the present study evaluated the expression of PDYN gene at mRNA level in the spinal cords of tolerant rats. We also assessed the methylation status of the promoter region of this gene.

Material and Methods: The Tolerance was induced by administration of intrathecal (i.t) morphine (22 nmoles) once daily from days 1-10. It should be mentioned that nociceptive testing was performed daily by the tail-flick test. Moreover, the real-time PCR was performed to assess changes in the expression of PDYN gene. Additionally, the status of gene promoter methylation was determined by MS-PCR on DNA samples modified by sodium bisulfite.

Results: Our results revealed that the level of PDYN mRNA was significantly up-regulated by the repeated morphine administration as compared to those in the saline group. Furthermore, we did not find significant differences between methylation status of promoter regions of the PDYN gene either in morphine tolerant rats or in saline-injected animals.

Conclusion: In summary, our data suggest that morphine tolerant rats show increased mRNA expression of the PDYN gene in the lumbar spinal cords. The evidence also suggests that the methylation status of PDYN promoter region in the spinal cord has not contributed to morphine tolerance.

Keywords: Morphine tolerance, PDYN, Epigenetic, Methylation

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ID:257

The protective role of the variant rs3088442 in the 3´UTR of the SLC22A3 gene in type 2 diabetes: a possible contribution of microRNA-147

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Objective: A guanine to adenine substitution in the variant rs3088442 created a microRNA (miR-147) binding site in the SLC22A3 messenger RNA, which resulted in a reduction in the expression of this gene. Considering the important roles of organic cation transporter 3 (OCT3) encoded by SLC22A3 in the transfer of various endogenous and exogenous compounds and its wide tissue distribution, in this study, therefore, we investigated whether this variant influence susceptibility to T2D in patients newly diagnosed with T2D.

Material and Methods: The case control study comprised of 150 newly diagnosed T2D patients diagnosed based on the WHO criteria and 152 control subjects. The genetic analyses were made by the restricted fragment length polymorphism (RFLP) after PCR amplification.

Results: The association of the rs3088442 variant with T2D showed a significant odd ratio (OR) for the A carrier genotypes (AG + AA) vs. GG genotypes (OR=0.37, $p<0.001$).

There was a statistically significant higher OR for A carriers vs. GG homozygotes in both men (OR=0.37, p=0.036) and women (OR= 0.38, p=0.001). A carriers also had a significantly lower OR vs. GG homozygotes in the BMI<30 kg/m2 group (OR= 0.23, p<0.001) compared with the BMI≥30 kg/m2 group (OR= 0.67, p= 0.34). In addition, A allele carriers had significant ORs vs. GG homozygotes for both the age<50 years group (OR= 0.31, p= 0.016) and the age≥50 years group (OR= 0.47, p= 0.008).

Conclusion: Our findings provide evidence for the protective role of the variant rs3088442 in susceptibility against T2D. The association of the A allele of rs3088442G>A with T2D become weaker in obese people than that of non-obese. The variant rs3088442 as a genetic marker may potentially assist in the identification of individuals at increased risk of T2D, and this would help to design targeted preventive programs. However, further research in different populations with a larger sample size is strongly recommended to confirm and clarify the role of this variant in susceptibility to T2D.

Keywords: SLC22A3, Organic cation transporter, rs3088442, type 2 diabetes, Genetic variant

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ID:260

Functional hepatocyte-like cells derived from human adipose tissue derived stem cells

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Objective: Human adipose tissue derived stem cells (hADSCs) are considered as a promising candidate for cell therapy of end-stage liver diseases. They possess the special affinity to acquire hepatocyte functions alongside of longer culture period and higher proliferation compared to mesenchymal stem cells (MSCs) derived from other sources. So far, wide varieties of strategies have been used for in vitro stem cell differentiation toward hepatocyte like cells. However, hepatic differentiation status of these cells has not been sufficient for clinical use, mainly because their metabolic activities are not fully induced. The aim of the present study was to explain a new protocol for the efficient hepatic differentiation of hADSCs.

Material and Methods: hADSCs were obtained from human adipose tissue and were cultured in hepatic differentiation medium containing fibroblast growth factor 4 (FGF4), hepatocyte growth factor (HGF), dexamethasone and oncostatin M up to 21 days. Afterwards, the hepatic functionality of differentiated cells was evaluated by analyzing specific hepatocyte genes and biochemical markers at different time points of differentiation induction.

Results: qRT-PCR analysis revealed significant up regulation of ALB, AFP, CK18, CK19 and HNF4a expressions in differentiated cells. Moreover, positive staining was detected for ALB and AFP using immunocytochemistry assay whereas negative control stained negatively. Also, the finding of glycogen deposits in differentiated cells and urea production suggested that most of cells differentiated into hepatocyte-like cells.

Conclusion: Summing all, our present report has provided a simple protocol for differentiation of hADSCs into functional hepatocyte-like cells.

Keywords: Human adipose tissue derived stem cells (hADSCs), Hepatic differentiation, Hepatocyte-like cells

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ID:264

Investigating the anticancer secondary metabolite production by Dendrostellera lessertii cell culture technique

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Objective: 3-Hydrogenkwadaphnin (3-HK) is a novel diterpene ester which is isolated from the leaves of Dendrostellera lessertii (D. lessertii) with anticancer properties. 3-HK is present at extremely low concentrations in the nature-harvested plants. This study was aimed to investigate the efficiency of plant cell culture for the production of this compound.

Material and Methods: Plant tissue culture was used to obtain callus (plural: calli). Thin layer chromatography (TLC) was then performed on ethanol extract of the calli to determine the most productive callus. These calli were chosen to be utilized in plant cell culture. The biological activity of the cell cultures medium was investigated every week for 60 days with brine shrimp lethality assay (BSLA) and MTT assay (K562 and 4T1).

Results: After 48 days, the lethal concentration 50 (LC50) reached 3 µl.ml-1 in BSLA and inhibitory concentration 50 (IC50) reached 20 µl.ml-1 in MTT assay for K562 and 30 µl.ml-1 for 4T1 cell lines. Furthermore, megakaryocyte differentiation was observed in K562 cells after 24h of treatment.

Conclusion: This study has shown that a biological active compound is produced and released from the cells to the medium, which

shares the 3-HK properties. These data suggest that 3-HK production can be achieved through plant cell culture.

Keywords: 3-Hydrogenkwadaphnin, Dendrostellera lessertii, anticancer secondary metabolite, Plant cell culture

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ID:270

Utilization of Scaffold Free 3D Cell Culture System to Study the Growth Kinetics and Drug Response of Spherical Breast Cancer Model

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Objective: Three-dimensional (3D) cell culture, scaffold-based and scaffold-free, is increasing in use today because of its ability to mimic in vivo condition. Cell-cell and cell-ECM interactions establish a 3D communication network maintaining the tissue specificity and homeostasis. Under 3D culture, cancer cells can generate the tumorsphere; a model for study of cancer.

Material and Methods: Herein, we used a scaffold-free method to generate the mammospheres from MCF-7 cell line to determine the growth and evaluate their drug resistance. In order to generate the mammospheres, MCF-7 cells were seeded with different cell number then their growth kinetics and cell viability were studied using light microscopy and Hoechst/PI staining. The cell viability of the 2D and 3D cultured cells was measured using MTT assay in the presence of a pro-apoptotic compound; Actinomycin-D. Then the mammospheres were treated with Actinomycin-D at the determined IC50. Afterward, their growth kinetics and cell viability were studied again.

Results: The growth kinetics shows that the best growth curve is obtained from mammospheres generated by fewer seeded cells, so the study was continued with the minimum cells. The obtained IC50 for 3D culture is higher than 2D. Mammospheres treatment showed growth inhibition and decrease in cell viability but in a very slow rate during a week.

Conclusion: Totally, this study shows that cells in the mammosphere have higher drug resistance in comparison to the cells cultured in 2D. It is suggested that this observation is due to the comprehensive cell-cll communication in 3D systems which is missed in 2D systems.

Keywords: Cancer, Mammosphere, 3D cell culture, Drug resistance

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ID:274

The effect of FADS2 gene rs174583 polymorphism on desaturase activities, fatty acid profile, insulin resistance, biochemical indices and incidence of Type 2 Diabetes

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Objective: In this study, we investigated the associations of erythrocytes fatty acid composition and activities of delta-5 desaturase and delta-6 desaturase, with T2D risk to determine if rs174583 polymorphism of FADS2 gene had any effect on these associations.

Material and Methods: Fatty acid profile of erythrocytes was determined using gas chromatography mass spectrometry (GCMS) in 95 T2D patients and 95 apparently healthy subjects. The genotypes of SNP of FADS2 gene were determined using the PCR-RFLP technique. Other biochemical parameters were measured in the serum using standard analytical procedures.

Results: Delta 6 desaturase (D6D) activity was increased ($p<0.001$) and, Delta 5 desaturase (D5D) activity was decreased in T2D patients ($p<0.001$) compared to controls. Insulin resistance index (HOMA-IR) was positively correlated with D6D ($r= 0.34$, $P<0.001$) and negatively correlated with D5D ($r= -0.19$, $P=0.02$). Palmitic acid ($p<0.001$) and dihomo-gamma-linolenic acid ($p=0.03$) were higher and linoleic acid ($p<0.001$) and arachidonic acid ($p<0.001$) were lower in T2D patients. The distribution of rs174583 genotypes which includes: C/T, C/C, and T/T was not different in the two groups ($p=0.63$).

Conclusions: In the population studied, there was a strong association between the distribution of rs174583 genotypes and the erythrocytes fatty acid composition and delta-5 and delta-6 desaturase activities. However, there was no association between the distribution of rs174583 genotypes and the biochemical parameters studied, i.e. HOMA-IR and the lipid profiles, except TG in T2D patients. In addition, the distribution of rs174583 genotypes did not differ significantly between T2D patient and controls and it did not appear to be an association between rs174583 SNP and incident of type 2 diabetes in the population studied.

Keywords: fatty acid desaturase, single nucleotide polymorphism, fatty acid profile
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ID:280

Trimethylamine-N-Oxide Induce the Expression of Toll like Receptor 4 in Murine Macrophage Cell line

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Objective: The exact mechanism by which gut microbiota-dependent trimethylamine-N-oxide (TMAO) induces inflammation and foam cell formation during atherosclerosis is not well understood. Activation of toll-like receptor 4 (TLR4) on macrophages has been shown to initiate a signaling pathway which resulted in to production of pro-inflammatory cytokines. The present study was designed to evaluate the expression of TLR4 at protein and mRNA levels in macrophages.
Material and Methods: J774A.1 murine macrophage cell line were treated with different concentration (37.5, 75, 150 and 300 µM) of TMAO for 24 h. The cells were also treated with tunicamycin, as a positive control for stress. Western blotting and RT-qPCR was used to evaluate the expression of TLR4 at protein and mRNA levels respectively. MTT assay was also used to monitor the viability of cells during different treatments.
Results: Unlike tunicamycin, high dose of TMAO significantly increased TLR4 at both protein and mRNA levels compared to the control cells ($p<0.05$). The viability of treated cells was higher than 96% and no cell death occurred.
Conclusion: Our results provide findings to contribution and alteration of TLR4 as a cell surface receptor in response to abnormal activation of macrophages by TMAO.
Keywords: Toll-like receptor 4, Atherosclerosis, Trimethylamine-N-Oxide, Macrophages
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ID:281

Induction of osteogenic differentiation in osteosarcoma cells by poly (ethylene glycol)-coated hydroxyapatite

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Objective: Hydroxyapatite nanoparticles have extensively been used in biomedical fields such as drug delivery system, tissue engineering, and bone reparation. Up to now, several methods have been employed for the synthesis of hydroxyapatite nanoparticles such as wet chemical deposition, biomimetic depositional sol-gel route and etc. The aim of this study was to synthesize poly (ethylene glycol)-coated hydroxyapatite (PEG/HAP) nanoparticles by the hydrothermal method and to evaluate their biological effects on osteosarcoma cells.
Material and Methods: PEG/HAP nanoparticles were synthesized by the hydrothermal method and characterized by XRD and FT-IR techniques. To detect the cytotoxic effect of nanoparticles on osteosarcoma cells (Saos2), MTT assay was utilized. The cellular morphology of Saos2 cells was observed by phase contrast microscope. Osteogenic differentiation was evaluated by the assessment of alkaline phosphatase activity (ALP).
Results: The XRD pattern of nanoparticles showed the formation of single-phase hydroxyapatite, and the spectrum matched well with the JCPDS value (09-0432). The FT-IR spectrum showed the adsorption the band at 604 cm-1 which is related to the bending vibration of phosphate groups and the band at 1044 cm-1 which is attributed to the stretching vibration of phosphate groups. The sharp absorption band at 3570 cm-1 corresponds to the stretching vibration of OH groups. Based on MTT assay and microscopic images, PEG/HAP nanoparticles increased the proliferation of Saos-2 cells at concentrations of 10 and 50 µg/ml while no significant effect was observed at higher concentrations up to 150 µg/ml. Moreover, it was found that PEG/HAP nanoparticles have ability to induce osteogenic differentiation in Saos-2 cells which was quantified by ALP activity. A significant increase was observed in ALP activity in Saos-2 cells as they were treated ith PEG/HAP nanoparticles.
Conclusion: Based on the obtained results, PEG/HAP nanoparticles possess high potency for the induction of osteogenic differentiation and could be considered as an appropriate biomaterial for cancer therapy.
Keywords: Osteosarcoma, Hydroxyapatite, MTT assay
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ID:282

MAA and SBA histochemical studies in human stomach adenocarcinoma

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Objective: Stomach adenocarcinoma is the second most common cancer in Iran. In this cancer, genetic and morphological changes occur in glandular stomach cells. In this study, we have evaluated the changes of some terminal and glycoconjugate in different degrees of stomach adenocarcinoma.

Material and Methods: Tissue samples of 40 stomach adenocarcinomas and normal tissues were selected from pathology Department of Imam Reza Hospital. H&E stained tissue slides were restudied and the adenocarcinomas were graded sections were stained with SBA and MAA (conjugated with HRP) lectins and Alcian blue pH 1, 2.5 for microscopically observation.

Results: Positive response to Alcian blue pH 1, was seen in the stroma of normal mucosa and cancer tissues, but normal glandular cells and cancer cells with different degrees of differentiation showed negative response. In Alcian blue pH 2.5 the response in normal glandular cells were intense but it decreased by the tumor progression. The response of normal glandular cells in comparison with cancer cells was not significant in SBA lectin histochemistry staining and also no reaction was observed in normal and cancer cells with MAA lectin histochemistry.

Conclusion: Genetic changes in gastric cancer cells probably resulted in reduction of carboxylated mucusubstances in comparison with healthy samples and not production of sulfated mucusubstances in these cells. It also seems that the two terminal sugars that have specific attachment to SBA and MAA (sialic acid α2-3 galactose/GalNAC and α and β GaL<α and β-GaLNAC) lectins don't have an important and fundamental role in cellular interactions and special biological behaviors which result from neoplastic changes in gastric glandular cells. It seems that each glycoconjugate follows a special pattern according to its specific role in different grades cancer so it may be the pathologic diagnostic marker.

Keywords: alcian blue, stomach adenocarcinoma, lectin histochemical

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ID:283

Spectroscopic study of the binding affinity of Alimta with DNA in the solution

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Objective: Alimta (pemetrexed disodium) is an anticancer drug widely used in the treatment of lung cancer. Alimta acts as antifolate which inhibits several folate-dependent enzymes, leading to a global reduction in DNA synthasis. In eukaryotes, genetic material (DNA) is complexed with histones and other nuclear proteins producing a defined structure known as chromatin. One of the most potent target of anticancer drugs in the cell is DNA molecule. To date there is no research about the interaction of Alimta with DNA. The aim of this study was to evaluate the binding affinity of Alimta anticancer drug to DNA.

Material and Methods: The present study focuses on the binding affinity of Alimta to DNA molecule employing spectroscopic techniques such as circular dichroism (CD) and thermal denaturation (Tm).

Results: The results showed that the binding of Alimta to DNA reduced absorbance at both 260 and 210 nm with different extents. Melting temperature (Tm) of DNA exhibited hypochromicity without any shift in Tm value. The binding of the drug induced structural changes in both positive at (275) nm and negative at (245) nm extremes of CD. In the presence of Alimta molar ellipticity is decreased at positive extreme and ellipticity at negative extreme becomes more positive.

Conclusion: From the results it is concluded that Alimta as a potent anticancer drug represents high binding affinity to DNA, suggesting DNA molecule as one of the target of Alimta cytotoxicity.

Keywords: Alimta, DNA, Circular dichroism, Thermal denaturation

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ID:284

In vitro interaction of anticancer drug Levofloxacin with DNA

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Objective: Levofloxacin is a fluoroquinolone antimicrobial agent which exhibits broad-spectrum bactericidal activity, recently the anticancer effect of Levofloxacin has been reported and shown contributions to deeper insight into the mechanism of action Levofloxacin. The interaction of this class of antibiotics with DNA might be important for a better understanding of their therapeutic efficacy.

Material and Methods: In this study the interaction of Levofloxacin with DNA has been assayed by Thermal denaturation analysis, UV/vis spectroscopy and circular dichroism.

Results: Results imply that the structure of DNA alters in both positive at (275 nm) and negative at (245 nm) extremes of circular

dichroism spectra after interaction with Levofloxacin. The UV absorption spectrum of DNA in the presence of Levofloxacin was decreased at both 260 and 210 nm. In thermal denaturation study of the binding of DNA to Levofloxacin revealed that the drug band to DNA and reduced absorbance at 260 nm (hypochromicity).

Conclusion: The data suggested that one of the most important target of anticancer drug Levofloxacin is DNA and it may affect cancer cells by possibly intercalating and changing the structure of target DNA.

Keyword: Levofloxacin, DNA, anticancer drgs, spectroscopy analysis

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ID: 285

Oligonucleotide aptamers: potential novel molecules against viral hepatitis

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Objective: Viral hepatitis, as an international public health concern, seriously affects communities and health system. In recent years, great strides have been taken for development of new potential tools against viral hepatitis. Among these efforts, a valuable strategy introduced new molecules called “aptamers”. Aptamers as potential alternatives for antibodies could be directed against any protein in infected cells and any components of viral particles.

Material and Methods: In this review, we will focus on recent advances in the diagnosis and treatment of viral hepatitis based on aptamer technology.

Results: In recent years, various types of aptamers including RNA and DNA were introduced against viral hepatitis. Some of these aptamers can be utilized for early and precise diagnosis of hepatitis infections and other group selected as therapeutic tools against viral targets. Designing diagnostic and therapeutic platforms based on aptamer technology is a promising approach in viral infections. The obtained aptamers in the recent years showed obvious potential for use as diagnostic and therapeutic tools against viral hepatitis.

Conculosion: Although some modifications to increase the biostability and half-life of aptamers are underway, it seems these molecules will be a favorable substitute for monoclonal antibody in near future.

Keywords: Aptamer, Hepatitis B, Hepatitis C, SELEX

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ID:286

The effect of dacarbazine on histone H1 subtypes expression and content in lung cancer A549 cells

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Objective: Dacarbazine is an antitumor drug which is used for the treatment of malignant metastatic melanoma and Hodgkin’s disease. Dacarbazine is a cell-cycle nonspecific antineoplastic agent, which functions as an alkylating agent that binds to specific sections of DNA and prevents cell division, resulting in cell death. H1 and related linker histones are important both for maintenance of higher-order chromatin structure and for the regulation of gene expression, however, its role in diseases, such as cancer, remains understudied. In this study we obtain the effect of dacarbazine on histone H1 subtypes expression and content in lung cancer cells.

Material and Methods: The cells were exposed to various concentration of dacarbazine and the viability was assessed by MTT assay. The cells were stained with ethidium bromide/acridin orange and examined with fluorescence microscope. Histone H1 proteins extracted from drug-treated and the control and analysed by western blotting also expression of H1 (H1.1 and H1.2) proteins were examined by real-time PCR.

Results: The result from MTT assay were showed that dacarbazine decreased cell survival of non-small lung cancer cells in a dose- and time-dependent manner. Dacarbazine, at 5 µM showed significant reduction in the content of histone H1.1 when analyzed on SDS-PAGE and western blot and its mRNA expression level reduced. Whereas, the content of intracellular H1.2 protein and mRNA expression level slightly changed. The morphological experiment showed occurrence of apoptosis in dacarbazine treated cells.

Conclusion: In conclusion, the result obtained from this study suggests that dacarbazine represents apoptotic effect on A549 cells. Histone H1.1 protein plays an important role in this process and can be considered as a target for dacarbazine.

Keywords: histone H1, chromatin, dacarbazine, lung cancer,

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ID:288

The role of long non-coding RNAs and autophagy in hepatocellular carcinoma: a review

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Objective: Long non-coding RNAs (lncRNAs) promote or repress the physiological and pathological processes such as autophagy, as a catabolic process. Several studies have revealed autophagy has a double-edged sword role in cancer; suppresses tumorigenesis or promotes cancer progression. Hepatocellular carcinoma (HCC) is a highly malignant cancer with poor survival rate and the third-leading cause of deaths from cancer worldwide. The aim of this review is investigate the relationship between lncRNAs and autophagy in HCC. The lncRNA highly up regulated in liver cancer (HULC), an oncogenic lncRNA, overexpress in human HCC. HULC decrease the miRNAs expression cause to increased ubiquitin-specific peptidase 22 (USP22) and silent information regulator1 (Sirt1) by which activate autophagy through enhanced LC3-II/I, decreased p62 expression and increased Atg5 and Atg7 deacetylation. Moreover, HOX antisense intergenic RNA (HOTAIR), other oncogenic lncRNA, activates autophagy by up-regulating Atg3 and Atg7 expression and promotes cell proliferation in HCC. Enhanced autophagy is a multi-drug resistance (MDR) mechanism in HCC cells. Metastasis-associated lung adenocarcinoma transcript1 (MALAT1) can regulate MDR by down-regulates miR-216b as a tumor suppressive miRNA and increasing LC3-II levels in HCC. Antisense transcript of HNF1A (HNF1A-AS1), another oncogenic lncRNA in HCC, significantly promoted autophagy via increased LC3-II/I and Atg5 expression but reduced miR-30b. Furthermore, PTEN homolog pseudogene1 (PTENP1), as a tumor suppressive lncRNA, provoke autophagy byinhibited PI3K/Akt signaling pathway. Conclusion: According to lncRNAs role in autophagy, it seems that lncRNAs is an important diagnostic marker and potential therapeutic target for reducing HCC risk and improving HCC therapeutic efficacy.
Keywords: Long non-coding RNA, Autophagy, Hepatocellular carcinoma
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ID:293

Zataria Multiflora Essenthial Oil Strongly Synergizes Human Prostate Carcinoma PC3 Cells to Doxorubicin-induced Growth Inhibition and Apoptosis

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Objective: One of the biggest challenges in the treatment of prostate cancer is lowering the toxicity of doxorubicin. Tantalizing evidence shows that the natural compounds as combinatory therapy for cancer has been successful. In present study, Zataria Multiflora Essential Oil(ZEO) was concomitantly employed with doxorubicin in order to reduce the doxorubicin dosage and toxicity.
Material and Methods: The IC50 of ZEO and doxorubicin was determined by MTT assay. Combination assay was done by combining 26.3; 15; 7.5 µg/mL of ZEO and 0.78; 0.39; 0.19; 0.09µg/mL of doxorubicin. Cells were treated with ZEO or DOX either together or first with ZEO for 24 h then with DOX, or vice versa, for a total of 48 h, and viability were determined by MTT assay. The combination index (CI) was calculated by the Chou-Talalay equation (CI <1synergism; CI =1 additive effect; and CI >1 antagonism). In order to verify ZEO-DOX induced apoptosis use AnnexinV-FITC/PI staining.
Results: IC50 of ZEO and DOX in 48 h was 26.3 and 1.89 µg/mL respectively. Also IC50 of ZEO and DOX can induce 44.4% and 48.64% primary and secondary apoptosis respectively. But in combination assay we find 15 µg/mL of ZEO and 0.19 µg/mL of doxorubicin together for 48 h with CI =0.35 has strong synergistic effect and it induce 41.4% in primary and secondary apoptosis compared to control.
Conclusion: The results showed that ZEO can act as an amplifier to sensitize cancer cells and heighten the efficacy of doxorubicin in lower dosage. It seems ZEO can be applied for the treatment of prostate cancer as combinatory therapy to enrich the armamentarium of therapeutic agents with acceptable safety and efficacy.
Keywords: Doxorubicin, Zataria Multiflora Essenthial Oil, Prostate Cancer, Synergy, Apoptosis
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ID:295

In-vitro Screening for cholinesterase and antioxidant activities of thymus vulgaris from Lorestan

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Objective: Cholinesterase is a family of enzymes that catalyzes the hydrolysis of the neurotransmitter acetylcholine to acetic acid and choline. It involves two types: Acetylcholinesterase and butyrylcholinesterase (plasma cholinesterase). The aim of present study was to evaluate the

chemical composition and antioxidant activity of the thymus vulgaris hydroalcoholic extract and its effect on the plasma cholinesterase enzyme activity.

Material and Methods: Thymus vulgaris was collected from Lorestan province and extracted by Maceration method. The extract was analyzed using GC-MS spectrometer. Antioxidant activity of the extract was evaluated by 2,2-diphenyl-1-picrylhydrazyl (DPPH) assay. Plasma sample was taken from healthy volunteer donor and plasma cholinesterase activity was estimated by Ellman method.

Results: Thirty-seven components comprising 95.9% of the total extract were identified, of which 1,2-Benzenediol (11.6%), 2-Methoxy-4-vinylphenol (9.75%), 2(3H)-Furanone, dihydro-4-hydroxy (8.05%), Hydroquinone (7.79%), 2, 6-dimethoxy Phenol, (7.50%) and p-Cymene (6.53%) were found to be the main components. The thymus vulgaris hydroalcoholic extract showed DPPH radical inhibition with IC50 value of 450 µg/ml. The extract at the 1 mg/ml concentration increased the plasma cholinesterase activity by 58.99% compared to control. The extract inhibitory and cholinesterase activation activities were concentration dependent.

Conclusion: Thymus vulgaris possesses potent antioxidant properties and significantly increase the plasma cholinesterase activity.

Keywords: Chemical composition, Thymus vulgaris, Antioxidant, Cholinesterase activity

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ID:296

In vitro increased cholinesterase activity produced by extract of the chrysanthemum flowers from Lorestan

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Objective: Plasma cholinesterase is a glycoprotein synthesized in the liver and found primarily in blood plasma. It is a serine hydrolase that catalyzes the hydrolysis of esters of choline. The objectives of this study were to evaluate the chemical composition and antioxidant activity of the chrysanthemum flower hydroalcoholic extract and its effect on the plasma cholinesterase activity in vitro.

Material and Methods: The Chrysanthemum flowers was collected from Lorestan province and extracted by Maceration method. The extract was analyzed using GC-MS spectrometer. Plasma sample was taken from healthy volunteer donor, plasma cholinesterase activity was estimated by Ellman method and antioxidant activity determined by 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging assay.

Results: Thirty-two components comprising 95.9% of the total extract were identified, of which 3,5-dihydroxy6-methyl-2,3-dihydro-4H-pyran-4-one (24.32%), (E)-2-Methylcrotonic acid (8.93%), 1-Pyrrolidine ethanamine (8.56%) and Thymol (5.41%) were found to be the main components. The hydroalcoholic extract showed DPPH radical inhibition with IC50 value of 480 µg/ml and at the concentration 1 mg/ml increased the plasma cholinesterase activity by 46.67% compared to control. The extract cholinesterase activation and antioxidant properties were concentration dependent.

Conclusion: Chrysanthemum flower extract exhibited significant plasma cholinesterase activation and antioxidant properties.

Keywords: Chrysanthemum, Chemical composition, Antioxidant, Cholinesterase activity

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ID:298

Quercetin interacts with doxorubicin in a dose-dependent manner in ovarian cancer therapy

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Objective: Ovarian cancer is one of the most common invasive types of cancer in women. To overcome multi-drug resistance (MDR) to Doxorubicin (DOX) as a chemotherapeutic drug, combination therapy has a special situation. Quercetin (QC) as a herbal medicine, is a phenolic compound that has antioxidant properties and anti-proliferative activity against many cancer cells. The aim of this study was to investigate the therapeutic effects of QC in combination with DOX in ovarian cancer cells.

Material and Methods: Human ovarian cancer cell line (OVCAR-3) was supplied from the Pasteur Institute of Iran (Tehran, Iran) and cultured in DMEM medium with 10% FBS (fetal bovine serum) (Gibco, Grand Island, USA) and penicillin-streptomycin (Gibco, Grand Island, USA) under standard condition (37ºC and 5% CO2 in a humidified incubator). QC treatment at various concentrations (10, 20, 30 and 40 µg/ml) was examined in combination with different concentrations of DOX (0.03, 0.07, 0.15 and 0.31 µg/ml) by colorimetric MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) tetrazolium reduction assay.

Results: Unlike low concentrations (5 µg/ml – 30 µg/ml) of QC augmented the cytotoxicity effects of DOX, high concentration (above 40

µg/ml) of QC resulted in varying degrees of attenuation of cytotoxicity of DOX.

Conclusion: These results suggest that QC at low concentrations synergistically promote the cytotoxicity effects of DOX and improve therapeutic index of DOX in ovarian cancer and also show during ovarian cancer treatment, combination regimens of high QC may reverse therapeutic response.

Keywords: Ovarian cancer, Quercetin, Doxorubicin, Synergism

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ID:301

Influencing factors on mitochondrial function as key mediator of glucose induced insulin release

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Objective: Pancreatic β-cells recognize changes in blood glucose and release insulin to create normoglycemia. Diabetes is a chronic disorder of insulin insufficiency leads to the disruption of glucose homeostasis and multiorgan problems. Since both prevention and treatment of type 2 diabetes should focus on mitochondrial targets for the improvement of nutrient stimulated insulin secretion, we decided that in this article review influencing factors on mitochondrial function as key mediator of glucose induced insulin release.

Material and Methods: About 110 articles with mitochondrial, diabetes and insulin keywords were studied from various databases including PubMed, ISI web of Knowledge, science Direct and Google Scholar that 85 of them were selected as references.

Results: The significant role of mitochondria is to provide controlling signals for the first and second phase of insulin secretion. All of the identified TCA cycle intermediates were identified as key components of biphasic insulin secretion, in particular for second-phase insulin secretion. The mitochondrial membrane potential (ΔψM), and its response to glucose, is the principal stimulus of mitochondrial ATP synthesis and is hence a central mediator of glucose induced insulin release. Also, changed mitochondrial dynamics in pancreatic β cells are seemed to trigger the development of type 2 diabetes mellitus.

Conclusion: The studies have the potential to enhance our understanding of the mechanisms mediating the triggering and the amplifying pathways of insulin release, which according to, will be helpful for understanding the mechanisms implicated in the progressive beta cell failure that results in type 2 diabetes.

Keywords: Diabetes, Insulin, Mitochondria

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ID:304

Carbohydrate components in the process of esophageal carcinoma differentiation in human

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Objective: Change in cellular glycoconjugates, is one of the most important phenomenon in the process of cancerization and indicates abnormal biological behavior of tumoral cells.

Material and Methods: Tissue samples of 40 esophageal SCCs (10 patients in each differential grade) were selected from pathology department of Imam reza hospital. After identifying tumor differentiation grade, 5micron sections in Alcian Blue (pH 1 and 2.5) staining, for detecting Sulfated and Carboxylated Mucosubstances and in lectin histochemistry procedure, MAA and SBA, which specifically sugar residues, sialic acid α2-3 galactose/GalNAC and α and β GaL<α and β-GaLNAC were used. The intensity of the staining, which showed the concentration of the terminal sugar residues was studied.

Results: None of the specimens in various grades cancer represented Carboxylated and Sulfated Mucosubstances, which was the same as the normal tissue, although stroma of the tumor and esophageal mucousal glands showed positive reactivity. In results for MAA lectin showed, no specific terminal sugar residue of sialic acid α 2-3 galactose/GalNAC in normal epithelium, different degrees of SCC cells, stroma and esophageal mucousal glands. SBA lectin respond was increased by degrading tissue differentiation with the exception of undifferentiated grade.

Conclusion: It seems that in the process of cancerization of esophageal squamous cells, functional changes which result in producing Acidic Carboxylated and Sulfated Mucosubstances and also changes in the presence of specific terminal sugar residue, sialic acid α 2-3 galactose/GalNAC do not occur. Whereas, different in presence of terminal sugar, α and β GaL< α and β-GaLNAC,

probably represent obvious and abnormal glycosilation of cellular proteins in the process of esophageal epithelium cancer.

Keywords: Squamous Cell Carcinoma (SCC), Glycoconjugates, MAA, SBA lectins, Alcian blue, esophagus

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ID:307

The effect of quercetin on oxidative stress factor and genes expression of PON1 and AhR in BDL cirrhotic rats

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Objective: Quercetin is a major suppressor of liver fibrosis through its antioxidant and anti-inflammatory properties. Aryl hydrocarbon receptor (AhR) is a ligand-activated transcription factor that stimulates Paraoxonase 1 (PON1), the most important antioxidant enzymes, transcription activation in mouse liver. This study aimed to determine the protective effect of quercetin on hepatic damage via the gene expression of AhR and PON1in biliary duct ligated (BDL) fibrotic rat model.

Material and Methods: To accomplish that, male Wistar rats were divided into four groups (n=8 for each): sham, sham+quercetin (30 mg/kg per day), BDL and BDL+quercetin (30 mg/kg per day). We measured the MDA level and in hepatic tissue of four groups. The expression of AhR and PON1 were measured at the levels of gene by real-time PCR.

Results: Our results demonstrated that AhR and PON1 gene expression significantly reduced in liver tissue of BDL rats compared with sham group ($P<0.05$). However, treatment with quercetin increased gene expression of AhR and PON1 in the liver tissue of BDL+Q group compared with BDL group ($P<0.05$). The liver MDA level significantly increased in BDL rats compared with sham group ($p<0.05$). It was found that quercetin could significantly decrease the formation of MDA in BDL-treated rats.

Conclusion: Quercetin demonstrated hepatoprotective activity against BDL-induced liver injury by influencing the gene expression of AhR and PON1.

Keywords: Querecetin, Oxidative stress, Bile duct ligation, Paraoxonase 1

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ID:325

Investigation of CCND1 gene expression in cancerous tissue compared to normal tissue in Iranian women with sporadic breast cancer by Real-Time RT PCR method

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Objective: Breast cancer is the most common cancer and leading to death in women. This cancer is a highly heterogeneous disease which divided into several types such as LCIS, DCIS and invasive carcinoma. Cyclines are one of the most important cyclic controls of Cell division in breast. Cyclin D1 is one of the main regulators of cell cycle, which plays a role in regulating the cycle of the cell from stage G1 to S. Regarding the high prevalence of breast cancer among women and the importance of early diagnosis of disease in early stages using advanced molecular techniques and the importance of CCND1 gene as a prognostic factor in breast cancer, expression of CCND1 gene in the cancerous tissue compared to normal tissue of women with sporadic breast cancer was investigated by Real Time RT PCR.

Material and Methods: Extracting of tissue samples (normal and cancerous tissue) with Thrysol, Total RNA, and after synthesis of CDNA, by Real Time RT PCR technique, examined CCND1 gene expression in women with sporadic breast cancer.

Results: Relative expression of CCND1 gene by Real Time RT PCR technique in cancerous tissues compared with normal tissue increased by 5.34-fold. Showed equality and a statistically significant difference in this case with P value=0.002.

Conclusion: Our study showed that there is a possible relationship between the high expression of CCND1gene and breast cancer and could be considered as a potential target for breast cancer treatment.

Keywords: Gene Expression, Breast Cancer, CCND1, Real Time RT PCR

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ID:329

Comparison of the effect of hydroalcoholic extract of aloe vera, chamomile and green tea on wound healing in diabetic rats

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Objective: The complications of diabetes mellitus delay wound healing. Since ancient times, the use of herbs and their derivatives have been used to treat diabetes and its complications, including plants such as aloe vera, green tea and chamomile.

Material and Methods: First, the hydroalcoholic extract of leaves of aloe vera, green tea and chamomile was extracted individually by Soxhlet apparatus. In this study, male rats who were diabetic with streptozotocin were used. We created an injured area of about 2 cm2 in the body of the Rat. Rats were divided into groups treated with chamomile extract, green tea and aloe vera at a dose of 25 mg/kg and a control group without treatment. The area of the wounds was measured on days 1, 5, 7, and 11.

Results: The results showed that the wound healing rate was higher in chamomile treated diabetic rats and less in the treated group with green tea than in other groups. But the rest rate in all three groups was significantly higher than the diabetic control group.

Conclusion: All three plants used in this study have antioxidant properties and effective in the reintroduction of epithelium, but chamomile was more effective and green tea had less effect.

Keywords: diabetes, wound, aloe vera, green tea, chamomile

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ID: 333

Candidate biomarkers in early diagnosis of Parkinson disease

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Objective: Parkinson's disease (PD) is a common neurodegenerative disease. Oxidative stress is considered as a key modulator in the development of PD. This study aimed to investigate associations between serum NOX1 (NADPH oxidase1), ferritin, selenium (Se) and uric acid (UA) levels and clinical parameters in patients with PD.

Material and Methods: Serum levels of NOX1, ferritin, Se and UA were measured in 40 PD patients and 40 healthy individuals. Receiver operating characteristic (ROC) analysis was performed to investigate incremental diagnostic value of each factor in the study groups.

Results: Mean serum NOX1 levels was markedly higher in patient group (22.36±5.80 ng/mL) versus healthy individuals (8.89±2.37 ng/mL) ($p<0.001$). Significant differences were also observed in the serum concentrations of ferritin ($p= 0.005$) and Se ($p= 0.001$) between patients with PD and healthy individuals. However, the serum concentrations of UA were not statistically significant between the study groups ($p= 0.560$). ROC analysis revealed a diagnostic ability of serum NOX1 and ferritin levels for PD with an area under ROC curve of ≥0.7 ($p<0.05$) and relatively high sensitivity and specificity. Combination of serum NOX1 and Se along with ferritin and UA levels increased the sensitivity up to 85%, specificity up to 97% and area under the ROC curve up to 0.94 (95% confidence interval (95% CI): 0.89 to 0.99, $p<0.001$).

Conclusion: Our findings indicated that serum concentrations of NOX1, ferritin and Se are significantly higher in the patients with PD. Therefore, these factors can be considered as potential diagnostic biomarkers for diagnosis and monitoring of PD patients.

Keywords: NADPH oxidase1, Ferritin, Selenium, Uric acid, Parkinson Diseases

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ID:335

Apoptotic and cytotoxic effects of carboxyl-functionalized single- and multi-walled carbon nanotubes: an in vitro and in vivo study

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Objective: Nanotechnology is under fast development in various fields. Carbon nanotubes (CNTs), with unique physicochemical properties, have attracted attention of numerous researchers and industries but their potential toxicity to life is not addressed well. Various factors can affect toxicity of these nanomaterials. Due to their widespread use, it is important to study CNT cytotoxicity. In the current study, toxicity of carboxyl-functionalized SWCNT and MWCNT was evaluated.

Material and Methods: In vitro studies: Toxicity of CNTs against A549 cells was evaluated by MTT assay. Morphological changes of the cells were evaluated using

acridine orange-ethidium bromide staining. In vivo studies: 5-7 weeks male BALB/c mice were injected intraperitoneally with a CNT dose of 75µg/mice and monitoring was continued in a period of five weeks after injection. Oxidative stress response was examined by measuring total antioxidant, total peroxide, malondialdehyde (MDA) and protein carbonyl in tissue (lung and liver) homogenates of treated mice. To assess liver damages, SGOT and SGPT enzymes were measured in serum of mice.

Results: Carboxylated CNTs at doses lower than 500µg/ml have no toxic effect against A549 cell line within 24 hours. During an incubation time of 48 hours, cell toxicity was seen at CNT concentrations more than 100µg/ml. The morphological studies showed that carboxylated CNTs could induce apoptosis in A549 cells. Both CNT preparations reduced the amounts of total antioxidant in the lung tissues of mice at the first week post-injection. No significant increase was observed in the amount of total peroxide. Results showed that carboxylated MWCNT could increase the amount of MDA in the liver after five weeks and carboxylated SWCNT could cause an increase in the amount of liver protein carbonyl. No significant liver injury was detected.

Conclusion: According to the obtained results, carboxylated CNTs do not induce acute toxic effects in BALB/c mice and A549 cell line at the examined dose.

***Keywords*:** Carbon nanotubes, Oxidative stress, Cytotoxicity assay, BALB/c mice, A549 cell line

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ID:340

Effect of Idarubicin-ZHER2 affibody conjugate on induction of death HER2 positive malignant cells

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***Objective*:** The targeting therapy of HER2-positive cancerous cell line by conjugation of a chemical toxin to a peptide is a new approach for specific representation of selective drugs and has also fewer undesirable side effects. ZHER2 affibody is a small engineered peptide that binds to HER2 receptors with high affinity. Our previous study indicated that idarubicin-ZHER2 conjugate could not induce an immune response in BALB/c mice.

Material and Methods: ZHER2 affibody was expressed in competent cells of E. coli, and purified by His-select affinity column chromatography. Affibody ZHER2 and idarubicin-ZHER2 conjugate were treated on the HER2-positive cancerous cell lines SKOV3, HN5, SKBR3, and MCF7 with different concentration (5-80 µM) and Idarubicin was treated on all cell lines with different concentration (0.01-1 µM). The cytotoxicity effects of idarubicin-ZHER2 conjugate on the cell lines were assessed through MTT assay. The expression of HER2 level was detected by western blot analysis.

Results: The purified Affibody ZHER2 was assessed by SDS-PAGE and Coomassie Brilliant Blue stain to confirm the affibody band. The conjugation's success was confirmed by UV-Visible and fluorescence spectroscopy. Although, the non-conjugated form of Idarubicin showed potential toxic effects against all four mentioned cell lines, however, the idarubicin-ZHER2 conjugate showed more cytotoxicity effect especially on the HER2 positive cell line.

***Conclusion*:** Our results indicated Idarubicin-ZHER2 conjugate has very weak cytotoxicity effect on the MCF7 cell line after 48 hours' treatment, however, in SKBR3 has more effect compared to negative control group. This cytotoxicity effect of the conjugate was much more in HN5 & SKOV3 cell line compared to the others. Higher overexpression of HER2 in HN5 & SKOV3 cell line was confirmed compared to SKBR3 cell line by western blot analysis.

***Keyword*:** Idarubicin-ZHER2, HN5, SKOV3, SKBR3, MCF7

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ID:344

Protective effects of selenium on parameters associated with kidney function in male wistar rats intoxicated with cadmium

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***Objective*:** Cadmium is an unessential heavy metal that is present in water, air, food as results of industrial manufactory and cigarette smoke. It's a serious threat to human health due to bioaccumulation in the liver and kidneys. Selenium is a necessary trace element and constituent part of several enzymes, including glutathione peroxidase (GSH-Px), thyroidoxin reducatas (TR), and selenoprotein p (SeP), which has some protective effects against the toxicity of cadmium. Purpose: the purpose of this study was to investigate the protective effects of selenium on serum parameter related to kidney function in cadmium-toxicity in rats and it investigates the acute and chronic effects of cadmium on the kidney.

***Material and Methods*:** The present study was conducted in a short-term period of 15 days and long-term period of 45 days on 60 male wistar rats. The rats were divided into 10 groups containing 6 in the short-term. The control group received 0.5mg/kg BW normal saline and groups 2 to 4 0.5mg/kg and 1 mg/kg BW normal saline and 2mg/kg BW of cadmium chloride (CdCl2.H2O), respectively. The control group received 0.5 mg/kg BW normal salin and other groups received 0.23mg/kg BW., 0.5 mg/kg BW sodium selenate (Na2SeO3), 1mg/kg BW cadmium chloride, 1mg/kg BW cadmium chloride + 0.23 mg/kg BW sodium selenate and 1mg/kg BW cadmium chloride+0.5mg/kg BW sodium selenate, respectively. All injections were administered intraperitoneally (i.p).

Results: After intraperitoneal injection to short-term group, a significant decrease in sodium, potassium and albumin ($p<0.05$) was observed while urea and uric acid levels were elevated significantly ($p<0.5$) as compared with control group. Serum creatinine and total protein levels did not change significantly in acute exposure with cadmium ($p>0.05$). Combined treatment with sodium selenite (0.5mg/kg) + Cadmium chloride (1mg/kg) showed significant increase in serum sodium, potassium, albumin, total protein and uric acid in the chronic period ($p<0.05$). In addition, serum level of sodium, potassium, albumin and total protein in combination treatment (sodium selenate 0.23+cadmium chloride 1mg/kg) revealed a significant increase as compared to the cadmium chloride group (1mg/kg) in the long-term period ($P<0.05$). Serum urea and creatinine did not change significantly in the long-term period as compared with control ($P<0.05$).

***Conclusion*:** The result shows that selenium has some protective effects against the toxicity induced by cadmium on the renal function of the rat.

Keywords: Rare elements, Kidney, Uric acid, Creatinine, Rat

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ID:359

PLGA-based nanospheres as efficient vaccine delivery vehicles for the design of subunit vaccine against Toxoplasama gondii

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***Objective*:** The application of safe and efficient adjuvant and/or delivery system is inevitable in new vaccine design strategy to achieve desired immune responses. PLGA particles as a FDA-approved vaccine delivery platform have attracted much attention regarding their remarkable features. Here, we adsorbed rSAG1 and rGRA2 (recombinant Toxoplasma antigens) on PLGA nanospheres (NSs) individually and evaluated the effect of both nanospheres in eliciting immune responses against acute toxoplasmosis infection in vivo.

***Material and Methods*:** Blank PLGA NSs were prepared using double emulsion solvent evaporation technique, then rSAG1 and rGRA2 adsorbed individually on them. All nanospheres were characterized by dynamic light scattering using spectroscopy technique. BALB/c were subcutaneously immunized two times with three weeks interval. The concentrations of IFNγ and IL-10 were determined in free spleen cells supernatant by ELISA kit.

***Results*:** Analysis demonstrated slightly polydisperse nanospheres (PDI<0.2) with the average size of less than 490 nm for both rSAG1-PLGA and rGRA2-PLGA, and their zeta potential was higher than blank NSs, showing antigen adsorption. The significantly increase of IFNγ and decrease of IL-10 (as key indicators of Th1 and Th2, respectively) in immunized mice with rSAG-PLGA or rGRA2-PLGA compared to control mice clearly demonstrated eliciting of desired cellular immune responses

***Conclusion*:** Adsorption of SAG1 and rGRA2 on PLGA NSs had no effect on their antigenicity. Antigens loaded on PLGA could elicit significantly higher Th1-associated immunity, confirming the role of PLGA.

***Keywords*:** PLGA, vaccine delivery, rSAG1/rGRA2, Toxoplasma, Adsorption

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ID:366

Promoter methylation analysis of miR-34a, miR-34b/c, miR-126 and miR-9-3 tumor suppressor miRNAs in colorectal cancer cell lines

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***Objective*:** MicroRNAs (miRNAs) are small, non-coding RNAs that have been implicated in the regulation of diverse cellular processes. Emerging evidence suggests that miRNAs are regulated by epigenetic mechanisms, and

aberrant promoter DNA methylation of miRNAs has an important role in different types of cancer invasion including colorectal cancer (CRC). To verify the role of DNA methylation in CRC progression, we analyzed promoter DNA methylation of five tumor suppressor miRNAs including miR-34 cluster (34a, -34b/c), miR-126 and miR-9-3 in a panel of five CRC cell lines

***Material and Methods*:** We used methylation specific PCR (MSP) technique to evaluate the methylation profile of the promoter CpG islands of miR-34 cluster (34a, -34b/c), miR-126 and miR-9-3 in a panel of five CRC cell lines (HCT116, HT29/219, SW741, Caco2 and LS180). After bisulphite treatment of DNA, which modify unmethylated but not methylated cytosines to uracil, DNA was amplified by two sets of primer pairs, which differentiating between unmethylated and methylated cytosines. PCR products were analyzed by electrophoresis on a 1.5% agarose gels and visualized under UV illumination.

***Results*:** The promoter methylation status of miR-34a, miR-34b/c, miR-126 and miR-9-3 were different in CRC cell lines. Among the cell lines, (3/5, 60%), (5/5, 100%), (5/5, 100%) and (5/5, 100%) showed promoter methylation for miR-34a, miR-34b/c, miR-126 and miR-9-3, respectively. miR-34b/c, miR-126 and miR-9-3 were fully methylated whereas miR-34a was the less methylated miRNA in five CRC cell lines.

***Conclusion*:** Promoter hypermethylation of miR-34b/c, miR-126 and miR-9-3 is a frequent epigenetic changes that is observed in CRC cell lines. The association between Clinicopathological features of these colorectal cell lines and their methylation status will be analyzed and the result will be used and presented as a potential biomarker for tumors classification. This study might provide further insights into mechanism of cancer development.

***Keywords*:** Colorectal cancer, Methylation specific PCR, MiR-34a, miR-34b/c, MiR-126

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Studying the molecular mechanism of interactions between novel 2-amino benzamides and Histone Heacetylase enzyme using molecular dynamic simulations

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***Objective*:** Histone deacetylases (HDACs) are attractive therapeutic targets for the treatment of cancer and other diseases. It has four classes (I-IV), among them especially class I isozyme are involved in promoting tumor cells proliferation, angiogenesis, differentiation, invasion and metastasis and also viable targets for cancer therapeutics. It was claimed that novel HDACIs were optimized as potential drug candidates, designed for regional or systemic release, and created as significant inhibitors.

***Material and Methods*:** Molecular dynamics simulation was used to evaluate a new 2-amino benzamide derivative as an inhibitor of histone deacetylase1. Simulation calculations were performed using the Nanoscale Molecular Dynamics NAMD 2.9 program with CHARMM27 force field in atomic details at real physiological condition aqueous solution at T = 37°C, P = 1atm. The visualization package Visual Molecular Dynamics (VMD) was used to analyze results. Analysis studies such as rmsd, rmsf, radius of gyration, short-range electrostatic and vander waals interactions energy, distance between coordinated Zn2+ ion with active site residues and also hydrogen bonding during the simulation were performed.

***Results*:** The obtained findings indicate mode of interactions and inhibition strengths of the studied inhibitor for HDAC1. The average RMSD value of ligand-bond protein was 2.27±0.15 A°, the average RMSF of ligand-bond protein was 0.73±0.456 A°, respectively. The ligand-bond protein potential energy was found to be -33259.5±13.35 kcal/mol indicating the stability of the system. These results improved the expected penta-coordination complex between HDAC1 residues and ligand with zinc ion at the enzyme active site.

***Conclusion*:** Molecular dynamics simulation showed interaction mode of -amino benzamide derivative with HDAC1 including zinc ion coordination, strong hydrophobic interactions and formation of hydrogen bond with benzamide derivative.

***Keywords*:** Histone deacetylase 1; 2-AminoBenzamide, Molecular dynamics simulations, HDAC1 inhibitors

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ID:372

Effect of losartan in cell proliferation and angiogenesis of colon cancer

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***Objective*:** Colorectal cancer (CRC) is one of the major cause of mortality worldwide. There are several therapeutic interventions that have been identified. Angiotensin II (Ang II) is a main component of the renin angiotensin system that was found to be expressed in tumor growth and angiogenesis. It is found that angiotensin II type 1 receptor (AT1R) is significantly up-regulated in tumor cells. AT1R blocker (ARB), including losartan was inhibited the growth of cancer cells and angiogenesis. The purpose of this study is to investigate the therapeutic potency of losartan in targeting cell cycle progression and angiogenesis in colorectal cancer cells.
***Material and Methods*:** CRC cell line, CT26, was treated with losartan and cell viability was measured by MTT assay. Next, Real-Time PCR was performed to evaluate the effect of losartan on the expression level of several genes involved in cell cycle and angiogenesis including cyclinD1 and VEGF. Consistently, Western blot was used to evaluate protein expression of these key proteins in colon cancer cells upon losartan treatment.
***Results*:** Cell cytotoxicity of losartan was evaluated and the IC50 for this drug was about 980nm in these cells. Our results showed that losartan down-regulates expression of cyclinD1 in colon cancer cells. Consistently, losartan decreased angiogenesis by suppressing VEGF activity in CT-26 cells.
***Conclusion*:** This study suggests that losartan by suppressing cell cycle progression and angiogenesis can elicit potent anti-cancer properties in colon cancer cells. These results support the therapeutic potency of this inhibitor for colon cancer patients. However, further in vitro, in vivo and clinical studies are required to determine the exact molecular mechanism of this drug in cancer patients.
***Keywords*:** Colorectal cancer, Losartan, Angiogenesis, Tumor progression
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Crocin inhibits the prenylation of Ras onco-protein in MCF-7 cell line

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***Objective*:** Ras family of onco-proteins is the most frequently mutated protein in cancer. Post-translational prenylation and thereby anchorage on cell membrane is inevitable for transducing activity of Ras in normal and cancer cells. Interestingly, inhibition of Ras prenylation have been targeted as an approach against cancer for past three decades. Crocin, as the main carotenoid of saffron have been reported for its anticancer effects both in vitro and in vivo. In the present study, the effect of crocin on inhibition of K-Ras prenylation was investigated in MCF-7 breast cancer cell line.
***Material and Methods*:** The present study was designed to conduct both in silico and in vitro. First, we estimated the spatial interaction between crocin and a ubiquitous crystal structure of prenyl transferase enzyme a Rat Farnesyl transferase enzyme [FT]) through a docking analysis by AutoDock vina. Then, MCF-7 was cultured in 10% FBS- enrich DMEM medium and treated with 3.5 mg/ml (IC50) crocin. Then, the level of protein expression and prenylation of K-Ras was examined by gel shift assay- Western blotting technique in the cell lysates after 6, 12, and 24 h of treatment.
***Results*:** Our in silico findings showed that crocin strongly (binding affinity~12 kJ/mol) binds with substrate- binding- site of rat FT through hydrogen and Van der Waals bonds. Concomitantly, our in vitro study has also shown that treatment of MCF-7 with crocin resulted in a time dependent, and significant diminish of K-Ras protein expression, as well as its prenylation.
***Conclusion*:** In conclusion, our data showed that crocin is a potent agent for inhibition of K-Ras prenylation in MCF-7 cancer cell line. We suppose that the prenyl-like structure of crocin may be responsible for its anti- prenyl transferase activity observed in the present study. The precise mechanism of crocin action needs for more studies.
***Keywords*:** K-Ras, Prenyl trsnsferase inhibitor, crocin, braset cancer
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Assessment of Insulin Like Growth factor (IGF1) and blood glucose levels in STZ-induced diabetic rats after administration of aqueous extract of Ficus carcia leaves

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Objective: Diabetes is a metabolic disorder which can cause many complications. Long term complications of diabetes consist of retinopathy, nephropathy, neuropathy and angiopathy and several others. The goal of treatment in diabetes mainly concentrates on keeping blood sugar levels as close to normal as possible, without causing low blood sugar. This can usually be accomplished with a healthy diet, exercise, weight loss, and use of appropriate medications. In addition, the use of some herbal medicine could have beneficial effects in patients. This study was designed to assess effects of aqueous extract of ficus carcia leaves on blood glucose and IGF1 in streptozocine STZ-induced diabetic rats.

Material and Methods: 24 male Wistar rats were randomly divided in 4 groups. Normal, diabetic, diabetic treated with (500 mg/kg/daily), diabetic treated with (1000 mg/kg/daily) of aqueous extract of Ficus Carcia leaves. Blood Glucose was measured by Glucose oxidase–Peroxidase Method and the quantitative determination of IGF1 was performed by use of IGF1-ELISA kit.

Results: Blood glucose levels significantly increased in diabetic rats compared with controls ($P<0.001$) and aqueous extract of ficus Carcia leaves decreased this levels ($P<0.05$). Serum IGF-1 was significantly lower in diabetic rats than normal controls ($P<0.05$). Although both concentrations of the aqueous extract of ficus Carcia leaves caused significant increase in serum IGF-1 in diabetic rats, there was more increase in IGF1 levels in 1000 mg/kg treated group.

Conclusion: This study showed that aqueous extract of ficus carcia has anti-diabetic effects through reducing blood glucose and increasing IGF1.It seems this extract might be a good candidate as a supplementary substace for control glucose levels in diabetes.

Keywords: IGF1, ficus carcia, diabetic, RATs

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Antioxidant and Chemopreventive effect of *Astragalus ovinus* against DMBA induced breast cancer in rats

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Objective: The aim of this study was to investigate the antioxidant and chemopreventive effect of *Astragalus ovinus* hydroalcoholic extract(AOE) against DMBA-Induced breast tumors in rats.

Material and Methods: The antioxidant activity was evaluated by DPPH, FRAP assays. Forty adult female Sprague-Dawley rats were divided into 4 equal groups. The first group served as control and treated with a single dose of olive oil orally, the DMBA (group II) and treatment groups (III & IV) were treated with a single dose of DMBA dissolved in olive oil at dose of 50 $mg.kg^{-1}$ body weight. Group I and II received normal salin and group III and IV treated with AOE orally at doses of 120 and 240 mg kg^{-1} respectively for 30 consecutive days. Chemopreventive effects were assigned by weight and volume of tumors, expression levels of PCNA, serum levels of $CA_{15.3}$, p53 protein, MDA, CAT, calcium, and histopathological studies.

Results: Results showed that the AOE contains a noticeable amount of phenolic and flavonoids compounds. This extract showed a potent antioxidant activity both *in vitro* and *in vivo* assays. Furthermore, orally treatment of rat with AOE decreased the final diameter and volume of tumors, as well as reduced the serum levels of $CA_{15.3}$, p53 protein, MDA, and calcium. AOE also decreased the expression of PCNA in cancerous tissues and reduced the histopathological deformity.

Conclusion: The present study showed the antioxidant and chemopreventive effects of AOE in DMBA-induced breast tumor in rats . This chemopreventive activity of AOE may be largely due to its antioxidant properties.

Keywords: *Astragalus Ovinus*, Breast Cancer, DMBA

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Effects of Different Doses of Metformin on SNARE Proteins Expression in Skeletal Muscle of Rats with Type2 Diabetes Mellitus

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Objective: Soluble N-ethylmaleimide-sensitive factor activating protein receptors, SNAREs, play important roles in membrane trafficking. Among the different isoforms of SNARE proteins, SNAP-23, syntaxin-4 and VAMP-2 are highly expressed in skeletal muscle tissue and play important roles in GLUT-4 trafficking and

vesicle fusion. The altered expression of these proteins can be one of the etiological causes of insulin resistance and type 2 diabetes. The aim of this study was to investigate the effect of metformin on the expression of SNARE proteins in an animal model of type 2 diabetes.

Material and Methods: Forty male Wistar rats were used. A single dose of streptozotocin/nicotinamide were injected to induce type 2 diabetes. Metformin (100 and 150 mg/kg) was administered orally for a month. FBS, body weight and insulin level were measured. The expression of SNARE proteins was assessed using Real-Time qRT-PCR.

Results: Mean delta Ct of SNAP23, syntaxin-4 and VAMP-2 were lower in diabetic rats compared with healthy rats, as a result, their expression increased, although differences were not significant. A dose of 100 mg/kg metformin did not change the expression of these proteins, while 150 mg/kg metformin decreased the expression of all three genes, the differences were not statistically significant.

Conclusion: Streptozotocin along with nicotinamide led to type 2 diabetes induction that was associated with a relative decrease in insulin secretion and insulin resistance. Depending on the dose, metformin can modify SNARE proteins expression in skeletal muscle. This may be another mechanism for metformin to improve diabetes.

Keywords: SNARE proteins, Type 2 diabetes, Metformin

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Protection against H2O2-induced cytotoxicity in PC12 cells by microalgae's extracts

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Objective: The aim of current research is to discover of new compounds with stronger neuroprotective potential and fewer side effects compared to synthetic drugs. Microalgae are microscopic organisms capable to convert solar energy to chemical energy via photosynthesis. Recently, microalgae researches has gained a lot of attention recently because of its roles to the production of renewable fuels, also several secondary metabolites which produced by alga cells such as polysaccharides, polyphenols, polyunsaturated fatty acids, carotenoids and sterols. These compounds show several pharmacological activities and have neuroprotective potential. Here we studied antioxidant and neuroprotective activity of the crude extract of some micro algae.

Material and Methods: Antioxidant activity of the extracts was determined by using 2,2'-azino-bis (ethylbenzthiazoline-6-sulfonic acid (ABTS. (+)) radical cation assay. Cell viability detection by MTT assay. Also mechanism of action was studied by mitochondrial membrane potential (MMP) and intracellular reactive oxygen species (ROS).

Results: The highest reducing power, ABTS radical scavenging, and chelating power were found in methanol extracts of microalgae. The results showed that the treatment of PC12 cells with microalgae extracts to H2O2 exposure effectively increased the cell viability. In addition, this treatment decreased the amount of intracellular ROS, stabilized the mitochondria membrane potential (MMP), and decrease the activity of apoptosis-related protein like caspase 3.

Conclusion: Marine algal are valuable sources for antioxidant agents and could be used for the detection novel functional ingredients for pharmaceutical aim for alleviate the neurodegenerative diseases or for delaying aging.

Keywords: Microalgae, Antioxidant activity, Neuroprotection, PC12 cell line, Bioactive compounds

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Eco-friendly functionalized magnetic nanoparticles as a novel nanocarrier for controlled loading of acyclovir as an anti-cancer agents

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Objective: Considering many applications of functionalized magnetic iron oxide nanoparticles (MIONPs); herein, a new strategy is developed for biosynthesis of MIONPs to improve their performance in the acyclovir delivery. Acyclovir has been the mainstream therapy for herpes viruses and recent studies have revealed the positive cytotoxic effects of antiviral-drugs in cancer treatment.

Material and Methods: A biological method for producing of MIONPs was introduced. The drug loading was studied by including MIONPs (0.01 g) into a phosphate buffered (1 ml, pH 9) containing acyclovir (1mg) with magnetic stirring (50°C, 5h). The accuracy of loading was investigated by FESEM, FT-IR and XRD

techniques and in vitro release of acyclovir was screened through the dialysis method. Then in vitro cytotoxicity of nanoparticles on MDA-MB231 cell lines was assessed.

Results: Biologically synthetized MIONPs was functional which stabilize the nanoparticles and can be exploited for the conjugation of other molecules to these particles. As results showed that the nanoparticles have displayed uniform spherical shape with an average size of 18.8-28.3 nm. The bands at 3355 and 2920 cm-1 in the FT-IR spectrum were ascribed to N–H and C–H stretching vibrations and corroborated that the amine groups in the surface of nanomagnetic. After acyclovier loading, the grafted amine group at the surface provided hydrogen bond interactions with the oxygen atoms of acyclovir and caused immobilization of drug. It can be concluded that loading and release of acyclovir from this biocompatible nanocarier can be controlled by pH.

Conclusion: Since, antiviral-drugs cause various allergenic side effects; therefore, design of a new biocompatible nanocarrier bearing less harmful impacts for oral delivery should be useful.

Keywords: Magnetic iron oxide nanoparticles, Acyclovir, Anti-cancer agents

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Evaluation of soluble expression of a single-chain antibody fragment against human epidermal growth factor receptor 2 (HER2) by three different E. coli strains

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***Objective*:** Several studies showed successful soluble expression of scFvs using genetically modified Escherichia coli species. Origami (DE3) has mutations which lead to higher formation of disulfide bonds and more soluble protein expression. ShuffleT7 is a novel modified strain which has DsbC isomerase more than Origami (DE3). In our previous work, single chain antibody of pertuzumab was overexpressed on E. coli but more of them were insoluble. The present study evaluate soluble expression of scFv against HER2 by different E.coli strains.

***Material and Methods*:** In this experimental study, scFv plasmid is transformed to strains of E.coli (BL21(DE3), Origami(DE3), Shuffle T7) by heating shock. Then expressed in LB broth with suitable antibiotics in different temperature (23, 30, 37) and differential concentration of inducer, IPTG. After leased cells by microsmash, soluble and insoluble protein separated by centrifuge. For analyse of scFv used SDS-PAGE, Western blot. Soluble scFv pured in affinity chromatography by Imidazole solution. Amount of disulfide bonds evaluated by Ellman method.

***Results*:** The primary results of this study showed that total expression of scFv was higher in BL21 (DE3) than Shuffle T7 and Origami (DE3) but soluble expression of scFv in BL21 (DE3) was a little more than Shuffle T7 based on SDS-PAGE analysis. scFv expression was higher in lower temperatures and lower concentrations of IPTG.

***Conclusion*:** Genetic modification and using two antibiotics may lead to decrease in expression of protein in Shuffle T7 and Origami (DE3) but after using only one soluble expression of scFv had no diffrence. pET plasmid in present of IPTG is toxic for E.coli and reduced culture temperature improve folding process in cells these can be why scFv protein expression was higher in lower concentration of IPTG and lower temperatures.

***Keywords*:** E. coli, soluble expression, disulfide bond, single chain antibody, HER2 receptor

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Anti-proliferative and apoptotic activity of Astragalus ovinus leaf extracts and its terpenoid fraction on MCF-7 cancer cell line

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***Objective*:** *Astragalus ovinus* (Fabacea) has been used in folk medicine to treat a different of diseases. Despite some reports about the antitumor effects of some species of this genus, there is no evidence addressing this effect in *Astragalus ovinus (A.ovinus).* Here, we studied the cytotoxic effect of methanolic extract of *A. ovinus* and its terpenoid fraction on MCF-7 breast cancer cell line.

***Material and Methods*:** MCF-7 cells were cultured and then incubated in the methanolic extract of *A. ovinus* and its fractions with various concentrations for 24 hours. Cell viability was measured by MTT assay. Furthermore, the effects of the indicated extracts were tested on some regulators of cell death such as Caspase-8, Caspase-9.

***Results*:** The estimated IC_{50} values of the methanolic extract, and terpenoid fraction on MCF-7 cell after 24 h were determined 979.44

and 372.134 µg/ml, respectively. *A. ovinus* extract and its fraction induced apoptosis by activation of caspase-8 and caspase-9.

***Conclusion*:** Our data confirmed the significant cytotoxic and antiproliferative effects of *A. ovinus* on breast cell line through induction caspase. These findings provide a basis for the therapeutic potential of *A. ovinus* in the management of breast cancer. Isolation of the compound responsible for this effect may lead to the development of a new anticancer compound against breast cancer.

***Keywords*:** *Astragalus ovinus*, MCF-7, Apoptosis, caspase, antiproliferative

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Investigation on the effects of green synthesized Copper oxide nanoparticles on the structure of calf thymus DNA

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***Objective*:** Copper oxide (CuO) is an important metal oxide and has many applications in different fields including medicine. Nanoparticles are synthesized through different methods such as sono-chemical route, hydrothermal approach, chemical reduction which have many disadvantages. So, in this study, we have used synthesized copper oxide nanoparticles using green chemistry method. This method can be a valuable substitute for toxic and destructive chemical methods and has fewer side effects. The side effects of the green synthesized Copper oxide nanoparticles were investigated via its interactions and induction of structural changes in calf thymus DNA.

***Material and Methods*:** In the present study, for the first time, we have investigated the interaction of CuO nanoparticles with calf thymus DNA using various spectroscopic methods of Uv-Visible, fluorescence and circular dichroism (CD) techniques.

***Results*:** By the analysis of UV- Visible data, it was found that CuO nanoparticles can change the structure of calf thymus DNA and induce denaturation in it. Extrinsic fluorescence emission spectra of intercalated ethidium bromide (EB) in the presence of DNA showed that by increasing the concenteration of CuO nanoparticles, a significant reduction of in EB intensity and quenching of EB fluorescence was observed. Also, the CD results suggested that CuO nanoparticles can change the structure of DNA.

***Conclusion*:** Result of the present study has shown that the green synthesized nanoparticles can bind and interact with DNA, and may have used this nanoparticle for the treatment of diseases, including cancer.

***Keywords*:** CuO nanoparticles, green chemistry, side effects, circular dichroism, fluorescence

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Rapid and sensitive nanobiosensor for human influenza A detection based on lateral flow immunoassay [Review Article]

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***Objective*:** Now day rapid recognition of various analytes at little concentrations has been provided using developing the several types of nanobiosensors. However, Rapid and sensitive point-of-care (POC) recognition remains a challenge in biomedical diagnostics application. Recently, appearance the lateral flow immunoassay (LFIA), has received increased interest as a means in order to POC screening and diagnosis the wide variety of analytes. Herein, a rapid test strip has been developed based on lateral flow immunoassay in order to detect H1N1 human influenza type A virus. Influenza A viruses is responsible for seasonal epidemics accounting for over 200000 hospitalizations and 30000-50000 deaths in each year. For this purpose, gold nanoparticles have been synthesis according to Mirkin and coworkers protocol. Then, monoclonal anti-NP protein has been conjugated at the surface of GNPs. Moreover, after the fabrication the LAFIA test strip, by applying 100 µL of the sample on a sample pad the LFIA was performed on the strip. Finally, the test strip was investigated by monitoring the color changed on the test line for15 min at room temperature. According to the results, LFIA test strip was successfully developed for a rapid and sensitive detection of the influenza A virus. In the presence of Influenza virus the test line NP was colored compare to negative control due to virus-conjugated gold nanoparticle complex concentration on the test line. The result showed that LFIA test strip is capable of detecting Influenza virus as low as 10 $pfu \bullet mL^{-1}$ within3 min. In conclusion, Rapid test strip has a wide and interest potential which could be useful for various medical and diagnostic applications.

***Keywords*:** Lateral flow immunoassay (LFIA), Influenza A virus, Nanobiosensors, Gold nanoparticle
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Determination of paraoxonase 1 (PON1)-Q192R phenotype distribution by double substrate method in patients with type 2 diabetes: effects on the association of PON1 activity with age

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***Objective*:** Low paraoxonase 1 (PON1) activity is associated with increased risk of coronary artery disease in patients with type 2 diabetes (T2D). In this study, we have determined the phenotypic distribution of PON1-Q192R as a common variant in the coding region of PON1 gene by double substrate method and the relationship of the phenotypes with age.

***Material and Methods*:** A total of 115 patients with T2D were enrolled in this study. Hydrolyses rates of the two substrates paraoxon (paraoxonase activity; POXase) and phenylacetate (arylesterase activity; AREase) were spectrophotometrically assayed. Blanks were used to correct for the nonenzymatic hydrolysis of the substrates. The molar extinction coefficient was 1,310 and 17,100 M-1 cm-1, respectively for AREase and POXase. The ratio POXase/AREase was determined for each person to assign individuals to one of the three possible phenotypes (individual genotypes): QQ (homozygous with low activity), QR (heterozygous with intermediate activity) or RR (homozygous with high activity).

***Results*:** The ratio of POXase/AREase was revealed a trimodal frequency distribution in the study patients. Accordingly, the study subjects were divided into the three phenotypes at the ratios of 1.3 and 2.7. Patients with a ratio below 1.3 were classified as QQ phenotype, between 1.3 and 2.7 as QR phenotype and patients with a ratio above 2.7 were defined to have RR phenotype. Our results showed that linear regression of POXase vs. AREase in each subgroup was significant: r=0.602, p<0.001 for QQ phenotype; r=0.837, p<0.001 for QR phenotype; r=0.893, p=0.007 for RR phenotype. According to correlation analyses, there was no statistically significant correlation between POXase and age (r=−0.016, p=0.881) in total data. When analyses were performed according to Q/R phenotypes, there was a negative and significant correlation between POXase and age in QR + RR group (r=−0.318, p=0.043). In people with QQ phenotypes, there was no statistically significant correlation between these two parameter (r=−0.091, p=0.514).

***Conclusion*:** Based on double substrate method, the frequency of Q phenotype (low activity) was 0.78 and of R phenotype (high activity) 0.22 in the study population. Considering age as a risk factor for cardiovascular diseases, our findings might show that the presence of the R allozyme potentiate the effects of age on susceptibility to the diseases in T2D.

***Keywords*:** Paraoxonase 1, Q192R phenotype, Double substrate method, Type 2diabetes, Age
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ID:449

Inhibition of lncRNA CBR3-AS1 induces apoptosis and inhibits cell proliferation in human gastric cancer cells

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***Objective*:** Gastric cancer is responsible for > 700,000 annual cancer-related deaths in the world. CBR3-AS1 (PlncRNA-1) is a newly identified long noncoding RNA encoded from the antisense direction of the CBR3 gene. Up-regulation of PlncRNA-1 has been reported in various cancer types. In the current study, we investigated the effects of suppression of this lncRNA by RNAi technique in a human gastric cancer cell line.

***Material and Methods*:** Real-time RT-PCR was performed to determine the relative expression of CBR3-AS1 in three gastric carcinoma cell lines. RNA interference technique was utilized to knock-down the expression of CBR3-AS1. Cell viability and apoptosis analyses were performed after treatment with siRNA.

***Results*:** Among three gastric cancer cell lines examined, CBR3-AS1 had the highest relative expression in AGS cell line. Over 99% reduction (p<0.0001) was observed in CBR3-AS1 expression level after siRNA treatment CBR3-AS1 knockdown significantly decreased cell viability in AGS cells with a significant 60-70% reduction rate. A significant increase in

the rate of Annexin V positive cells was also detected after CBR3-AS1 knock-down.

***Conclusion*:** In conclusion, these findings suggest that CBR3-AS1 is over-expressed in AGS gastric cancer cells and affects cell survival of these cells. More work needs to be performed for exploration of the molecular mechanisms underlying CBR3-AS1 functions in cancer cells. This lncRNA may be a promising molecule that might/could be used as novel biomarker of cancer diagnosis, prognosis and therapy.

***Keywords*:** CBR3-AS1, Gene Expression, RNA Interference, Stomach Neoplasms

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CBR3-AS1 and TUG1 are over-expressed in gastric cancer tissues: Supportive evidence from TCGA Pan-Cancer Data

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***Objective*:** Gastric cancer (GC) is the third leading cause of cancer death worldwide. Despite the current improvements of life expectancy and survival rate, most of the patients are diagnosed when their cancer has been progressed to advanced stages. Therefore, unraveling the molecular mechanisms of GC to find early-stage biomarkers is urgent. Based on the critical roles of CBR3-AS1, TUG1 and FAM83H-AS1 genes in cancer pathogenesis, in this study, we aimed to assess the expression profile and clinicopathological features of these lncRNAs in human gastric cancer. Furthermore, gene expression, clinicopathological characteristics and overall survival data of these lncRNAs were retrieved and analyzed from the Cancer Genome Atlas (TCGA) cohort.

***Material and Methods*:** Total RNA extraction, cDNA synthesis, and quantitative real-time PCR were performed for 80 paired GC tissues. Furthermore, expression and clinicopathological data of the lncRNAs from 318 gastric cancer patients were retrieved from TCGA database.

***Results*:** Expression of CBR3-AS1 and TUG1 were significantly up-regulated in GC tumoral tissues compared with their paired adjacent non-tumoral ones. FAM83H-AS1 showed no differential expression between tumoral and non-tumoral tissues. Consistently, the expression of CBR3-AS1, TUG1 and FAM83H-AS1 were significantly higher in TCGA tumor tissues than those in normal ones. The Kaplan-Meier survival curves demonstrated that none of the studied lncRNAs correlated with GC overall survival.

***Conclusion*:** In conclusion, CBR3-AS1 and TUG1 lncRNA genes may play a critical role in GC progression and may serve as potential diagnostic biomarkers in GC patients.

***Keywords*:** CBR3-AS1, TUG1, Gene Expression, Stomach Neoplasms, TCGA

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ID:455

Desipramine induces apoptosis in human chronic myeloid leukemia K562 cells

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***Objective*:** Antitumor effects of antidepressants have been reported in some cancer cell lines. However, to our knowledge, there is not any study about anti-proliferative effects of desipramine, a tricyclic antidepressant, in human chronic myeloid leukemia. Therefore, in this study, we examined the effects of desipramine in human leukemia k562 cells.

***Material and Methods*:** The cytotoxic effects of desipramine were studied using MTT assay. K562 cells were cultured and treated with various concentrations of desipramine and incubated for 24 h, then IC50 value was determined. Morphology changes of cells was evaluated by reverse phase microscopy. The activity of caspases 8 and 9, gel electrophoresis of DNA and Nitric oxide (NO) production were used for apoptosis investigation.

***Results*:** In the present study, desipramine drug reduced cell viability of K562 cells and induced apoptosis by increases activity of caspases 8 and 9, stimulation DNA fragmentation and inhibition of NO production. These results confirm that desipramine displays anti-proliferative effects in k562 cells mediated by promotion of apoptosis.

***Conclusion*:** With respect to the results of the present study, desipramine inhibited the growth of K562 cell line and induced cell death in this cell line. These results showed that it may be possible to use this drug in cancer research fields, although more clinical researches are needed.

***Keywords*:** Antidepressants, Desipramine, K562 cell, Anti-proliferative, Apoptosis

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ID:461

Nrf 2 Polymorphism at rs6721961 in Breast Cancer Patients with No Precedent Chemotherapy among Kurdish Population

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***Objective*:** Owning to the putative role of Nrf2 in activation of several protective genes in response to oxidative stress and pathological conditions, the aim of present study was to investigate the role of Nrf2 expression and it's polymorphism in Breast cancer patients with no previous therapy.

***Material and Methods*:** Breast cancer patients (34 cases) and controls (80 cases) from western Kurdish population of Iran were selected to evaluate the genotype of Nrf2 (rs6721961) by PCR-restriction fragment length polymorphism. In addition, the statistical association between Nrf2 (rs6721961) was analyzed with the expression of Nrf2, ER, PR, Her2, SOD, catalase and other clinicopathological characteristics.

***Results*:** The mean age of patients and controls were 43.55±1.89 and 46.44±2.16, respectively. In control group, Nrf2 rs6721961 polymorphism deviated from Hardy-Weinberg Equation with a p=value of 0.035 while among the patients, SNP exact test for HWE, showed a satisfied association with HWE (p=0.7). Besides, there was no significant relation between Nrf2 expression with catalase (p=0.28) while SOD had a meaningful association with Nrf2 expression (p=0.02). There were no meaningful association of SNP with the expression levels of Her2 (p=0.30), ER (p=0.60) and PR (0.63). Besides, SNPSTAT showed that the expressions of Her2, ER and PR were in agreement with hardy-Weinberg equations.

***Conclusion*:** The results clearly indicated that Nrf2 is involved in the risk of breast cancer. In addition, geographical and racial differences are the imperative effectors in the appearance of several genes in patients that would be considered in all studies.

***Keyword*:** Nrf2, Polymorphism, Catalase, SOD, Oxidative stress

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ID:462

Study of glutathione S-transferase P1 Ala114/Val114 genotypes specific polymorphism in Iranian population with considering gender differences in lung cancer

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***Objective*:** Lung cancer continues to be the leading cause of cancer death in both men and women in the United States, with more than 158 900 deaths expected in 1999. Among tobacco-smoke structures, polycyclic aromatic hydrocarbons (PAHs), such as benzo-a-pyrene (BaP), play a major role in lung chemical carcinogens. Many of the Xenobiotic-metabolizing enzymes (XMEs) are similar to cytochrome P450, glutathione S-transferases (GSTs), and hydroxyl epoxide in BaP metabolism, which can lead to the prevalence of high-mutagenic metabolites such as 7 and 8-diol-9 and 10- epoxied BPDE). GSTP1 is highly expressed in lung tissue and is considered the predominant GST in the lungs.

***Material and Methods*:** We selected 120 lung cancer patients tissue, 120 normal cases (as control) The GSTP1 genotypes were determined in all cases. The ARMS-PCR method was used for diagnosis of techno-specific single nucleotide polymorphisms (SNP). The primary ARMS PCR was used in order to conclude the Ala114→Val114 genotype.

***Results*:** For those with Ala114/Ala114 genotype, the odds ratio of lung cancer was 34% higher than the odds for people with Ala114/Val114 heterozygote genotype (P=0.515; OR=1/34; 95% CI=0.556-3.22), although it is not statistically significant. The results also showed that for those who had the Ala114/Ala114 genotype (P=0.071), the odds ratio for lung cancer was 65% higher than the odds for people with homozygous Vla114/Val114 genotype (P=0.089; OR=0.606; 95% CI=0.34-1.08).

***Conclusion*:** We found no relationship between the homozygote genotype Ala114/Ala114 (P=0.071) and Ala114/Val114 (P=0.515) and Vla114/Val114 (P=0.089).

***Keywords*:** Lung cancer, Glutathione S-transferees P1 Ala114/Val114, Genetic polymorphism, ARMS

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The comparison of catalase and superoxide dismutase activities in individual's exposure to outdoor air pollution in the cities of Arak and Zanjan

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***Objective*:** Nowadays, Air pollution is the most important health and environmental problems in developing cities. Long-term exposure to Outdoor air pollutants is a major risk factor for morbidity and mortality from chronic

diseases such as cardiovascular disease, diabetes, cancer and pulmonary disease.

***Material and Methods*:** In this cross-sectional study, a total of 203 healthy adult men never-smoking (111 exposed subjects and 92 controls) were enrolled. The levels of superoxide dismutase enzyme were assessed by ELISA assay and antioxidant enzyme activity of catalase in the serum samples was determined using a spectrophotometric method.

***Results*:** Data analysis showed a significantly lower level of superoxide dismutase enzyme activity in the exposure group compared to control group. On the other hand, there were no differences in the levels of enzymes activity of catalase between residents in the cities of Arak and Zanjan.

***Conclusion*:** This study suggests that activity of superoxide dismutase enzyme could be useful biomarker of environmental stresses such as in exposure of air pollution. On the other hand, our result did not support the hypothesis that catalase could be considered as an oxidative stress marker following exposure to outdoor air pollution.

***Keywords*:** Air Pollution, Catalase, Superoxide dismutase enzyme, Arak, Zanjan

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ID:483

Investigation of cytotoxicity and apoptosis induction in human leukemia K562 cell line by an active compound from pyrazine family

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***Objective*:** It has been recently showed that pyrazine derivatives have various biological activities including anti-bacterial, anti-viral and anti-cancer. Some pyrazines are essential for all forms of life due their DNA strand breakage activity and their apoptosis inducing effects. The present study aimed to evaluate the cytotoxicity and induction of apoptosis in human leukemia K562 cells by (2)-3-phenyl prop-2-enyl-pyrazin-2-carboxylate (2-P. P) a new compound from pyrazinoic acid family.

***Material and Methods*:** The K562 cells were treated with various concentration (10-120 µM) of the 2-P. P for 24-72 hours. Cell viability was determined by MTT growth inhibition assay. Apoptosis, as the mechanism of cell death, was investigated morphologically by Hoechst staining, cell surface expression assay of phosphatidyl serine by annexin-V/PI technique, as well as, DNA fragmentation assay. The effect of 2-P.P on K562 cell cycle was studied by flow cytometry.

***Results*:** He results revealed that 2-P.P inhibited viability with IC50 of 70 µM for 72 h. Assessment of Annexin V/PI double staining by flow cytometry, morphological changes by fluorescence microscope and the formation of DNA ladders upon treatment of the cells with the 2-P.P showed that this compound induce apoptosis at IC50 value. Cell cycle arrest was observed in G0/G1 phase and sub-G1 cell opulation increased after 24- 72 h of treatment.

***Conclusion*:** It is concluded that 2-P.P can be suitable candidate for further pharmaceutical evaluations.

***Keywords*:** Pyrazines, Apoptosis, K562, Chronic Myeloid Leukemia

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Impact of digoxin on the cisplatin sensitivity in bladder cancer cells

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***Objective*:** Cisplatin-based chemotherapy improves the overall survival of patients with bladder cancer. However, most of these patients show resistance to cisplatin, when used as a monotherapy. This study was conducted to investigate the potential of digoxin as a chemosensitizer for increasing the therapeutic efficacy of cisplatin in bladder cancer cells.

***Material and Methods*:** MTT assay was used to determine the cytotoxic effect of cisplatin and digoxin on 2 human bladder cancer cell lines (EJ138 and 5637). To evaluate the effect of digoxin on the sensitivity of cells against cisplatin, cells were pretreated with low cytotoxic concentration (IC30) of digoxin and then various concentration of cisplatin.

***Results*:** Digoxin and cisplatin inhibit the growth of bladder cancer cells in dose-dependent manner. 5637cell line was more resistant to cytotoxic effect of digoxin and cisplatin than EJ138. Pretreatment with digoxin markedly sensitized both cell lines to the cytotoxic effects of cisplatin.

***Conclusion*:** Taken together our findings, show for the first time that pretreatment with low dose of digoxin significantly enhanced the cytotoxic property of cisplatin on bladder cancer cells. The combination of digoxin and cisplatin may be considered as a potential new chemotherapy regimen to overcome cisplatin resistance in patients with bladder cancer.

***Keywords*:** Digoxin, Bladder cancer, Cisplatin, Chemotherapy

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Investigation of in vitro aldose reductase inhibitory potential of effective fraction of salvia officinalis

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***Objective*:** Aldose reductase (AR) is the key enzyme of the polyol pathway, which plays an important role in the pathogenesis of diabetic complications. AR inhibitors can be used as an important strategy in the treatent of diabetic complications.

***Material and Methods*:** The aim of the present study was to investigate effect of effective fraction of salvia officinalis on the activity of the bovine lens aldose reductase. For this purpose, the phenol and flavonoid contents, IC50 values of different fractions of the salvia officinalis were first measured to scavenge the DPPH free radicals. Then, the effect of crude extract and effective fraction of the plant on the enzyme activity were investigated.

***Results*:** Results indicated that ethyl acetate fraction had the highest of phenolic and flavonoid contents by 412.6±1.55 and 372.5±6.47 mg/ml, respectively. Also, the ethyl acetate fraction showed the lowest IC50 content of 1.18µg/ml for scavenging of the free radicals and 9.25µg/ml for the inhibition of AR activity. According to the lineweaver–Burk plot, the ethyl acetate fraction acts as an uncompetitive enzyme inhibitor.

***Conclusion*:** One short sentence which summarizes the contents of the article, presenting the final outcome of and concluded from the research or proposing further study on the subject, may be given at the. These findings revealed that different fractions showed significant amount of AR activity, where in ethyl acetate fraction it was found to be maximum which may be due to its high phenolic and flavonoid content.

***Keywords*:** Salvia officinalis, Aldose reductase, Ethyl acetate fraction, Inhibititory effect

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ID:496

The Kinetic Study of Permuted and Non-permuted Renilla luciferase

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***Objective*:** Circular permutation is a nature-based strategy in protein engineering methods and so applicable in zymogen construction. A zymogen is an inactive form of an enzyme which is activated by a proteolytic digestion.

***Material and Methods*:** In this study, we have benefited from circular permutation strategy to design a biosensor in the form of zymogen. Indeed, we have changed the position of N and C terminal domain of Renilla luciferase. This rearrangement results in enzyme inactivation unless it is exposed to the caspase-9, the processing protease. All the standard protocols for the cloning and protein purification were done for both form of luciferase, intact and engineered. The effect of circular permutation on enzyme activity, the decay rate of emitted light and the kinetic parameters were investigated.

***Results*:** Examining the enzyme activity of these enzymes showed that in the absence of caspase-9, the permuted form of luciferase has no activity, however, it regains its activity after cleavage by caspase-9. Measuring and comparing the decay rate of bioluminescent emission for both enzymes do not show a significant difference. Afterward, the enzyme kinetics studies have been done and the Michaelis-Menten plots were graphically depicted. The results show kinetic parameters Km and Vmax values, decreases in the permuted luciferase rather than non-permuted one.

***Conclusion*:** In conclusion, the study showed that circular permutation of Renilla luciferase changes its kinetic parameters. It may be due to the conformational changes in substrate binding site that occur during permutation process.

***Keywords*:** Circular permutation, Enzyme kinetics, Renilla luciferase

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An overview of the quality control process for Andrology tests and set up a method for new SCSA test in a medical diagnostic laboratory

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***Objective*:** The quality control process results in increase of accuracy and precision in analytic detection in the clinical laboratory. Medical diagnostic laboratories have the existing rules for quality control in most subclinical section. However, quality control process in the Andrology department have been underestimated, and many infertility laboratories are not aware of the rules and procedures for implementing quality control in this section. Also, the introduction of new tests

in the Andrology department such as SCSA (sperm chromatin structure assay) and TUNEL requires standardization of new quality control procedures. In this study, in addition to a review of the quality control processes for Andrology department section, we provide a novel and accurate method for SCSA quality control.

***Material and Methods*:** For pool control sample, semen samples were selected from individuals with concentration > 60 million/ml and semen volume>3 cc, were liquated divided on 500 µl micro tube and then were storage in -20 refrigerator. After 1 week, first micro tube of semen was thawed and this SCSA results was considered as references value. Then every month one micro tube of semen samples was thawed and the obtained results were compared with references value. In addition, samples were prepared and were send to other laboratories for assessment the SDI.

***Results*:** The results show when the samples were kept at a – 20°C for one year, the SCSA results did not have a significant clear difference with the samples that were read after one 1 week from pool control production. We observed CV about 8%, which was acceptable. In addition, the produced control samples and which were sent to other laboratories did not differ significantly in the SCSA results and CV content was reported 7%.

***Conclusion*:** The method used for assessing the quality control process is was appropriate for the SCSA test and result in improvement in accurate and precision of this test results. Quality control procedures in the Andrology department have a great importance in order to improvement the accuracy and precision of the results in this Andrology section.

***Keywords*:** Quality control, Andrology, SCSA test

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ID:499

Inhibitory effect of Irisin on LDL oxidation as a newly atherosclerosis diagnostic biomarker In vitro

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***Objective*:** Recently, Irisin has been identified as a new glycopeptide and myokine and that is result of the proteolysis of the FNDC5. This peptide is secreted from the heart muscle while exercising. The low level of irisin in the bloodstream is associated with signs of atherosclerosis and the effect on LDL oxidation, causing to make delayes in the oxidation process and will be prevent the formation of foam cells and vascular endothelial destruction. This study aimed to investigate the effect of irisin on reducing LDL oxidation as an effective factor in atherosclerosis.

***Material and Methods*:** Fasting blood samples were collected from normal people and serum was isolated by ultracentrifugation gradient medium. At the end the effect of certain concentration of irisin on activity of LDL oxidation induced by CuSo4, the oxidation kinetics was studied in vitro.

***Results*:** The results of this study showed that the 5 (µg/ml) concentration of the irisin had the most effective concentration on reducing LDL oxidation and significantly increased the lag phase as a factor affecting the incidence of atherosclerosis ($p<0.001$).

***Conclusion*:** Findings showed that the irisin secreted from the heart muscle tissue as a newly biomarker on inhibition of serum lipid oxidation such as LDL as an indicator of heart disease, including atherosclerosis by strengthening the antioxidant properties of the lipoproteins internal particle and inhibition of free radicals result from CuSo4 in vitro, was significantly effective, and probably will have similar effects in vivo.

***Keywords*:** Irisin, Atherosclerosis, LDL oxidation, FNDC5

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Neuroprotective effect of hydralazine upon dopaminergic SH-SY5Y human neuroblastoma cells in a 6-hydroxydopamine model of Parkinson's disease

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***Objective*:** The prevalence of neurodegenerative diseases such as

Parkinson's disease (PD) is clearly growing in all the world's societies and it cannot be completely cured by present prescriptions. Recent findings have confirmed that activating the hypoxia HIF-1α/VEGF signaling pathway could mediate neuroprotective procedures. In the present study, we determined to assess the neuroprotective capacity of hydralazine, a mimetic agent of the hypoxia pathway, in vitro model of PD.

***Material and Methods*:** At the beginning of the experiment, the effects of various concentrations of hydralazine on SH-SY5Y human neuroblastoma cell viability were considered to obtain the non-cytotoxic concentrations of a drug by MTT-assay. Additionally, the cells exposed to different concentrations of 6-hydroxydopamine (6-OHDA) (100 µg/ml) to evaluate 6-OHDA-induced SH-SY5Y cell toxicity by MTT and apoptosis detection assays. Afterward, the cells were pretreated with 25, 50, 75 and 100 µg/ml concentrations of hydralazine for 6 h, followed by incubation with 6-OHDA (100 µg/ml) for 24 h. Eventually, protein expression of HIF-1α and VEGF in experimental groups was analyzed by western blotting.

***Results*:** Hydralazine at 50 µg/ml concentration significantly attenuated 6-OHDA-induced cell apoptotic cell death in SH-SY5Y cells. Pretreatment with hydralazine significantly up-regulated the protein expression of HIF-1α and VEGF in the cells incubated with 6-OHDA versus 6-OHDA group alone.

***Conclusion*:** The present data suggest that hydralazine pretreatment via regulation of transcription factor HIF-1α expression levels and correlated target genes may mediate beneficial properties in reversing 6-OHDA-induced deteriorations and provide a useful therapeutic strategy for preventing PD.

***Keywords*:** Parkinson disease, Hydralazine, HIF-1α, 6-OHDA, SH-SY5Y cells

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Therapeutic effect of combination Silibinin and Sodium Butyrate on a mouse model of ulcerative colitis

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***Objective*:** Intestinal inflammation (IBD) is a complex multifactorial disease that includes two Crohn's disease and ulcerative colitis (UC). Ulcerative colitis is a disease in which the inner lining of the colon is inflamed. So far, this disease has no definitive cure, and the drugs used, such as anti-inflammatories, can stop the disease for a while, in addition to having complications. Our goal in this study is to find the appropriate drug for the improvement or definitive treatment of the disease without side effects.

***Material and Methods*:** In this study, 48 Balb/C male mice weighing 25 to 35 g were divided into 6 groups of 8. They were administered for 2 weeks with an effective dose of Silibinin (SB) or sodium butyrate (BU) or a mix of two. To compare the therapeutic effects of these compounds, an anti-inflammatory drug such as Mesalazine (Mz) was also used. After 12 days of treatment, colitis was induced by rectal acetic acid injection in mice, and 48 hours later, on day 14, all mice were sacrificed. In order to verify the results, histomorphologic and immunohistologic studies were performed on the blood and the colon tissue.

***Results*:** Histomorphologic examination of colonic biopsy specimens according to the available classification: mild, moderate and severe colitis, shows that groups treated with SB or BU alone have no significant difference with the MZ group, but the combination of SB and BU shows a significant difference with this group and the negative control. Immunohistological studies, TNF-α, IL-6, glutathione tests on tissue and blood confirm the results observed above.

***Conclusion*:** The present investigation outlines the anti-inflammatory activities of SB+BU against experimental ulcerative colitis. The anti-ulcerogenic effect was confirmed by the histological preservation of the colon architecture, inhibiting neutrophil infiltration and promoting the antioxidant capacity of the damaged colonic tissue.

***Keywords*:** Ulcerative colitis, Intestinal inflammation, Silibinin, Sodium Butyrate, Mice

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Nano-biosensor-based Early Detection of Breast and Colon Cancers by Targeting Plasma miR-155

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***Objective*:** Cancer treatment is facilitated by early-phase diagnosis. The molecular diagnosis of cancer tumor markers can provide a sensitive and highly specific method for detection of cancers. Among molecular detection methods, nano-bio-sensing technology could serve as a point-of-care and cost-effective method with high specificity and sensitivity. MicroRNAs are preferred among many tumor markers mainly because of a key role in metastasis and apoptosis that mostly appear in the early-stage of cancer.
***Material and Methods*:** MiRNA-155 was selected for investigation in the plasma of the suspected patients with/without chemotherapy to check whether the expression of the biomarker was dysregulated or not. MiRNAs from plasma of 10 suspected patient to breast and colon cancers were extracted. Subsequently, the extracted samples were subjected to the designed optical nano-bio-sensor in which mi-RNAs are targeted by nano-probes.
***Results*:** The color changing of the nano-biosensor from red to violet were observed in testing of six out of ten samples of suspected patients which could be occurred because of upregulation in miRNA-155. However, the intensity of the violet shift in samples with clinical symptoms was higher and faster than two samples that were in the early stages of cancer. This could be attributed to the amount of expressed miRNA-155. The other four samples didn`t show any color change that could be related to chemotherapy treatment which was probably resulted in lowered amount of miRNA-155.
***Conclusion*:** In conclusion, nano-biosensor approach targeting miRNA-155 was successfully analyzed as a potential method for early detection of cancer as well as evaluation of prescribed therapeutic methodologies.
***Keywords*:** MiRNA-155, Nano-bio-sensing, Tumor marker
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ID:522

Homology Modeling of Desmoteplase: The Important Enzyme for Plasminogen Activation

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***Objective*:** The Desmodus rotundus plasminogen activator (DSPA-α, desmoteplase) from vampire bat saliva is plasminogen activator that does not exhibit NMDA (N-methyl-D-aspartate) associated neurodegeneration. Three-dimensional structure of protein is very important for novel insights into safe plasminogen activator discovery and design.
***Material and Methods*:** For modeling the structure of protein, the sequence of target protein was obtained from UniprotKB database (Accession number P98119). A PSI-BLAST Search with default parameters was carried out against the Protein Data Bank (PDB) to find suitable templates for homology modeling. The multiple sequence alignment of target sequence and selected templates was performed with Clustal Omega web server. Than 1000 models of target protein were generated with Modeller software using multiple sequence alignment of target and known templates. Internal scoring functions such as DOPE score (discrete optimized protein energy), molpdf and GA341 were used to select the best model.
***Results*:** The quality of final model was evaluated by various tests. Finally, the validated model was subjected to energy minimization with Gromacs, molecular dynamic package, with steepest descent algorithm and CHARRM forcefield parameters. The Ramachandran plot of selected model obtained from RAMPAGE server showed that 99.1% of residues were in favored and allowed regions. The Z-score of ProSA-Web server was -8.88 which indicated that it was reliable and accurate model.
***Conclusion*:** The model was accurate and reliable for further computational study about structure and function of protein.
***Keywords*:** DSPA-α, Plasminogen activator, Homology modeling
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In Silico Modeling of DSPA-β

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***Objective*:** Four type of plasminogen activator have been identified as Desmodus rotundus salivary plasminogen activators (DSPAs). Lack of adverse effect within the central nervous system is a prominent feature of DSPAs. Model of protein is important for further studies about design and discovery of plasminogen activator drugs.

***Material and Methods*:** Sequence of target protein, salivary plasminogen activator Beta of Desmodus Rotendus, was retrieved from UniprotKP database (Accesion number P98121). The template search for the target sequence was conducted in PSI-BLAST against Protein Data Bank database. The sequences of target protein and templates were aligned with the Clustal Omega web server. The modelling procedure of target sequence completes with generation of 1000 models of target sequence with associated known templates. The output is a best model for the target sequence with respect to internal scoring functions, such as least DOPE score, least molpdf and highest GA341.

***Results*:** Final model evaluation was carried out with Prosa-Web, RAMPAGE and verify-3D web servers. Prosa Z-score for best model (-7.66) suggests good quality for selected model. Best model indicated 91.1 % of the residues in favored regions, 6.9 % residue in allowed region and 2% residue in disallowed region. Appraisal of three dimensional profile with VERIFY 3D showed good quality and reliability for selected model (86.84% of the residues had an averaged 3D-1D score≥0.2). Then, the validated model was subjected to energy minimization with molecular dynamics simulation package, GROMACS, to accomplish low energy 3D structure.

***Conclusion*:** The model was accurate and reliable for further computational study about structure and function of protein.

Keywords: DSPA-β, Plasminogen activator, Homology modeling.

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ID:536

The salivary creatinine, urea and prostate-specific antigen (PSA) positively and significantly associated with the serum creatinine, urea and PSA in prostate diseases

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***Objective*:** In recent years, the use of saliva as a specimen, due to its non-invasive and easy access increased. But their roles have not been confirmed yet. Therefore, our aim was to evaluate the correlation between salivary, serum creatinine, urea and prostate-specific antigen (PSA) ratio in patients with prostate diseases.

Material and Methods: This case control study included 20 prostate cancer (PCa) patients and 20 benign prostatic hyperplasia (BPH) patients. The PSA, creatinine and urea levels in their saliva and serum were measured with the enzyme-linked immunosorbent assay and Biochemical kits, respectively. The derived data was compared using the Mann–Whitney U test. The correlation between salivary and serum creatinine, urea and PSA was determined using Spearman's correlation test.

***Results*:** Significant differences were observed between the PCa and BPH groups in terms of the creatinine, urea and PSA levels in the serum and saliva ($P<0.001$). The correlation was positively and significantly between salivary and serum creatinine in PCa and BPH groups ($r=0.753$, $P<0.05$) and ($r=0.729$, $P<0.05$) respectively. The serum urea in PCa ($r=0.747$, $P<0.05$) and BPH ($r=0.798$, $P<0.05$) groups was positive and statistically significant correlated with salivary urea. As well as, the salivary PSA in the PCa ($r=0.610$, $P<0.05$) and BPH ($r=0.531$, $P<0.05$) groups was positively and significantly associated with the serum PSA in the two groups.

***Conclusion*:** According to the results of the present study, the salivary creatinine, urea and PSA can be used as an alternative to the serum creatinine, urea and PSA for diagnosis and monitoring of prostate diseases.

***Keywords*:** Creatinine, Urea, PSA, Saliva, Postate diseases

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Serum irisin changes following consumption of fenugreek seed's alcoholic extract in hypertriglyceridemic rats

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***Objective*:** There is a hypothesis that indicates irisin as an adipomyokine, can boosting energy consumption and heat generation via burning fat. The aim of this study was to investigate whether irisin changes following the use of fenugreek seed's alcoholic extract coincide with triglyceride changes?

***Material and Methods*:** In this experimental study, 38 male Wistar rats (180-250g) were divided into five groups: standard control (STC), hypertriglyceridemic control (HTC) and test groups include fenugreek extract200 (FE-200), fenugreek extract400 (FE-400) and gemfibrozil (GEM). The test groups were received doses of 200 mg/kg/day or 400 mg/kg/day of fenugreek seed's alcoholic extract and gemfibrozil at 100 mg/kg/day dose. The first 16 weeks were used to apply the especial model (High Fat-high

Carbohydrate diet for long-term) for inducing hypertriglyceridemia, followed by five weeks treatment with gavage. The lipid profile was measured by spectrophotometry and irisin by ELISA method.

***Results*:** The model we used to induce the hypertriglyceridemia (p=0.000) was significantly successful. Serum triglyceride levels decreased after the treatment (p=0.001); while there were not significant changes in other component of lipid profiles and serum irisin concentration (p=0.197). Moreover, the serum concentration of irisin and triglyceride was not correlated (p=0.693, r=0.071).

***Conclusion*:** The result of this study suggested that, fenugreek seed's alcoholic extract and gemfibrozil significantly reduced serum triglyceride levels. There was no correlation found between the concentration of triglyceride and irisin.

***Keywords*:** Diet, Fenugreek, gemfibrozil, Hypertriglyceridemia, irisin

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ID: 570

Investigation of the effect of Teucrium polium extract on inhibiting fibrillation of hen egg white lysozyme

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***Objective*:** The mistakes in protein folding and their self-accumulation as amyloid deposits are known as the cause of many fatal and disabling disorders, such as Alzheimer's disease, Parkinson's disease, and contagious spongiform encephalopathy. The process of intermolecular interaction in accumulations is complicated and numerous factors affect on it. Restrain of producing protein assemblies can reduce the damage caused, as a result, a variety of work has been done to identify anti-myeloidogenic compounds. In this research, hen egg white lysozyme was used as a protein model and the effect of Teucrium polium extract on inhibiting the fibrillation of this protein was investigated.

***Material and Methods*:** Amyloid accumulation induced in hen egg white lysozyme with protein incubation in acidic ph and 57°C temperature. The effect of Teucrium polium extract on Inhibition of fibrillation using 420 nm THT fluorescence intensity, Congo red spectrophotometer spectrum in the range of 400-700 nm, and observation of fiber morphology by atomic microscope was investigated.

***Results*:** It was observed that Teucrium polium extract has inhibitory effect on fibrillation of this protein.

***Conclusion*:** Due to the inhibitory effect of Teucrium polium extract on fibrillation of lysozyme protein, by separating and purifying the active compounds of the plant, it can be used to prevent and treat amyloid-dependent diseases.

***Keywords*:** Teucrium Polium Extract, Protein Fibrillation, Lysozyme, Amyloidosis

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Combinatorial Effects of Aurapten and X-radiation in Mouse Colon Adenocarcinoma Cells

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***Objective*:** Application of ionizing radiation is a routine approach in cancer treatment. Nevertheless, resistance to radiotherapy, which resulted from the presence of DNA repair systems in cancer cells, is an important obstacle that needs to be overcome. Auraptene (7-geranyloxycoumarin) is a coumarin derivative with valuable biological activities, such as anticancer and chemopreventive effects. To improve efficacy of radiotherapy in animal model of colon adenocarcinoma, we investigated cytotoxicity of X-radiation alone and in combination with auraptene on CT26 cells.

***Material and Methods*:** Cells were treated with non-toxic concentrations of auraptene (10 and 15 µg/ml) for 24, 48 and 72 h, while untreated cells and cells treated with 0.4% DMSO were considered as control groups. Afterwards, irradiation was applied in different doses (2, 4 and 6 Gry) and cells were recovered for 48 h. For quantitative colorimetric assay of cell viability, alamarBlue was used.

***Results*:** Our findings revealed that in combination with control treatments, auraptene (15 µg/ml) increased cytotoxicity of 4 and 6 Gry radiation up to 19% and 22%,

respectively. To evaluate in vitro results, combinatorial effects of auraptene and radiotherapy will be studied in tumour induced animals.

Conclusion: Present findings indicated that auraptene could be used in combination with other therapeutic options against cancer.

Keywords: Auraptene, Radiotherapy, Colon adenocarcinoma, CT26 cells

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The use of natural products to target cancer stem cells Review

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Objective: From wide range of natural products with pharmaceutical effects, the privileged structures of polyphenols, flavonoids and alkaloids let them to influence multiple cellular pathways simultaneously. In case of cancer cells, for instance, such potential is valuable since survival, self-renewal and re-emergence of cancer is due to activity of many different mechanisms. Polyphenols, mostly consist of aromatic benzene rings bonded to hydroxyl groups, negatively affect angiogenesis, proliferation and migration of cancer cells. Well known examples of polyphenol derivatives are resveratrol and curcumin that possess anti-oxidative and chemopreventive effects, as well as apoptosis inducing activity. Flavonoids are major class of polyphenolic secondary metabolites, and their structure includes two phenyl rings and one heterocyclic ring. Quercetin and kaempferol are great examples of flavonoid derivatives that act as angiogenesis inhibitors, apoptosis inducers and inflammation regulators. Alkaloids are compounds with nitrogen and aromatic rings in their structure that beside anti-neoplastic and anti-metastatic effects, could reverse drug resistance of cancer cells. Capsaicin is an alkaloid derivative with the ability to promote separate modes of cell death–autophagy and apoptosis in different cancer cells. Another example is piperine that could induce cell cycle arrest and endoplasmic reticulum stress in malignant cells. Conclusion: It could be concluded that natural products reviewed above are good candidates for designation of novel chemotherapy regimens against cancer, since they interact with various cellular targets, and thus harness cancer cell population via different aspects.

Keywords: Anticancer activity, Polyphenols, Flavonoids, Alkaloids

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Construction, expression, and characterization of 1F5 human-mouse chimeric anti-CD20 monoclonal antibodies

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Objective: Despite the unparalleled success of anti-CD20-targeted immunotherapy, the currently available mAbs are not sufficiently efficacious in the treatment of lymphoma. 1F5 is one of a panel of anti-CD20 mAbs, and it was the first mAb used in the serotherapy of human B-cell lymphoma. Despite the efficacy of murine 1F5 mAbs in the lymphoma patients, the 1F5 chimeric antibodies with human effector functionality are yet to be approved and widely used in the treatment of lymphoma

Material and Methods: MRNAs were extracted from human peripheral blood mononuclear cells (PBMC) and 1F5 hybridoma cells (ATCC HB-9645). The mRNA was reverse transcribed into cDNA. The method for constructing 1F5 chimeric antibody genes involves the following: (1) Primary PCR amplification of VH and VL, and CH and CL genes from 1F5 hybridoma and human PBMC cDNAs, respectively; (2) Joining of the VH and CH, and VL and CL sequences via overlap PCR to create chimeric heavy-chain and chimeric light-chain genes, respectively. Subsequently, a bicistronic expression vector (pBudCE4.1-HC-LC) encoding chimeric antibody heavy-chain and light-chain driven by elongation factor-1α (EF-1α) and cytomegalovirus (CMV) promoters, respectively in the pBudCE4.1 was constructed. CHO-K1 cells were transfected with the plasmid pBudCE4.1-HC-LC and stable clones were selected under Zeocin selective pressure. 1F5 chimeric antibodies were purified by HIS-Select Nickel Affinity chromatography and biological activities were investigated.

Results: In this study, the conversion of 1F5 mAb from mouse IgG2a to human–mouse chimeric IgG1 was achieved. The generated 1F5 chimeric mAbs mediate enhanced complement-dependent cytotoxicityagainst a Burkitt's lymphoma cell line in vitro, and exhibit superior cell growth inhibition activity in vitro, compared to rituximab.

Conclusion: The 1F5 chimeric anti-CD20 mAbs with increased potency in CDC are promising reagents for improved clinical efficacy. Our work contributes to the future studies involving in vivo biological functions and application of 1F5 chimeric antibody.

***Keywords*:** CD20, Chimeric 1F5, Complement-dependent cytotoxicity, Monoclonal antibody
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ID:584

Construction and characterization of monoclonal antibodies against the extracellular domain of B-lymphocyte antigen CD20 using DNA immunization method

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***Objective*:** To date, several new anti-CD20 monoclonal antibodies (mAbs) have been developed for potential efficacies compared with familiar mAb rituximab. Despite the recent advances in development of anti-CD20 mAbs for the treatment of B cell malignancies, the efforts should be continued to develop novel antibodies with improved properties. However, the development of mAbs against CD20 as a multi-transmembrane protein is challenging due to the difficulty of providing a lipid environment that can maintain native epitopes. To overcome this limitation, we describe a simple and efficient DNA immunization strategy for the construction of a novel anti-CD20 mAb with improved anti-tumour properties.

***Material and Methods*:** Using a DNA immunization strategy that includes intradermal (i.d.) immunization with naked plasmid DNA encoding the CD20 gene, we generated the hybridoma cell line D4, which secretes functional mAbs against an extracellular epitope of CD20. Binding specificity was examined by immunocytochemistry analysis and a cell-based enzyme-linked immunosorbent assay using a Burkitt's lymphoma cell line. Moreover, the binding specificity of D4 mAbs was determined by western blot analysis. Cell proliferation was examined by the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay. Apoptosis was detected by the annexin V/propidium iodide staining and dye exclusion assay.

***Results*:** Immunocytochemistry analysis and a cell-based enzyme-linked immunosorbent assay showed that D4 mAbs are capable of binding to native extracellular epitopes of CD20. The results showed that D4 anti-CD20 mAbs produced by DNA immunization exhibit potent growth inhibitory activity and have superior direct B-cell cytotoxicity compared to rituximab.

***Conclusion*:** Taken together, the data reported here open the path to DNA-based immunization for generating pharmacologically active monoclonal antibodies against CD20. In addition, the data support future in vivo animal testing and subsequent procedures to produce a potential therapeutic mAb.

***Keywords*:** Apoptosis, CD20, DNA immunization, Monoclonal antibody, Proliferation
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ID:585

Adsorbtion of leflunomide upon multiwall carbon nanotube: anti-cancer effect investigation upon Hela cell line and differentiation induction of mesenchymal stem cells evaluation

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***Objective*:** Leflunomide [HWA 486 or RS-34821, 5-methyl-N-(4trifluoromethylphenyl)-4-isoxazole carboximide] is an immunosuppressive agent effective in the treatment of rheumatoid arthritis. Many attempts have been carried out to design and synthesize new targeted biocompatible compounds with a high capacity for loading and controlled release of desired drug molecules which show minimum leak of drug molecules before reaching to the target organ and studying their activities for combating human diseases.

***Material and Methods*:** After functionalization of multi wall carbon nanotube (MWCNT), the drug loading content of the nanocarrier was computed by, loading content= M0-Mt /MN × 100 %, Where, M0 and Mt are the amounts of leflunomide in primary and filtered solutions, respectively. MN is the amount of functional MWCNT used in the loading process. Anti-cancer effect and differentiation of mesenchymal stem cells into neural level evaluation was performed with MTT Assay and real time PCR respectively.

***Results*:** After loading of leflunomide on MWCNT, the nanocarrier were washed and the scoured test was further analysed by XRD, TEM and SEM. The effect of the drug in free and connected to nanocarrier forms on Hela cell line cytotoxicity was examined. Death rate of cancer cells is related to dose and adjacent time. The MWCNT-leflonomide can have a somewhat increased effect and induce the stimulating of differentiation induction of mesenchymal cells into Nerve cells. In this thesis, this effect was investigated by measuring the increase of Nestin and nurofilament gene expression.

***Conclusion*:** Functional MWCNT involve relatively large surface area; which enable them as potential carriers in drug delivery with multiple practical applications in medicine and biology.

***Keywords*:** Leflunomide, MWCNT, Anti cancer effect

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Effect of crocin carotenoid on BDNF and CREB gene expression in brain VTA of morphine treated rats

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Objective: It has been demonstrated that morphine dependence could reduce the CREB gene expression and serum level of BDNF. The BDNF and CREB are essential for regulation of neural cells proper functions. The main objective of this study was to investigate the effect of crocin carotenoid on BNDF and CREB gene expression in brain VTA (ventral tegmental area) and the serum level of BDNF in morphine treated rats in comparison to control.

Material and Methods: In this study, 40 male wistar rats (200-250g) were used in 5 experimental groups: 1) Non morphine treat rats (control) 2) non morphine treated rats 25mg/kg crocin carotenoid (i.p., for 21 days) 3) morphine treated rats (10 mg/kg twice a day, s.c., 21 days) 4 and 5) morphine treated rats + 12.5 and 25mg/kg crocin carotenoid. At the end study, BDNF and CREB expression were determined by real-time-PCR method. ELISA analysis was also applied for evaluating the serum BDNF level.

Results: the data revealed that, morphine tratment could cause significant reduction in brain VTA BDNF and CREB gene expression as well as serum level of BDNF compared to control group. Treatment with 25mg/kg crocin caused significant increase in BDNF and CREF gene expression and serum level of BDNF in morphine treated rats compared to morphine treated group.

Conclusion: According to obtained results, crocin carotenoid could prevent unfavorable effects of morphine on neural system to some extent through increasing BDNF and CREB gene expression in VTA and serum level of BDNF

Keywords: Morphine, BDNF, CREB, Crocin, VTA

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Hepatoprotective and Antioxidant Activity of Quercetin on Hepatic Cholestasis Induced by Bile Duct Ligation in Rats

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***Objective*:** Quercetin is a flavonoid with antifibrotic, and hepatoprotective properties. The current study was to evaluate effects of quercetin on oxidative stress markers in bile duct ligation (BDL)-induced liver fibrosis in rats.

***Material and Methods*:** The male Wistar rats divided into three groups including SC (sham control), BDL (Bile duct ligation surgery) and BDL+Quercetin (administration of 50 mg/kg per day by intraperitoneally). Ten days later the rats were sacrificed, the blood was collected for liver enzymes determination and the liver was separated for the measurement of oxidative stress markers and hematoxylin and eosin staining, respectively.

***Results*:** The application of BDL clearly increased the malondialdehyde (MDA) levels and decreased the glutathione peroxidase (GPX) activity. Quercetin treatment significantly decreased the elevated tissue MDA levels and increased the reduced GPX enzyme activity in the liver tissue ($P<0.05$). Another interesting finding was that the protein carbonyl groups were decreased in quercetin-treated BDL rats compared to BDL rats ($P<0.05$). Histopathological studies further confirmed the protective effects of quercetin on cholestasis-induced hepatic injury in rats.

***Conclusion*:** Quercetin treatment might be beneficial in cholestasis-induced

hepatotoxicity through increasing GPX activity and decreasing lipid and protein oxidation.

***Keywords*:** Oxidative stress, Cholestasis, Quercetin, Antioxidant

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Cytogenetic Abnormalities with Interphase FISH Method and Clinical Manifestation in Chronic Lymphocytic Leukemia Patients in North-East of Iran

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***Objective*:** Chronic lymphocytic leukemia (CLL) is one of the most prevalent adult leukemias. This malignancy is known by lymphocytosis for a duration of more than 3 months. In fact, it is a heterogeneous clinical disease with changeable progression. Chromosomal aberrations are significant parameters to predict result and survival rate and find treatment strategies for each patient. Cytogenetic methods are known as sensitive and relatively new procedures to detect abnormalities in genome.

***Material and Methods*:** In order to identify CLL-related chromosomal abnormalities, 48 CLL patients included 38 Men and 10 Women with mean age of 58.25±36 were enrolled in this case series study. The survey was done at Cancer Molecular Pathology Research Center, Mashhad University of Medical Sciences. Interphase fluorescent in situ hybridization (I-FISH) was done on unstimulated peripheral blood or bone marrow samples, which were cultured in whole medium culture; it was used to detect chromosomal abnormalities such as 11q, 13q14, 17p, 6q and trisomy 12 in CLL patients.

***Results*:** Analysis demonstrated that 45.5% of CLL cases had chromosomal abnormalities; 13.63% had del 17p, 40.90% had del 13q14 and 9.09% had del 11q. Statistical analysis of data revealed a significant relevancy between age variable and splenomegaly occurrence (P value<0.05). The younger the patients were, the less the splenmegaly occurrence.

***Conclusion*:** Laboratory findings were correlated with clinical data.

***Keywords*:** Chromosomal aberration, Chronic lymphocytic leukemia (CLL), Interphase FISH (I-FISH), Polymerase chain reaction (PCR)

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Thrombosis and thromboembolism risk factors in HIV positive individuals in Southern Iran

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***Objective*:** The reported incidence of venous thromboembolism (VTE) in patients with human immunodeficiency virus (HIV) infection has ranged from 0.25 to 0.96% in clinical studies, and up to 17% at autopsy. Among HIV positive patients there are several factors that may lead to thromboembolism, it means that many of factors are contributing to increasing the risk of thromboembolism. The present study was performed to find the reasons and risk factors of VTE among HIV patients.

***Material and Methods*:** This cross-sectional study analyzed a total of 100 HIV serology positive patient between 2015 to 2017 in behavioral disease consoling center in Shiraz, Southern Iran. First, based on enzyme-linked immune sorbent assay (ELISA) patients were identified, then confirmation was obtained by western blot and PCR methods. From all participants, a total of 10 ml blood sample was collected, then using a centrifuge 3000 rpm for 10 min, serum and plasma was separated from the cell. CD4 was assessed using standard Cy flow counter (partec), HIV viral load was assessed with Qia gene and hematologic parameters determined using IL –AC9000 with the hemophile kit.

***Results*:** Our data shown a higher prevalence of VTE in patients under age 50 who are HIV-positive compared to those who are HIV-negative. Also, there was a statistically significant association between the stage of AIDS (P=0.002), low CD4+ cell count (P=0.001), using HAART treatment regimen (P=0.03), smoking (P=0.01) and drug injection (P=0.001) with higher risk of VTE.

***Conclusion*:** Currently available epidemiological evidence suggests that chronic HIV infection is associated with a two to 10-fold increased risk of VTE in comparison with a general. Some risk factors demonstrated a strongest association with VTE such as stage of AIDS, low CD4+ cell count especially in the

presence of clinical AIDS, protein S deficiency, and protein C deficiency.

***Keywords*:** Venous thromboembolism (VTE), HIV/AIDS, Risk factors, ELISA, PCR

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Nanostructured Lipid Carriers (NLCs) enhance Letrozol Efficacy in MCF-7 Breast Cancer Cells

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***Objective*:** Side effects of anti-cancer agents and resistance to treatment is an obstacle in cancer chemotherapy and novel delivery systems, like NLC, can diminish these problems. In this study we formulated Letrozol (LTZ)–aromatase blockage used in treatment of breast cancer in NLCs to enhance efficacy and diminish harmful effects of LTZ.

***Material and Methods*:** We prepared NLC formulation with dissolving LTZ in Miglyol and adding into compritol. Then poloxamer 4% as surfactant was added under homogenization. After sonication, this hot nano-emulsion was cold down. The average size of LTZ-loaded NLCs was measured with particle size analyzer. We used scanning electron microscope to investigate morphology of particles. In order to cytotoxicity study, MTT assay was done. The flow-cytometry was used to determination of apoptotic cells and cell cycle analysis.

***Results*:** The size distribution of NLC formulations was 60 to 135 nm with a poly dispersity index (PDI) of 0.165. IC50 value for LTZ was 2.2±0.2 µM. LTZ-loaded NLCs suppressed proliferation of MCF-7 cells more effectively than LTZ alone(p<;0.05). There were no differences between cells incubated with NLCs alone and control cells which demonstrated biocompatibility and low cytotoxicity of carriers. Our results showed that LTZ-loaded NLCs increased cells in apoptotic phase 42±3.45 %(p<0.05). Exposed cells with LTZ-loaded NLCs led to accumulation of them in subG1 phase up to 13±3.2%. Treatment of cells with LTZ-NLCs caused 30±2.8% apoptosis and 34±0.7% G2/M arrest.

***Conclusion*:** The use of LTZ as an anti cancer drug along with NLC, new generation of lipid-based drug delivery system, improved the sensitization of cancer cells to this chemotherapy agent.

***Keywords*:** Apoptosis, Nano structured lipid carrier, Letrozol

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Sonic hedgehog pathway suppression and reactivation accelerates differentiation of rat adipose-derived mesenchymal stromal cells toward insulin-producing cells

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Objective: Sonic hedgehog (Shh) is an intercellular signaling molecule that regulates pancreas development in mammals. Manipulation of Shh signaling pathway can be used as reliable approach to improve the generation of functional insulinproducing cells (IPCs) from mesenchymal stromal cells (MSCs).

Material and Methods: In the present study, a novel differentiation protocol was used to produce IPCs from adipose tissue–derived MSCs (ATDMSCs) based on sequential inhibition and reactivation of Shh pathway. ATDMSCs were differentiated into IPCs via a 14-day basic protocol using 1% insulin transferrin selenium (ITS) and 1% nicotinamide in Dulbecco's Modified Eagle's Medium medium. A mixture of 0.25 mol/L cyclopamine + 64 ng/mL basic fibroblast growth factor at day 3 of differentiation and 150 ng/mL recombinant Shh at day 11 of differentiation were used, respectively, to promote sequential inhibition and reactivation of Shh pathway. Insulin granule formation, glucose-stimulated insulin secretion and gene expression pattern related to the pancreatic endocrine development and function were analyzed in manipulated and unmanipulated IPCs.

Results: IPCs obtained after Shh manipulation secreted higher amounts of insulin in vitro. This phenotype was accompanied by increased expression of both genes critical for β-cell function and transcription factors associated with their mature phenotype including Pdx1, MafA, Nkx2.2, Nkx6.1, Ngn3, Isl1 and insulin at day 14 of differentiation.

Conclusion: Our findings indicated that the early inhibition and late reactivation of Shh signaling pathway during the differentiation of ATDMSCs improved the functional properties of IPCs, a novel method that could be considered as an alternative approach for cell-based therapy for type 1 diabetes.

Keywords: adipose tissue–derived mesenchymal stromal cells, insulin-producing cells, sonic hedgehog manipulation

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Protective effect of Pomegranate Peel Extract on Renal Ischemia Reperfusion Injury in mice

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Objective: ROS are recognized as the most important involved mechanisms in pathogenesis of renal ischemia reperfusion injury. So, antioxidant therapy is proposed as a beneficial solution for treatment of ischemia-reperfusion (IR) injury. Punica granatum which known as pomegranate is a native plant pf Iran with various antioxidant properties. Therefore, we decided to evaluate the protective effect of Pomegranate peel extract on renal ischemia reperfusion injury in rats.

Material and Methods: Forty male Sprague-dawley rats (200-250 g) were randomly divided into 5 groups as follow: control group, IR + water group, sham group (only received pomegranate peel extract), pomegranate peel extract and IR + 100 mg/kg pomegranate peel extract. After that, the rats were treated for two weeks. Then, both renal arteries were obstructed for 45 minutes and subsequently 24 hours of reperfusion. Antioxidant enzymes activity of kidney including catalase, glutathione peroxidase and glutathione level were measured biochemically. The results were analyzed by using Mann-Withney test and SPSS software.

Results: Catalase and glutathione peroxidase activities glutathione level was decreased significantly in IR + water group in comparison with control and sham group. Increased activity of catalase and glutathione peroxidase and glutathione level were observed in pre-treated groups with pomegranate peel extract.

Conclusion: 14 days pre-treatment with pomegranate peel extract decreased renal ischemia reperfusion injury through increased activity of renal antioxidant enzymes such as catalase, glutathione peroxidase and glutathione activities. Therefore, herbal medicines can be utilized as suitable choice for the ischemia reperfusion injury.

Keywords: Renal, Ischemia-Reperfusion, Pomegranate Peel extract, kidney, rat

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ID:613

Investigation of presence norA gene in clinical isolates of staphylococcus aureus

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Objective: Staphylococcus aureus is one of the most important causes of hospital opportunistic infections around the world. One of the mechanisms of Staphylococcus aureus resistance to antibiotics, including ciprofloxacin, is the existence of anthropometric pumps such as norA. The aim of this study was to evaluate the antibiotic resistance pattern and to investigate the presence of Effluxe norA pumps in strains of Staphylococcus aureus strains isolated from the reference laboratory of Kermanshah.

Material and Methods: In this study 100 clinical isolates of Staphylococcus aureus were collected from the referral laboratory Kermanshah. All of 100 Staphylococcus aureus were detected after biochemical tests and identification of the isolates. DNA extraction was performed by lysostaphin and identification of norA gene was performed by PCR method.

Results: Of the patients with Staphylococcus aureus, 55 were male (55%) and 45 were female (45%). Of 100 isolates, PCR results showed that norA gene was present in 40 isolates (40%).

Conclusion: In this study, the prevalence of the study gene is higher than other studies, which can be due to the prevalence of recent years in the country.

Keywords: Staphylococcus aureus, antibiotic resistance, norA, PCR

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Study of the prevalence of norB gene in Staphylococcus aureus strains isolated from the reference aboratory of Kermanshah

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Objective: Staphylococcus aureus is a positive cocci that is found everywhere. It is colonized in humans and domestic livestock and is considered an opportunistic pathogen. Staphylococcus aureus is one of the most important causes of acquired hospital infections. The aim of this study was to presence of Effluxe norB pumps in strains of Staphylococcus aureus.

Material and Methods: In the present research 100 clinical isolates of Staphylococcus aureus were collected from the referral laboratory Kermanshah. All of 100 Staphylococcus aureus were detected after biochemical tests and identification of the

isolates. DNA extraction was performed by lysostaphin and identification of norB gene was performed by PCR Technique.

Results: Of the patients with Staphylococcus aureus, 55 were male (55%) and 45 were female (45%). Of 100 isolates, PCR results showed that norB gene was present in 28 isolates (28%).

Conclusion: As shown in the results of this study, the prevalence of norB gene is relatively high, which can be due to the increased use of antibiotics in recent years in the country

Keywords: Staphylococcus aureus, Effluxe pumps, norB, PCR Technique

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ID:616

Characterization of a wound dressing mat composed of polycaprolactone(PCL) and silversufadiazine(SSD)

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Objective: Due to effective applications of nanoscale methods in a variety of medicine fields, this study focused on designing and fabricat a polymeric nanofibrous mat for wound dressing. Evaluation of PCL nanofibrous mat containing silversulfadiazine(SSD) in vitro was applied.

Material and Methods: A PCL/SSD mat was fabricated by using electrospinning. The electrospun nanofibers were characterized by field emmision scanning electron microscopy (FE-SEM), differential scanning calorimetric(DSC), contact angle, and Energy-dispersive X-ray spectroscopy(EDX). Cytotoxicity studies performed to examine the effects of SSD on cultured cells with MTT analysis. Antibacterial activity of PCL/SSD mat were examined with Staphylococcus aureus (ATCC29213), and Pseudomonas aeruginosa(ATCC27853). Presences of inhibition zone around nanofibrous mat containing SSD showed antibacterial activity due to the presence of Ag in SSD.

Results: The PCL/SSD nanofibrous mat showed applicable characteristics as a wound dressing.

Conclusion: This nanofibrous mat could be an ideal biomaterial for wound dressing applications in future.

Keywords: Polycaprolactone, Silver-sulfadiazine, Electrospining, Tissue engineering

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ID: 626

Investigating the effect of ice water on liver enzymes in serum of rats

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Objective: According to Persian medicine resources, ice water causes the functional damage of the liver. Therefore, we designed a study to measure the alanine amino transferase (ALT) and aspartate amino transferase (AST) enzymes in serum of rats.

Material and Methods: In this experimental study, 12 adult male Wistar rats weighting 220-200 g were used. The rats were divided into 2 equal groups including, control and experimental groups. The control and experimental groups respectively received normal water (20°C) and ice water (4°C) for 8 days. At the end of the eighth week, blood was taken from the heart of animals. After separating the serum, concentration of ALT and AST were measured by biochemical kits. Data were evaluated by Student's t-test.

Results: Results showed that ice water significantly increased the levels of ALT and AST levels in experimental group ALT (U/L):231.2 ±16 and AST (U/L):73±2.2 compared to control group ALT (U/L): 172.8±11.7 and AST (U/L): 61.8±1.4 ($P<0.05$).

Conclusion: Ice water increase serum ALT and AST, so probably can change the pattern of liver activity. Which can cause liver disease in the long-term. Although more studies are needed.

Keywords: ice water, liver enzymes, serum

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ID:628

Study of effects of novel synthetic acridine derivatives on acetylcholinesterase enzyme activity

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Objective: Alzheimer's disease (AD) is the most common age-related neurodegenerative disease causing neurological and cognitive disorders and finally leading to death. According to the cholinergic hypothesis of AD pathogenesis, the clinical features of the disease are attributed to the reduction of

acetylcholine synthesis, a neurotransmitter involved in the memory and learning process. Therefore using acetylcholinesterase inhibitors is one of the major therapeutic strategies for relative improvement of AD symptoms. Today, worldwide research is being conducted to find more powerful new drugs with fewer side effects for Alzheimer's. In the present study the effect of eight novel synthetic acridine derivatives on the inhibition of acetylcholinesterase activity has been assessed.

Material and Methods: The activity of acetylcholinesterase enzyme was measured using Ellman's method at different concentrations of substrate, then the enzyme activity plot was drawn and Km and Vmax parameters were determined. At the next step, at constant concentration of substrate, the enzyme activity was measured in the presence of various concentrations of acridine derivatives and neostigmine (a well-known acetylcholinesterase inhibitor) and then the half maximal inhibitory concentration (IC50) of each compound was calculated.

Results: Comparing the IC50 values of acridine derivatives with neostigmine IC50 showed all eight acridine compounds have the ability to inhibit the acetylcholinesterase activity, but one of them is a powerful inhibitor of the enzyme.

Conclusion: These novel synthetic acridine derivatives can inhibit the acetylcholinesterase activity and one of the compounds has a potential to use as a drug to treat Alzheimer's disease. It is clear that additional studies should be conducted on this compound to give a definite opinion.

Keywords: Alzheimer's disease, Cholinergic hypothesis, Acetylcholine, Acetylcholinesterase inhibitor, Acridine derivative

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ID:635

Evaluation of BAALC gene expression in normal cytogenetic acute myeloid leukemia patients in north-east of Iran

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Objective: Acute myeloid leukemia (AML) is known as one of the most common leukemia among adults. Environmental and different genetic factors affect disease process, prognosis and treatment. Among different genetic factors NPM1, FLT3, MLL and BAALC genes are the most effective on patient's survival rate. The aim of this study was to assess amount of BAALC gene expression in AML patients, and its relation to survival rate.

Material and Methods: In this case-control study, from all 94 individuals referred to Ghaem Medical Center during 2012-2015, 47 cases were normal cytogenetic AML and others were healthy individuals that were studied as control group. Real-time PCR method was applied for gene expression evaluation. Other information of patients was extracted from medical documents. SPSS v.21 was used for data processing.

Results: Mean age of studied cases was 31.50 years. The most of BAALC gene expression was seen in M1 and M2 subtypes, and the less was in M5. A significant relation was found between amount of gene expression and patient's survival rate.

Conclusion: BAALC gene expression was increased significantly in AML cases. BAALC expression had reverse relation with patients' survival rate in North-East of Iran.

Keywords: Acute myeloid leukemia, Survival rate, Prognosisampus

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ID:637

Association of high expression levels of SOX2, NANOG and OCT4 in gastric cancer tumor tissues with progression and poor prognosis

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Objective: Expression of the essential regulator genes, SOX2, NANOG and OCT4, so called as stemness factors, are prerequisite for the tumorigenic capability of cancer stem cells (CSC) and their potential role in the formation and progression of various human cancers. This study explored the expression and prognostic effect of these genes in gastric cancer patients by a quantitative real-time PCR (qRT-PCR) approach.

Material and Methods: In this study, the expression levels of SOX2, NANOG and OCT4 were quantified by a qRT-PCR method in 100 gastric cancer tumor tissues versus the paired adjacent normal tissues. Then, the relationship between the expression of the three genes in gastric cancer tumor tissues and the clinicopathological characteristics and overall survival of patients were investigated.

Results: Higher expression levels of SOX2, NANOG and OCT4 were found in gastric cancer tumor tissues compared with those in paired adjacent normal tissues (P=0.000). Overexpression of the mentioned genes in gastric cancer tumor tissues
as resolved to be significantly associated with tumor size (P<.05), TNM stage (P=0.001), tumor grade (P<0.01) and shortened overall survival time (P=0.0001).

Conclusion: These findings indicted that the stemness factors SOX2, NANOG and OCT4 are significantly overexpressed in gastric cancer and may serve as potential biomarkers of gastric cancer progression and prognosis.

Keywords: Gastric cancer, SOX2, NANOG, OCT4, Tumor tissue

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ID:641

Purification and Characterization of Cellulase from Caspian Sea Gammarous

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Objective: In recent years the interest in cellulases has increased due to the many potential applications for these enzymes in various industries including textile, laundry, food, pulp and paper industry. So, significant attentions have been devoted to the different organism for purification of cellulases with different properties. For this purpose, cellulase was purified from Caspian Sea Gammarous and its activity were determined using carboxymethyl cellulose (CMC) as a substrate.

Material and Methods: A portion of Gammarous hemoganate was concentrated by precipitation with ammonium sulfate at 60% and 90% saturation. Then, the fraction percipiteted with 60% of ammonium sulfate were applied to DEAE Sepharose columns, equilibrated with 50 mM tris buffer, pH 8 and eluting by same buffer with a salt gradient.

Results: Cellulase was purified 3.53 fold with specific activity of 90 U/mg in comparison to crude enzyme extract using ammonium sulfate precipitation. With the analysis of SDS–PAGE, the molecular weight of the purified cellulase was estimated to be 54 kDa.

Conclusion: It is concluded that this enzyme has great potential for use in cellulose biodegradation technologies.

Keywords: Gammarous; Gammarous; Cellulase; Purification; DEAE Sepharose columns

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ID:643

SOX2OT stable knock down enhances chemo-toxicity to Cytarabine in cancer cells

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Objective: SOX2 Overlapping transcript (SOX2OT) is a long non-coding RNA overexpressed in tumor tissues. SOX2OT encompasses SOX2 gene, master regulator of stemness and both are transcribed in same direction. Since the discovery of SOX2OT in 2003, its function has been studied in different contexts of stem cell biology and carcinogenesis; however, its mechanism of action is not clearly defined yet. Regarding the overexpression of SOX2OT in tumors of different origins (Breast, Lung and liver) and the previously reported function of SOX2 in drug resistance, here we aimed to explore the chemo-toxicity of two common nucleoside analogues (Cytarabine and 5-fluorouracil) in SOX2OT knocked down cancer cells of Glioblastoma (U87-MG) and teratocarcinoma (NTERA-2).

Material and Methods: U87-MG and Ntera-2 cancer cell lines were transduced with SOX2OT-shRNA or control-shRNA expressing lentivirus and the stable cells were selected by puromycin marker. The derived cells: SNT2, LNT2, SU87 and LU87 were treated with different concentrations of Cytarabine and 5-fluorouracil for 48 hours in complete culture medium. The NT2 (NTERA-2) and U87-MG cells were also treated as controls. The cell viability was measured with MTT assay. The results were analyzed with GraphPad Prism v.7 software.

Results: Cell viability of SNT2 cells treated with Cytarabine at different concentrations was significantly lower than NT2 cells (p value<0.001, ~36% decline in 0.8 µg/ml); however, chemo toxicity in U87-MG cells was achieved at higher drug concentrations with less significant difference between SOX2OT knocked down cells and control (p value<0.01, ~15% decline in 1.2 µg/ml). Similarly, 5-flurouracil treatment killed SOX2OT knocked down cells less efficiently in comparison to control (U87-MG: p value<0.01, ~10% increased viability in 5 µg/ml and NT2: p value>0.05, ~5% increased viability in 1 µg/ml).

Conclusion: Our findings suggests that SOX2OT knockdown can potentially improve the Cytarabine chemotherapy outcome in brain and teratocarcinoma cancer cell lines.

Keywords: SOX2OT, Cytarabine, 5-fluorouracil, Cell viability

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ID:648

Relationship of tissue DNA lesion (8-OHdG) with serum antioxidant activity in Iranian patients diagnosed with high-grade oral squamous cell carcinoma

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***Objective*:** Oral squamous cell carcinoma (OSCC) is strongly associated with oxidative damage and oxidative stress. Tobacco and alcohol consumption are important etiological factors for this cancer and sources of reactive oxygen species (ROS). The extent of oxidative DNA damage could be related with antioxidant factors. In this study, changes in serum total antioxidant status was determined in relation to DNA lesion (8-OHdG) levels in tumor biopsies from Iranian patients diagnosed with OSCC.

Material and Methods: Samples from patients (n=40) comprising of 80% pathologically well differentiated and moderately differentiated and 20% poorly differentiate tumors were collected Blood samples and gingival biopsies (n=35) from normal individuals were also processed and considered as control. Plasma total antioxidant capacity (TAC) was estimated using FRAP assay. Tissue biopsies were processed for DNA samples were isolated for estimation of 8-OHdG levels using ELISA.

***Results*:** Results showed that the plasma TAC in OSCC patients was significantly depleted (~25%; P<0.05) compared to normal individuals. The 8-OHdG formation in DNA showed that in DNA isolated from tumors was increased (4-5 folds; P=0.03) compared to normal samples. A significant decline in plasma TAC in one-third of OSCC patients was well correlated with DNA damage factor.

***Conclusion*:** Overall results suggest that oxidative DNA damage is an important index of OSCC (r=0.8; P=0.001). Attenuation of TAC in these patients clearly show the protective role antioxidant factors in DNA damage-repair system and causation of OSCC

***Keywords*:** DNA damage, Antioxidant factors, Oral squamous cell carcinoma(scc), Tissue DNA lesion (8-OHdG)

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ID:656

A meta-analysis of circulating visfatin levels and cancer risk

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Objective: Lack of specific biomarkers is one of the main challenges in early detection of cancers. Aberrant expression of visfatin as a pro-inflammatory adipocytokine, has been reported to associate with risk of many types of cancers. However, epidemiological studies are controversial. Some studies showed that increased visfatin levels were associated with cancer risk. Therefore, we performed a meta-analysis to assess the association between circulating visfatin levels and cancer risk.

Material and Methods: An electronic literature search of Medline, EMBASE, Scopus, and Cochrane Library was conducted to identify all relevant studies involving circulating visfatin and malignancies up to March 2018. Data related to Standard mean differences (SMDs) with 95% confidence intervals (95% CIs) were collected and pooled using a random-effect model. Egger's linear regression test were conducted to examine the risk of publication bias.

Results: The analysis included twenty seven studies with 2693 cases and 3040 healthy controls that met the study criteria and described the relationship between circulating visfatin levels and cancer risk. A total of 27 studies were included in meta-analysis for pooling SMD analysis. The results of the meta-analysis showed a significant higher visfatin levels in patients with various cancers, with a pooled SMD of 0.88 ug/ml, (95% CI=0.56-1.20, P=0.000). Further, subgroup, meta-regression, and sensitivity analysis also did not change the obtained results. No evidence of publication bias was also observed for pooling SMD analysis.

Conclusion: This meta-results collectively suggest that high circulating visfatin levels are associated with a higher risk of various cancers. However, further well designed studies are needed to confirm the role of visfatin as a potential biomarker for early detection of cancers.

Keywords: visfatin, Cancer, circulating level, Meta-analysis
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ID:657

Tumor derived exosomes over expressed Let-7i could promote Dendritic cell maturation

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Objective: Exosomes are nano-vesicles which are released by any kind of cells such as immune cells and tumor cells. They are known by their immune suppression effects as well as initiation mediators in cancer progression and metastasis. Although TEX contains inhibitory molecules leading to decrease the cytotoxicity and promote to regulatory microenvironment, they consist of tumor antigens to induce immunity against tumor cells. The aim of this study is using manipulated TEX with miR-155, miR-142 and let-7i as immune stimulators and evaluate their effects on dendritic cell maturation.

Material and Methods: Mouse mammalian breast cancer cell line; 4T1, was cultured. Differential ultracentrifugation was used for isolation and purification of exosome population from exosome free medium. Bone marrow derived DC was differentiated from bone marrow progenitors and miRNAs electroporated exosomes were used for DC maturation. The expression level of target miRNA was determined.

Results: Morphology, size distribution and protein expression of exosomes: We isolated nano-vesicles with spheroid morphology using electron microscopy and dynamic light scattering. Isolated exosomes were positive for CD81, CD63 and TSG101 as exosome markers using western blotting and flow cytometry. DC differentiation and maturation: Dendritic cells were generated from mouse bone marrow using IL-4 and GM-CSF cytokines. Immature DCs were incubated with LPS, tumor exosomes and manipulated tumor exosomes as control positive, control negative and test groups respectively. MHCII, CD80 and CD40 as maturation markers were assessed by flow cytometry. Upregulation of miRNAs was confirmed in exosomes and mature dendritic cells.

Conclusion: We found that Let-7i could efficiently increase DC maturation status also miR-155 and miR-142 have enhancing effect on DC maturation. The manipulated TEX would be a hopeful cell-free vaccine for cancer treatment.

Keywords: Tumor derived exosome, miRNA, manipulate, Dendritic cell

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ID:658

Urine Metabolomics Profile Revealed Molecular Signature of Steroid Resistance in Focal Segmental Glomerulosclerosis: A Pilot Study

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Objective: Focal segmental glomerulosclerosis (FSGS) is considered as one of the most severe glomerular diseases and around 80% of cases are resistant to steroid treatment. Since a large proportion of steroid resistant FSGS patients progress to end-stage renal disease (ESRD), and this population may benefit from treatment with other therapeutical strategies before ESRD, identification of non-invasive biomarkers to predict these high risk population is needed. The current work aimed to identify the non-invasive candidate predictive biomarkers to distinguish steroid resistant FSGS patients using metabolomics approach. The important pathways impaired in non-responder patients and identification the possible molecular mechanism of resistance was the alternative aim.

Material and Methods: Urine was collected from more than 50 biopsy proven patients diagnosed with idiopathic FSGS at Shahid Labbafinejad Hospital Medical Center. After evaluation the patients, only 17 FSGS patients were recognized eligible for monotherapy with steroid drug. These patients were treated with prednisolone (1 mg/kg) and followed for 6-8 weeks. Ten and seven patients was categorized s steroid sensitive and steroid resistant respectively based on the level of 24h protein excretion. Metabolomic profile of urine samples were analyzed by one dimensional 1H-nuclear magnetic resonance (1H-NMR). The predictive candidates and their diagnostic

importance were determined using statistical analysis. The impaired molecular pathways in resistant patients were identified using pathway analysis and the common target molecules and functional classes between candidates and prednisolone were predicted using bioinformatics analysis.

Results: Homovanillic acid, 4-methylcatechol and tyrosine were suggested as the significant ($P<0.05$) predictive biomarker candidates while L-3,4-dihydroxyphenylalanine (L-DOPA), norepinephrine and gentisic acid had high accuracy (AUC>0.78) as well. Tyrosine metabolism was the most important pathway that is perturbed in steroid resistant FSGS patients and molecules contributed in apoptosis were the common target of action of candidates and prednisolone.

Conclusion: Our findings demonstrate that metabolomic approach is a valuable technique in biomarker discovery platform and, urine metabolites including homovanillic acid and tyrosine may serve as potential non-invasive predictive biomarkers for evaluation the responsiveness of FSGS patients to steroid therapy. Furthermore, tyrosine metabolism as well as apoptosis pathways are the target of regulations in the future validation studies.

Keywords: Focal segmental glomerulosclerosis, predictive biomarker, prednisolone, steroid resistant, steroid sensitive

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ID:659

Decreased Na^+/K^+-ATPase activity and altered susceptibility to peroxidation and lipid composition in the erythrocytes of metabolic syndrome patients with coronary artery disease

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Objective: The increased generation of reactive oxygen species that occurs in the condition of metabolic syndrome (MetS) may be responsible for the increased oxidative injury to erythrocyte membranes in coronary artery disease (CAD). Therefore, we have looked into the effects of MetS on both indexes of oxidative damage and biochemical properties of erythrocyte membranes in CAD patients.

Material and Methods: We analyzed markers of oxidative stress, Na^+/K^+-ATPase activity, and the total cholesterol content (CEM) and fatty acid compositions of the erythrocyte membrane in 82 patients with stable CAD and 39 non-CAD subjects. The fatty acid composition of the erythrocytes membrane was determined by gas chromatography-mass spectrometry. Lipid peroxides in plasma and membrane samples were measured by a flourimetric method. Plasma total antioxidant status, erythrocyte superoxide dismutase (SOD) activity, Na^+/K^+-ATPase activity and CEM were measured by spectrophotometric methods.

Results: The CAD patients had higher levels of CEM, membrane lipid peroxidation, erythrocytes SOD activity and Na^+/K^+-ATPase activity compared with non-CAD subjects. The Na^+/K^+-ATPase activity was correlated negatively with membrane lipid peroxidation, and positively with the CEM. In CAD patients with MetS compared with those without MetS, we found that the membrane lipid peroxidation and CEM were increased, whereas the n-3 fatty acids content, SOD activity, Na^+/K^+-ATPase activity were decreased.

Conclusion: These findings suggest an impairment of erythrocyte membrane biochemical properties in stable CAD patients as consequence of oxidative injury that may contribute to the development of CAD. In ddition, MetS may be related to increased oxidative injury to erythrocyte membranes.

Keywords: Coronary artery disease, Metabolic syndrome, Erythrocyte membrane, Oxidative stress, Na^+/K^+-ATPase activity

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ID:672

A DFT study of synthetic drugs aminophosphonates: HOMO, LUMO

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Objective: Molecular modeling, consists of a set of features and visualization software, construction, editing and analysis of molecules providing as the basis of pharmacological planning; characterization of such a structure, their bond distances and their angles dihedral is not so simple to perform on a trial basis ,if necessary, then use methods in silico for the characterization may, by theoretical calculations based on quantum physics that optimize the geometric structure, until it reaches its most stable conformation, but also can indicate some very important indexes for the design of new drugs such as energies of HOMO orbital border (Highest Occupied Molecular orbital) and LUMO (Lowest Unoccupied Molecular orbital), minimum otential energy, dipole moment and the specific layout of each atom in the molecule.

Material and Methods: All calculations were performed in the framework of DFT with the Lee-YangParr correlation functional (B3LYP) computational level, using the 6-31G basis set for the ground state optimization. The frontier

molecular orbital's and the HOMO e LUMO energy gap has been computed.

Results: Referring back to Table, it can be seen that tetramethyl ((1,4 phenylenebis(azanediyl))bis((4-methoxyphenyl)methylene))bis(phosphonate) is the most reactivity, among the four drug.

Conclusion: The chemical hardness (ɳ) is useful in studying the stability and reactivity of compounds. It is formulated in terms of the energies of the HOMOs and LUMOs.ɳ =[EHOMO-ELUMO]/2 This formula indicates the more reactivity compounds have small chemical hardness, while less ones have large chemical splittings. In other words, the more reactivity compounds have small excitation energies, that is, their electron densities are easily altered, while less ones have large excitation energies or their electronic densities are difficult to modify.

Keywords: DFT, HOMO, LUMO

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ID:688

Association between HLA-G 3'UTR 14-bp ins/del polymorphism and susceptibility to prostate cancer

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Objective: Human leukocyte antigen G (HLA-G) is a non-classic MHC class I molecule that is highly expressed in tumor cell to inhibit different immune-competent cells. A 14-bp insertion/deletion polymorphism in exon 8 of the 3' untranslated region of the HLA-G gene has been recommended to be correlated with HLA-G mRNA stability and the expression of HLA-G. This finding revealed to evaluate the association of 14-bp ins/del polymorphism in HLA-G gene and prostate cancer in 150 cases and 146 controls of Tehran (Iran) men.

Material and Methods: This finding revealed to evaluate the association of 14-bp ins/del polymorphism in HLA-G gene and prostate cancer in 150 case and 146 control of south-east Iranian men. We designed a rapid and simple PCR for detection of 14-bp ins/del polymorphism in the HLA-G gene.

Results: The frequency of the Del allele was 58.0% in prostate cancer patients and 56.2% in the control group and the difference was not statistically significant (OR=1.074, 95%CI 0.774-1.489, P=0.334).

Conclusion: Our proofs, for the first time, suggest that the 14-bp insertion/deletion polymorphism in HLA-G gene was not associated with prostate carcinoma. Further studies on larger populations with different ethnicities are required to verify our findings.

Keywords: Polymorphism, HLA-G, Prostate cancer

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Evaluate the oxidative stress on chondrogenic ability of mesenchymal stem cells

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Objective: Oxidative stress involved in cartilaginous disorders such as osteoarthritis may affect mature chondrocyte. Therefore, mesenchymal stem cells (MSCs) present in synovial fluid can exhibit a different behavior when differentiated into chondrocyte under oxidative conditions. The aim of the present study is to investigate the oxidative stress effects on the differentiation of MSCs to chondrocyte.

Material and Methods: The isolated MSCs from adipose tissue were immunophenotyped and then differentiated into chondrocytes in the presence of 10 and 50 µM H2O2. After cell viability determination, the reactive oxygen species (ROS), glycoseaminoglycans level and hydroxyproline content were analyzed. In addition, gene expression of aggrecan type-II, collagen, and Sox9 transcription factor as well as safranin staining were also determined.

Results: Reactive oxygen species, which was significantly induced by higher hydrogen peroxide, significantly increased the content of glycoseaminoglycan and hydroxyproline to that the control cells both on the 9th day and 21st days post differentiation. The significant increased level of the gene expression of aggrecan, type-II, collagen, and Sox9 was also observed in concomitant with higher safranin staining on the 21st day ($p>0.05$).

Conclusion: The Results indicate a positive role of oxidative stress on differentiation into chondrocyte, which may lead to over chondorgenesis and its consequences during the oxidative state.

Keywords: Chondrocytes, Differentiation, Oxidative stress, Mesenchymal Stem cells

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ID:698

Berberine in combination with theophylline enhances apoptosis of MDA-MB-231 cells via BCL-2 family pathway

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Objective: Breast cancer is the most common female cancer and novel therapeutic agents are needed to treat this disease. Berberine, a natural isoquinoline alkaloid, has been shown to possess anticancer activity and induces apoptosis in various cancer cell lines. Theophylline, a methylxantine, has been widely used to the treatment of airway diseases including asthma and COPD. The aim of the present study was to investigate the effects of berberine alone and in combination with theophylline on MDA-MB-231 breast cancer cells.

Material and Methods: The cells were exposed to different concentrations of berberine alone and in combination with theophylline and the viability determined by MTT assay. BAX and BCL-2 mRNA expression were studied by Real-time PCR and Bax protein level and production of reactive oxygen species (ROS) determined using ELISA method.

Results: MTT assay showed that theophylline in combination with berberine increased toxicity of berberine in a dose dependent manner. Real-time PCR analysis of BCL-2 and BAX expression revealed that berberine alone and in combination with theophylline downregulated BCL-2 expression and upregulated BAX mRNA as compared to the control. Anion superoxide production increased significantly when the cells pretreated with theophylline compared to berberine treatment alone ($P<0.01$). Also the content of Bax protein level increased as berberine concentration increased, whereas in the presence of berberine and theophylline, the content of Bax was significantly increased ($P<0.001$).

Conclusion: Theophylline increases sensitivity of the MDA-MB-231 breast cancer cells to berberine through induction of ROS generation and increase in BAX/BCL-2 ratio. These findings provide an insight in to the potential application of berberine and theophylline in combination for the treatment of breast cancers.

Keywords: Berberine, Theophylline, Bcl-2 family, MDA-MB-231 breast cancer cells

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Carotid intima media thickness (cIMT) and liver stiffness (LS) predictors in T2DM and NAFDL patients

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Objective: Nonalcoholic fatty liver disease (NAFLD) is a spectrum of progressive liver disease which includes simple steatosis, NASH, fibrosis and eventually cirrhosis. Several studies have indicated that NAFLD had a significant relationship with the features of metabolic syndrome, such as abdominal obesity, glucose intolerance or diabetes mellitus type 2 (T2DM) and insulin resistance. There is little information concerning cIMT and LS predictors in the context of NAFLD and T2DM.

Material and Methods: We evaluated the clinical and subclinical features in healthy control and patients with NAFLD, T2DM and NAFLD + T2DM. T2DM was diagnosed based on American diabetes association (ADA) criteria. NAFLD was diagnosed using ultrasonography and Liver Stiffness was determined by elastography. Carotid intima and media thickness and the amount of visceral fat measured by ultrasonography.

Results: Multiple stepwise linear regression with LS as the dependent variable showed that ALT (β [SE]= 5.395 [0.917], $p<0.001$) and SBP (β [SE]=0.03 [0.011], $p<0.010$) were two predictor factors for LS. Strikingly, Multiple stepwise linear regression showed that SBP (β [SE]=0.002 [0.001], $p<0.007$) was an independent factor for cIMT.

Conclusion: Our results suggested ALT, BP and SBP can be associated factors with cIMT and LS in NAFLD and T2DM pathogenesis.

Keywords: NAFLD, T2DM, liver stiffness, carotid intima and media thickness

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ID:701

1 H NMR-based metabolomics study of serum in metabolic healthy and unhealthy obesity

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Objective: Metabolically healthy obese (MHO) has a lower risk of developing metabolic diseases compared with the metabolically unhealthy obese (MUHO). The molecular basis for this discrepancy remains unclear. Our objective: was to investigate metabolic profiles of both healthy and unhealthy obese subjects to identify new biomarkers and underlying metabolic pathways.
Material and Methods: Plasma samples of 22 MHO and 22 MUHO individuals were collected and subjected to nuclear magnetic resonance (NMR) analysis for metabolite profiling. Multivariate statistical analyses (PCA and PLS-DA) were applied to uncover metabolites that differed between two groups, and pathway analysis was performed to find responsible pathways.
Results: The results showed several differential metabolites between MHO and MUHO groups. Glutamine, proline, methionine, betaine, taurine, choline, 2-Aminobutyrate, tagatose were found to be lower in MUHO phenotype compared to MHO ones. On the other hands, two metabolites, palmitoleic acid and D-sphingosine, were higher in the MUHO group. In this line, three metabolites, proline, methionine and choline were negatively correlated with insulin resistance. Moreover, pathway analysis revealed impairment in some metabolic pathways including protein biosynthesis, ammonia recycling, glutamate metabolism and urea cycle in MUHO group.
Conclusion: Specific metabolomic profiles could distinguish MHO and MUHO groups. Some of differential metabolites had a correlation with insulin resistance, which could provide useful clues to study the underlying mechanisms of the development of abnormal metabolic phenotypes.
Keywords: Metabolomics, healthy obese, unhealthy obese, NMR
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ID:703

Saliva Metabolomic profile of patients with Chronic Hepatitis B

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Objective: Hepatitis B virus (HBV) causes chronic Hepatitis B virus infection (CHB), cirrhosis and hepatocellular carcinoma (HCC). Because liver biopsy is the gold standard approach for diagnosis of this disease, it is essential to find non-invasive and accurate methods for CHB. Therefore, the aim of this study was to investigate the saliva metabolic profile of CHB patients and to identify potential biomarkers of disease.
Material and Methods: Saliva from 16 healthy persons and 20 patients with CHB were analyzed by nuclear magnetic resonance. Then, multi variate statistical analysis was performed to identify discriminative metabolites between two groups.
Results: A set of metabolites were detected, including propionic acid, putrescine, acetic acid, succinic acid, tyrosine, lactic acid, butyric acid, pyruvic acid, 4-pyridoxic acid and p-aminobenzoic acid, which in combination with one another could accurately separate CHB patients from healthy controls.
Conclusion: It demonstrated that metabolomics has the potential to be developed into a novel clinical tool for hepatitis diagnosis and could contribute to an improved understanding of disease mechanisms.
Keywords: Saliva, Metabolomics, Hepatitis B virus, Biomarkers
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ID:714

Chondroitin sulfate degradation and eicosanoid metabolism pathways are impaired in the focal segmental glomerulosclerosis

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Objective: Focal segmental glomerulosclerosis (FSGS), the most common primary glomerular disease, is a diverse clinical entity that arises after podocyte injury. Although numerus studies suggested molecular pathways responsible for development of FSGS, many unknowns about its pathogenic mechanism is still remained. The present study investigated and confirmed the role of two important pathways that were predicted as candidates for pathogenesis of FSGS in our previous in silico analysis.

Material and Methods: The expression level of four enzyme genes that were representative of "chondroitin sulfate degradation" and "eicosanoid metabolism" pathways were investigated in the urinary sediment of biopsy proven FSGS patients (n=20) and healthy subjects (n=17) using quantitative real time polymerase chain reaction (Q-RT-PCR). These target genes were arylsulfatase, hexosaminidase, cyclooxygenase-2 and prostaglandin I2 synthase. Mann–Whitney U test was used to compare different variables between patient and control groups, patients with proteinuria of >3 gr/day and <3 gr/day, as well as patients with eGFR >60 ml/min/1.73 m2 and <60 ml/min/1.73 m2. Correlation of target genes and clinical and pathological characteristics of the disease was calculated. Receiver operating characteristic (ROC) analysis was performed to assess and compare the diagnostic accuracy of gene expression level between the study groups. Combination of target genes as a diagnostic or prognostic panel for ROC analysis was carried out using multiple logistic regression.

Results: The ROC analysis revealed that combination of three target genes (i.e. hexosaminidase, arylsulphathase and cyclooxygenase-2) improve the diagnosis accuracy of patients group to 76%, however, the mean difference between healthy and patients groups was not significant. The expression level of prostaglandin I2 synthase was lowers the limit of RT-PCR detection. Hexosaminidase were correlated with the level of proteinuria where cyclooxygenase-2 were correlated with interstitial inflammation and the serum creatinine level in the disease group. A combined panel of these three target genes improved the discriminant accuracy of disease progression in terms of proteinuria and glomerular filtration rate to 87% and 74% respectively.

Conclusion: Our data indicated that these target genes contributes in the pathogenesis of FSGS and can be considered as biomarkers for non-invasive evaluation of disease progression.

Keywords: Focal segmental glomerulosclerosis, molecular pathway, biomarker, Chondroitin sulfate, eicosanoid metabolism

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ID:723

Optimization of the Induction Conditions for Over-expression of a Recombinant Urate Oxidase in E. coli.

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Objective: Urate oxidase, an enzyme belonging to the class of oxidoreductases, catalyzes the conversion of uric acid to Allantoin. This enzyme has been used to treat hyperuricemia, gout, and tumor lysis syndrome. Because of the high demand for this drug, the development of a recombinant system for the production of urate oxidase is required.

Material and Methods: A strain of E. coli (BL21) which was carrying a codon optimized A. flavus urate oxidase gene on pET28a vector was used in this study. In order to improve the level of expression of Urate Oxidase in E. coli, the effect of different induction temperatures (18, 22, 30, 37°C), different IPTG concentrations (0.25–1.5mM), and various agitation rates (100-300rpm), and several post-induction harvest times (3-24hrsa) were examined. The level of protein expression in these conditions was investigated by SDS-PAGE and Bradford methods.

Results: Through these tests, an improved condition for the maximum enzyme expression was found. It included an induction temperature of 35°C, IPTG concentration of 1 mM, an agitation rate of 170rpm, and also a post-induction harvest time of 5hrs. Following further experiments, it was shown that the Urate Oxidase enzyme expressed in this condition were soluble.

Conclusion: The above-mentioned parameters were lead to a significant increase in the level of Urate Oxidase expression in E. coli. This would result in a further decrease in the production costs for the manufacture of this clinically important drug.

Keywords: Recombinant Urate Oxidase, A. flavus, Expression, E. coli, Culture Optimization
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ID:724

Cloning, Expression, Purification, and Characterization of the Recombinant Aspergillus flavus Uricase from Escherichia coli

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Objective: Accumulation of uric acid is a complication in the hyperuricemia, gout, etc. Uricase can convert uric acid to Allantoin, a compound with higher solubility. Since this enzyme is commonly used in treatment of these conditions, development of a reliable source for the production of uricase is essential. Our aim was to codon optimize an A. flavus Uricase gene for expression in E. coli.

Material and Methods: The Uricase gene was codon optimized based on the available E. coli codon usage table. Then, the synthesized gene was cloned into pET28a, which was afterwards transformed into E. coli (BL21). Thereafter, the expression of this gene was induced with 1 mM IPTG in Terrific Broth (TB) supplemented with Kanamycin. After investigating the protein solubility test, the His-tagged uricase was isolated from this crude extract by Ni-Sepharose affinity chromatography. The protein concentration and purity tests were performed by Bradford method and SDS-PAGE analysis, respectively. Ultimately, the activity of the purified protein was measured by the standard spectrophotometric tests.

Results: The codon optimized uricase gene was expressed in a soluble form in E. coli. Additionally, it was shown that this protein could be purified in a single step to a high degree of purity. The activity tests revealed that the purified uricase as a specific activity of 15.6 U/mg.

Conclusion: We revealed that the recombinant A. flavus uricase could be produced by E. coli. Our uricase showed a satisfactory activity compared to the commercially available enzymes, including Rasburicase.

Keywords: Uricase, Recombinant, E. coli, Codon optimization, specific activity
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ID: 726

Comparison of Apelin level in hypertensive patients receiving different hypertension medication

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Objective: Apelin as an adipokine secreted from adipose tissue has an important role in regulating the blood pressure and hypertension. The aim of this study was to evaluate and compare the plasma apelin level in hypertensive patients under treatment with amlodipine, losartan and amlodipine+losartan.

Material and Methods: In this case control study, the serum level of apelin was compared in 4 groups as follows: Healthy subjects group (n=31) who did not have high blood pressure and other known disease. Hypertensive patients were treated with amlodipine (n=31), hypertensive patients were treated with losartan (n=45) and the fourth group of 33 patients that treated with amlodipine and losartan. Apelin level in serum samples was measured using Human Apelin ELISA Kit according to the manufacturers' instructions.

Results: The average blood level of apelin in the control group, and groups receiving amlodipine, losartan and amlodipine + losartan were 366.16±36.04, 247.19±27.77, 282.93±47.08 and 289.84±32.20 pg/dl, respectively. Losartan+amlodipine group had the higher level of apelin compared with amlodipine alone ($p<0.05$).

Conclusion: The Results of this study showed that apelin has definite protective effect in the prevention of hypertension in treatment subjects. Also according to the Results: of this study, the renin-angiotensin aldosterone system inhibitors such as losartan cause more apelin increase resulting better blood pressure control.

Keywords: Apelin, Hypertension, Losartan, Amlodipin
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ID:727

Determination of acute hepatotoxic effect of orally administrated aqueous and hydro-alcoholic extract of Echium amoenum Fisch & C.A.Mey in rat

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Objective: People believe that medicinal plants are safe because of their natural origin. This public conviction has been led to a dramatically increasing rate in employment of herbal remedies to treat the disorders. Echium amoenum fisch & C.A.Mey (Boraginaceae) grows in most regions of Europe and in northern parts of Iran. In Iran its dry violet-blue petals have been used as an antidepressant, sedative, tranquillizer, tonic and anti-cough agent. One of the most important active components of E.amoenum petals is pyrrolizidine alkaloid. It has been previously reported that pyrrolizidine alkaloids lead to hepatic deterioration. The aim of this study is to assessment of safety range for E.amoenum hydro-alcoholic extract (EAHAE) and aqueous extract (EAAE) about liver toxicity.

Material and Methods: Adult wistar rats fed different doses of EAHAE, 400, 600, 800 mg/kg or EAAE, 800, 1000, 1400, 2000 for 28 days in the separated groups. The negative control animals received normal saline while the positive control was injected 1 ml/kg of CCl4. Then, the serum activity of ALT, AST, and ALP and the serum total bilirubin were measured, by a spectrophotometer method.

Results: The Results show, 800 mg/kg EAHAE remarkably increased the hepatic biomarker compare to normal. None of the treated doses of EAAE caused significant increase in the markers. The histopathological Results: confirmed the biochemical observations.

Conclusion: Our findings illustrate, EAAE didn't show any hepatotoxic effect. Indeed it is entirely safe for the liver even in the high doses administered for a long period. But EAHAE caused hepatic dysfunction when administered at the high dose.

Keywords: Echium amoenum, Aqueous extract, Hydro-alcoholic extract, Hepatotoxic, Safety

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ID:728

Immunomodulatory Effects of probiotic lactobacillus acidophilus in healthy adults: a double-blind, randomized, controlled trial

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Objective: The role of probiotics in management of chronic diseases, principally due to their role in immune system modulation and the anti-inflammatory response, has recently been experienced a renewed interest in society. In this study, we investigated the effect of daily consumption of probiotics on serum pro-inflammatory cytokines levels in healthy adults.

Material and Methods: Healthy adults (n=60) aged 18–40 years were randomly assigned to control and probiotic groups. The probiotic group received one capsule of probiotics containing 109 cfu lactobacillus acidophilus daily for 30 days, while the placebo group received similar capsules with no bacteria for the same duration. At the end of the study, levels of serum TNF-α, IL-2, and C- reactive protein were measured.

Results: The present study showed that daily consumption of probiotics significantly reduced the levels of serum TNF-α and CRP (P= 0.000), while there was no significant change in the level of serum IL-2.

Conclusion: In conclusion, probiotics are able to modulate the immune system and reduce production of pro inflammatory mediators and probiotics consumption provide benefits in healthy adults. In conclusion, probiotics could significantly reduce the serum levels of pro-inflammatory cytokine (TNF-α) and CRP.

Keywords: probiotics, Immunomodulatory, TNF-α, Healthy, CRP

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ID:729

IRAK inhibitor increase insulin sensitivity in mouse model of Insulin resistant

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Objective: Insulin resistance is a characteristic feature of most patients with type 2 diabetes mellitus and is one of the defining clinical features in the metabolic syndrome or syndrome X. Insulin resistance (IR) is a common pathologic state in which target cells fail to respond to ordinary levels of circulating insulin. Epidemiological evidence suggesting a correlation between inflammation and insulin resistant states such as obesity, but the mechanistic links were unknown. Interleukin-1 receptor-associated kinases (IRAK) play a central role in inflammatory responses by regulating the expression of various inflammatory genes in immune cells. This study was aimed to investigate the effect of IRAK inhibitor on gene transcription and serum concentration of adiponectin in insulin resistant mice.

Material and Methods: Experimental mice were randomly divided into 6 groups: the control group was fed a regular chow diet while other group fed with a high-fat diet(HFD) for 12 weeks. After the first 12 weeks, the animals were treated with IRAK inhibitor, both IRAK and pioglitazone,

pioglitazone, DMSO, for two weeks. Adiponectin and IL6 Gene expression level was analyzed by real-time PCR. Additionally, Serum adiponectin levels were measured by ELISA.

Results: our study showed that IRAK inhibitor significantly reduces serum Glucose (390 mg/dl to 240 mg/dl), Insulin (22 mIU/L to 14 mIU/L) and HOMA-IR (21 to 9) in comparison with control group. IRAK inhibitor also increase serum level of Adiponectin (10 µg/ml to 18 µg/ml) and in mRNA expression level, our study revealed that this agent significantly reduces IL6 mRNA and increases adiponectin mRNA in adipose tissue.

Conclusion: The study findings revealed that IRAK inhibitor might be a protective candidate against insulin resistance through increase in adiponectin levels.

Keywords: IRAK inhibitor, inflammation, insulin resistance, adiponectin, HFD

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ID:734

IMPDH1 retinal isoform have higher catalytic activity than canonical isoform in the mouse

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Objective: RP (Retinitis Pigmentosa) is a hereditary degenerative retinal disorder causing photoreceptor dystrophy. Mutations in the IMPDH1 gene cause RP10 disease. Mechanism of the IMPDH1 interference in RP10 disease has not really been clear. Inosine 5-monophosphate dehydrogenase 1 (IMPDH1) catalyzes the oxidation of IMP to XMP using NAD+ as the cofactor. This is the rate-limiting step in de novo guanine nucleotide biosynthesis. The IMPDH1 gene is highly expressed in the mammalian retina and has some retinal specific transcripts created by alternative splicing or translation start site. It has been suggested that the IMPDH1 should have a specific function in the retina, mediated by retina-specific variants, so there is an essential need for a functional assay of retinal isoforms to identify the mechanism of IMPDH1 mutations pathogenicity.

Material and Methods: After expression and purification of recombinant mouse IMPDH1 retinal and canonical isoforms, we performed enzymatic activity assay for each isoform and calculated catalytic activity separately. The reaction was started by addition of 5µg/ml purified recombinant IMPDH1 to assay solution and monitoring the absorbance increase at 340 nm for 15 min.

Results: Enzyme activity for canonical mouse IMPDH1 isoform was achieved at 1.1 µmol.min-1 and for retinal isoforms, H1 (546) was about 1.07 µmol.min-1 and H1 (603) about 1.7 µmol.min-1.

Conclusion: The higher retinal isoform activity may be due to more frequency of these isoform compared to canonical isoform in the retina and can be related to mechanism of RP10 disease.

Keywords: RP, IMPDH1, Retinal isoform, Catalytic activity

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Liposomal Gold and Silver Nanoparticles

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Objective: Liposomes can be described as artificially made vesicles composed of one or more phospholipid bilayer(s). They are being used to encapsulate different material including medicinal and nutritional compounds as well as cosmetic and diagnostic agents. Recently, liposomes have also been employed for the entrapment and delivery of a number of different trace elements (e.g. selenium), divalent cations (such as calcium and magnesium) and metal nanoparticles. Because of their unique optical and physical properties, silver and gold nanoparticles are widely used in many fields as ideal materials for labelling, imaging, and sensing. This review article addresses the use of liposome-encapsulated silver and gold nanoparticles in targeting drugs and diagnostic agents with reduced cytotoxic effects in patients with various cancers and many other diseases.

Keywords: cancer, encapsulation, gold nanoparticle, liposome, nanosilver

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ID:739

Effect of curcumin on serum metabolomic profile in patients with non-alcoholic fatty liver disease

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Objective: Curcumin, a natural polyphenolic compound in the spice turmeric, has been found to have potent anti-oxidative and anti-inflammatory activity. Curcumin may benefit non-alcoholic fatty liver disease (NAFLD) through its beneficial effects on biomarkers of oxidative stress (OS) and inflammation, which are two feature of this disease. However, the effects of curcumin on NAFLD remain poorly understood. This investigation evaluated the effects of curcumin administration on metabolic status in NAFLD patients.

Material and Methods: Fifty eight NAFLD patients participated in a randomized, double-blind, placebo-controlled designed study. The subjects were randomly allocated into two groups to receive either 250 mg curcumin (n=30) or placebo (n=28) one capsule per day for a period of 8 weeks. Fasting blood samples were taken from each subject at the start and end of the study period. Subsequently, metabolomics analysis was performed for serum samples by NMR.

Results: Compared with the placebo, curcumin supplementation resulted in significant decreases in serum 3-methyl-2-oxovaleric acid, 3-hydroxyisobutyrate, kynurenine, succinate, citrate, α-ketoglutarate, methylamine, trimethylamine, hippurate, indoxyl sulfate, chenodeoxycholic acid, taurocholic acid, and lithocholic acid. This panel of metabolic biomarkers could effectively distinguish NAFLD subjects treated with curcumin and placebo groups, achieving an area under receiver operating characteristic curve (AUC) values of 0.99.

Conclusion: Curcumin intake for 8 weeks to NAFLD patients had beneficial effects on mitochondrial dysfunction and gut microbiota dysbiosis associated with NAFLD.

Keywords: Metabolomics, NMR, Curcumin, Medicinal herb

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ID:741

The Expression of mir320 is reduced by metformin in insulin resistant 3T3L1 adipocytes

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Objective: MicroRNAs are small non-coding double stranded RNAs with 19-22 nt long repress activity of complementary mRNA regulate 30% of mammalian gene products. Some miRNAs as miR320 play any role in the development of insulin resistance in adipocytes, an important pathophysiological effect in diabetes. There is a new idea of miRNAs as biomarker in insulin resistant. Metformin is currently the drug of first choice for the treatment of T2D that reduce hepatic glucose output and increase uptake of glucose by the periphery, including adipocyte tissue. However metformin reduces insulin resistance. The aim of this study was whether metformin change expression of miR320 in insulin resistant 3T3L1 adipocytes.

Material and Methods: 3T3L1 cells were cultured in 6 plates in Dulbecco's modified Eagle's medium (DMEM) containing 10% FBS and differentiated to adipocytes with differentiation medium. Than the cells were induced to insulin resistance. metformin treatment was done at 2 and 24 hours in different concentrations (2.5 ,5,10 and 20 mmol/l). Quantitative real-time PCR was performed to determine miR-320 expression in insulin-resistant 3T3L1 adipocytes and compared with insulin resistant cells without metformin(control). Each sample was measured in triplicate, and gene expression levels were calculated using the 2-ΔΔct method.

Results: The results indicate that the expression of miR320 was increased in insulin resistant adipocytes. The expression of miR320 was inhibited in 2 hours metfornmin treatment for all concentrations so the maximum effect of metformin was 10 mmol/l (11.5 fold, p-value 0.02).

Conclusion: This study demonstrated that metformin reduced miR320 expression in insulin resistant 3T3-L1 adipocytes. More studies about IR-related miRNAs assessment serve therapeutic strategy to control insulin resistance

Keywords: MiR-320, 3T3-L1, metformin, insulin resistance

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ID:744

Hotair, new marker in patients suffer from breast ,colon, thyroid and glioma cancer

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Objective: Thyroid cancer is a one of important endocrine cancer. the cellular and biochemical mechanism of thyroid cancer is not well known. Recent years, noncoding RNAs were investigated by researchers. In this regard, hotair is homeo box transcript antisense RNA, this encoded antisense to the HOXC locous.

Material and Methods: To measure Hotair level, tissue and plasma can be prepared from cancer patients and examined by using immunological and genetic methods in different samples. The tissue samples are

available in the surgical department of the affected patients, and a plasma sample is also available in coordination with cancer patients. The ANOVA method can be used to analyze the results.

Results: Several researches and studies have shown that Hotair level changes in many cancer patients compared to the control group, and these changes is measurable and significant changes can be used for early diagnosis and differential diagnosis.

Conclusion: It is likely that Hotair, will be useful in the detection of cancers in a timely manner and before the onset of cancer and metastasis. Also, having these features better than previous markers, have a better diagnostic advantage.

Keywords: Hotair, new marker, cancer

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ID:746

Lower omega-3 index is associated with obesity in men with metabolic syndrome

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Objective: Diet plays a pivotal role in the development of metabolic syndrome (MetS) and its cardiovascular consequences. Fatty acids (FAs) composition of dietary intake, affects blood FAs concentration, cell membrane composition, insulin sensitivity and different unfavorable metabolic consequences. In this study, association between omega-3 index (red blood cell concentrations of eicosapentaenoic acid (%EPA) and docosahexaenoic acid (%DHA)) with anthropometric measurements and obesity was investigated in men with MetS, using gas chromatography/mass spectrometry (GC/MS).

Material and Methods: A total of 50 men with MetS, between 40 and 60 years of age and 30 normal men matched for age, sex and dietary intake were investigated from Isfahan Cardiovascular Research Center. Anthropometric measurements include height, weight, body mass index (BMI), waist and hip circumference (WC and HC respectively) were taken from all the subjects. To determine the omega-3 index, FAs composition of erythrocyte membranes was analysed using GC/MS.

Results: Negative associations were seen between the omega-3 index and anthropometric measurements of obesity include: BMI ($r=-0.283$, $p=0.049$), weight ($r=-0.285$, $p=0.045$), WC ($r=-0.359$, $p=0.011$) and HC ($r=-0.354$, $p=0.013$) in men with MetS. Such negative association was not observed in normal group ($P>0.05$).

Conclusion: Omega-3 index was negatively associated with BMI, weight, WC and HC in men with MetS. In conclusion, lower level of omega-3 index is associated with a higher level of unfavorable anthropometric indices and can improve by lifestyle modification.

Keywords: Gas chromatography/mass spectrometry, metabolic syndrome, Omega-3 index

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ID:748

Comparative Study on the effects of B and I derivatives of Cucurbitacin on ceramide metabolism in liver cancer cell line Huh-7

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Objective: The two derivatives of Cucurbitacin, B and I both belong to triterpenoid constituent of Cucurbitaceae species with cancer prevention potential. However, their mechanism of anti-cancer activity remains unknown, particularly in liver cancers. Here, we demonstrate, for the first time, that CuB and CuI inhibited the cell death of human liver cancer Huh-7 cells through a ceramide-dependent mechanism.

Material and Methods: In this study, Huh-7 cells were treated with two derivatives of CuB and CuI in the concentration range: 0, 0.5, 1, 2, 4, 6, 8 and 16 µM. Cell viability determined by the MTT method. Ceramide level, ceramidase, glucosylceramide synthase (GCS) and sphingomyelinase (SMase) activities were evaluated by spectrophotometer and HPLC in cell extract after 24 h treatment.

Results: The results showed that both derivatives were able to induce apoptosis in Huh-7 cells in ceramide generation pathways by which ceramide increase in dose dependent manner. This increase was attributed to to ceramide catabolism inhibition by decrease in ceramidase and glucosylceramide synthase (GCS) activities. On the other hand it was contributed to the rising activity of sphingomyelinase (SMase). Increasing in Caspase-3 activity also was related to program cell death that caused by both derivatives in which CuI was more potent than CuB. This difference may be attributed to structural modifications.

Conclusion: Our data explains the programmed cell death caused by both derivatives of CuB

and CuI and demonstrates its therapeutic potential against Huh-7.

Keywords: Cucurbitacin B, Cucurbitacin I, ceramide metabolism, Cell line Huh-7

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ID:752

Induction of cell cycle arrest by Britannin, a Sesquiterpene Lactone isolated from Inula aucheriana, in breast cancer cells

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Objective: Breast cancer is currently the most common cause of cancer-related death in women, especially in western populations and industrialized countries. Despite advances in therapies using chemotherapy, surgery and radiation, breast carcinoma remains a great challenge for clinical therapy. In the recent years, there has been growing interest in the use of natural products with more potent anticancer properties and reduced adverse effects. Increasing evidences demonstrate that plant-derived compounds could alter the natural history of cancer. Sesquiterpene lactones (SLs) are the active constituents of a variety of medicinal plants used in traditional medicine for the treatment of human diseases such as inflammation, headache and infections. Parthenolide, Artemisinin, and Tehranolide are examples of such compounds and have already reached cancer clinical trials. Britannin is a sesquiterpene lactone which in our previous works was isolated from the Inula aucheriana aerial parts and its anticancer activity was demonstrated. In this study, we evaluated the effects of Britannin on the cell cycle distribution and also cell cycle related proteins in breast cancer cells.

Material and Methods: Analysis of cell cycle distribution was carried out by flow cytometry. The effects of Britannin on Cyclin D1 and CDK4 expression were evaluated by Western blot.

Results: The obtained results show that Britannin at the low concentrations induces cell growth inhibition mainly via G1 phase arrest while it seems that apoptosis contribute to cell growth inhibitory effect of high doses of Britannin. Reduction of Cyclin D1 and CDK4 protein levels was also observed after treating cancer cells with Britannin.

Conclusion: The obtained results demonstrate that Britannin can inhibit MCF-7 and MDA-MB-468 breast cancer cells proliferation via arresting cell cycle progression through Cyclin D1/CDK4-mediated pathway.

Keywords: Britannin, sesquiterpene lactone, Cell cycle, CDK4, cyclin D1

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ID:756

Anticancer activity of Drimia maritima in human breast cancer cell lines MCF7 and MDA-MB-468

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Objective: One of the major concerns in conventional therapeutic approaches is the risk of undesired and severe side effects arising from the non-specific targeting of both normal and cancer cells. Therefore, the discovery of natural plant products with low toxicity has attracted considerable scientific interest in the recent years. After survey on the historical Pharmacopoeia of Iranian Traditional Medicine and medicinal plants which had been used to manage cancer-like disorders, Drimia maritima (D.maritima) has been subjected to investigate the anticancer features of D.maritima as well as its possible molecular mechanisms of action in two breast cancer cell lines, MCF7 and MDA-MB-468 cell lines.

Material and Methods: To observe cell viability and proliferation, MTT assay were carried out. Apoptosis was assessed with the Propidium iodide and Annexin-V staining, mitochondrial membrane potential ($\Delta\Psi m$) measurement, cytochrome c release, and Bcl-2 and Bax protein expression.

Results: D.maritima was found cytotoxic against MCF-7 and MDA-MB-468 cells with IC50 value of 20.48±1.17 µM and 25.74±2.05 µM, respectively. Flow cytometric analysis showed that D.maritima induced apoptosis that was associated with the loss of mitochondrial membrane potential ($\Delta\Psi m$), cytochrome c release, and increasing Bax/Bcl-2 ratio.

Conclusion: Our results suggest that D.maritima exerts effective anticancer activity against human breast cancer cell lines MCF-7 and MDA-MB-468 through induction of apoptotic pathway.

Keywords: Drimia maritima; Anticancer; Apoptosis; Breast cancer

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ID:769

Study of serum lead and cadmium levels of mine workers and their relation with liver function

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Objective: Work in mines in all countries of the world is accompanied by an accident and danger. Because health has different physical, psychological, social and spiritual dimensions, so measuring health with miners needs togo beyond disease and mortality and activity limitation. Therefore, the main objective of this study was to examine the level of serum lead and cadmium in mine worker and the evaluation liverdisorders in these workers.

Material and methods: This study was a descriptive case-control study with target population of workers employedin different mines. By conveying the type of study and the study objectives, by obtaining written consent, 270 employees working in mines as case group and270 individuals healthy non-employment was selected in the mines as a control group and 10 ml ofblood was taken from them. All blood samples taken were transferred to a freezer at -80^{o}C and stored until the tests were performed. Cadmium and lead concentrations were directly measured by the CTA-3000 atomic absorption spectrophotometer (Chemtech Analitical Instruments Limited UK). The amount of AST, ALT, ALP and Y-GT activity in serums were measured by colorimetric method. The levels of 5'-Nocleotidas in subjects serum measurd by ELISA method.

Results: According to demographics of workers, the average employment rate in mining was 7.2 years. The level of lead and cadmium in miners (case group) was significantly higher than the control group (Respectively p-value equal 0.025 and 0.001). The mean level of serum AST and ALT activity in the case group was significantly higher than the control group (p-value was 0.004 and 0.045 respectively). The rate of AST/ALT increased in case group. The level of ALP activity in the two groups did not show a significant difference, but YGT and 5'-Nucleotidease activity in the case group showed a significant increase compared tothe control group (in both cases p<0.0001).

Conclusion: The findings of this study show that the prolonged increase in lead and cadmium in the blood of mines' workers has asignificant effect on the level of liver enzymes. Screening for liver tests in these workers can be helpful in maintaining their health.

Keywords: Mine Workers, Trace Elements, Liver Disfunction

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Protective effects of Arbutin against tert-butyl hydroperoxide-induced oxidative stress in human foreskin fibroblasts (HFFs) through regulation of P53 and BAX/Bcl-2 ratio

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Objective: The integrity of human skin as a main target of oxidative stress is endangered by multiple insults such as exposure to UV irradiation and chemical stressors, which can trigger the production of reactive oxygen species (ROS). Anti-oxidative responses include activation of many stress-response genes (e.g. p53) and their signaling pathways. Tert-Butyl hydroperoxide (t-BHP) is widely used to study cellular injuries such as oxidative damage and cell apoptosis. T-BHP was found to induce the apoptotic process in cells through the up and down regulation of Bax/Bcl-2 protein. Arbutin (p-hydroxyphenyl-β-D-glucopyranoside), a natural polyphenol, is identified as a herbal medicine that possesses beneficial functions including anti-inflammatory, antioxidant and anti-tumor activities. Accordingly, we evaluated the cytoprotective effect of arbutin and the mechanism related to oxidative stress in t-BHP induced fibroblast cells.

Method: The cell viability was estimated by MTT and the percentage of apoptotic or necrotic cells was determined using a double staining Annexin V Fluorescein Isothiocyanate (FITC) Apoptosis Detection kit (eBioscience, San Diego, CA, USA). The mRNAs of P53, BAX and Bcl-2 were measured by Quantitative PCR.

Result: The viability of fibroblast cells decreased after 24 h of incubation with t-BHP

in a dose-dependent manner ($p<0.01$). Arbutin pre-treatment markedly promoted fibroblasts viability, in a dose-dependent manner ($p<0.01$). Additionally, arbutin significantly reduced P53 expression and the ratio of Bax/Bcl-2 ($p<0.01$). As well as, arbutin inhibits necrotic death induced by t-BHP in fibroblast cells ($p<0.01$).

Conclusion: Arbutin showed a protective effect against t-BHP-induced oxidative damage by increasing cell viability and reducing necrosis, Bax/Bcl-2 ratio and P53 expression in fibroblast cells. Our results confirm that arbutin possesses antioxidant properties, and may be useful for the prevention of free radical-induced skin damage.

Keywords: Arbutin, oxidative stress, fibroblast cells, apoptosis, tert-butyl hydroperoxide

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Molecular Docking Studies of tyrosine kinase inhibitors targeting DDR1

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Objective: The discoidin domain receptors1 (DDR1) that functions as cell surface receptor is activated by the binding of matrix fibrillar collagen and regulates proliferation, invasion, migration and adhesion. Deregulated DDR1 signaling has been linked to the pathogenesis cancer. DDR1 plays a relatively critical role in the development and survival of cancer cells, and their inhibitors are the main approaches to targeting tumor suppression. Cancer related tyrosine kinases such as DDR1 might provide new therapies for diseases such as cancer. Since the DDR1 is overexpressed in tumor cells, so the inhibition of the DDR1 kinase activity would be a significantly effective strategy in cancer therapy.

Material and methods: In this study we examined the insilico inhibition of DDR1 by the tyrosine kinase inhibitors imatinib, ponatinib, gefitinib, erlotinib, sorafenib, sunitinib, dasatinib and DDR1-IN-1 using AutoDock.

Results: Our results indicate that DDR1-IN-1 has an interesting inhibitory activity on DDR1 insilico, and can be used in further studies to develop therapeutic modalities for the treatment of metastatic cancers. Among the eight compounds investigated, DDR1-IN-1 exhibited potent binding energy ΔG = -10.59 kcal/mols with DDR1 receptor compared to commercially available tyrosine kinase inhibitors.

Conclusion: In the current study DDR1-IN-1 was suggested as a specific DDR1 inhibitor and strongly suggested that DDR1-IN-1 is a potent anti-cancer compound as ascertained by its potential interaction with DDR1. This hypothesis provides a better insight to control metastasis by blocking DDR1.

Keywords: DDR1, Inhibitor, Docking analysis, Cancer

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ID:780

Evaluation of relationship between serum levels of osteocalcin with atherosclerotic coronary arteries in people undergoing angiography at Bushehr Heart Center

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Objective: The aim of this investigation was to evaluate the relationship between serum levels of osteocalcin with coronary artery plugs in people undergoing angiography.

Material and methods: In this case-control study, 138people who referred to Bushehr Heart Center for routine examination were participated. Demographic information of the participants was registered by a standard questionnaire. Before undergoing the angiographic processes, 10 ml blood was collected from all the participants and stored at – 80°C until the analysis. After the angiography was performed, those who found to be normal entered the control group, and those with one or more arteries blocked were placed in the case group. Finally, serum levels of osteocalcin were measured in all the samples, by using ELISA kits.

Results: Serum levels of osteocalcin in the case group were significantly higher than the control ($P=0.019$). Moreover, no relationship was found between the osteocalcin levels and the number ofblocked arteries and the severity of atherosclerosis ($P=0.95$). By separating the two factors like age and T2DM disease in both the groups, a difference was found in the concentration of osteaocalcn and coronary artery atherosclerosis ($P=0.034$).

Conclusion: The results of this investigation showed that a significant relationship exists

between the increase in the concentration of serum osteocalcin and coronary artery atherosclerosis.

Keywords: Osteocalcin, atherosclerotic coronary arteries, angiography

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Correlation of trypsin inhibitory capacity with antineutrophil cytoplasmic antibody in multiple sclerosis

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Objective: Alpha-1 antitrypsin (AAT) is an inhibitor of proteinase3, an autoantigen for antineutrophil cytoplasmic antibody (ANCA). AAT deficiency is an inherited genetic disorder caused by mutations in the SERPINA1 gene that manifests as liver cirrhosis, lung diseases and auto immune diseases, and is characterized by low serum levels of AAT. This protein has been associated with a variety of autoimmune diseases. In this study sera from Iranian patients with multiple sclerosis were investigated in order to detect correlation between AAT activity with ANCA.

Material and methods: The activity of Alpha-1 antitrypsin as its potential trypsin inhibitory capacity (TIC) was measured spectrophotometrically with BAPNA substrate and ANCAs were detected in patients sera using the standardized indirect immuno fluorescence test.

Results: Seventy-three percent of patients were c-ANCA whereas no one was p-ANCA positive. The mean of TIC was detected 2.23 µM/mL/min.

Conclusion: We concluded that there was a significant difference between Alpha-1 antitrypsin activity and ANCA- positive tests in patients with multiple sclerosis.

Keywords: Alpha-1 antitrypsin, Antineutrophil cytoplasmic antibody, Multiple sclerosis

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Chronic pregabalin administration impairs memory of rat in Object Recognition Task

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Objective: Pregabalin is used as an adjunctive therapy in patients with partial seizure, fibromyalgia and central neuropathic pain associated to spinal cord injury and generalized anxiety disorders. This study is designed to determine the effects of pregabalin on memory of rat using object recognition task.

Material and methods: Male wistar rats were intraperitoneally injected 10 or 30 or 100 mg/kg/day of pregabalin for 28 days according to their respective group (n=7). In parallel the group of animal received a same volume of saline as the vehicle. After the end of treatments animals were undergone the new object recognition task (ORT) for evaluation of their spatial memory. For this reason the discrimination (d2) and recognition (R) indexes as well as the frequency of new object exploration were calculated. The data were analyzed using one way analysis of variance followed by Tukey post hoc tests. The P-values less than 0.05 were considered as statistically significant.

Results: Our results show that administration of pregabalin at the dose of 10, 30 or 100 mg/kg for 28 days significantly reduces the d2 and R indexes and frequency of exploration in the T2 trials compare to the control group. 100 mg/kg of pregabalin shows more decrease in the above factor compare to the 10 mg/kg.

Conclusion: The findings of the present study indicate, long term exposure to the pregabalin impairs spatial memory of rat in the object recognition task. The pregabalin induced cognitive deficit shows a dose dependent manner in this study.

Keywords: Pregabalin, Chronic, Memory, Rat, Object recognition task

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ID:784

Assessment of urinary Ca, Na, K and it's relationship with urinary iodine excretion and during pregnancy in Urmia county

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Objective: Iodine is a trace element and is required for the biosynthesis of thyroid hormones. Determination of urinary iodine concentration in pregnant women especially in iodine deficient areas is important. Random spot UI concentrations and UI/Cr is most widely used for UI measurements. Renal iodide clearance depends on glomerular filtration rate (GFR) and tubular reabsorption of urinary iodine is affected by osmotic diuresis. The ame of this study was to evaluate the relationship between deuresis and iodine excretion and thyroid function during pregnancy.

Material and Methods: In this cross-sectional study 131 pregnant women at 1st trimester and 60 no pregnant women were enrolled. Random urine was collected at 1st, 2nd, 3rd trimester. UIC was determind by Sandal-Kolthoff technique. Urinary calcium and creatinin were analyzed by CPC and gaffe method respectivly. Na+ and K+ measured by flame photometer. serum TSH was determind by chemiluminescence.

Results: The amounts of I/creatinine ratio in 1st, 2nd, 3rd trimester were 0.008 µg/g, 0.02 µg/g, 0.01 µg/g, respectivly. The corresponding values for the means of Ca/Cr, Na/Cr, K/Cr ratios were 0.08, 0.12, 0.12; 1.39,1.73,1.93; 0.5, 0.6, 0.6 respectivly. Mean of TSH values in 1st, 2nd. 3rd trimester was 1.1(mIU/L),1.7 (mIU/L), 1.5 (mIU/L) during the three gestation stages.

Conclusion: In this study, increasing values of urinary Ca, Na, K and iodine during pregnancy and correlation between them in first and second trimester suggests that increase in deuresis due to pregnancy causes high iodine excretion, that may mask the iodine deficiency in pregnant women at iodine defficient areas.

Keywords: Urinary iodine concentration (UIC), Glommerular filtration rate (GFR), iodine defficient (ID)

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Evaluating the association of single nucleotide polymorphism (SNP) rs6983267 with esophageal cancer in Iranian patients

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Objective: Esophageal cancer is one of the leading causes of death worldwide. The main problem with esophageal cancer is related to its late diagnosis and therefore poor prognosis. Single-nucleotide polymorphisms (SNPs) in several genes may increase the risk of different cancers. Several genome-wide association studies in various populations have proposed rs6983267 as a susceptibility marker for multiple cancers such as prostate, colorectal, breast, bladder, ovarian, thyroid and lung cancers. Therefore, rs6983267 in chromosome 8q24 was selected for further analysis in esophageal cancer patients.

Material and methods: In this case–control study, 30 patients with esophageal cancer and 45 control samples were collected from different hospitals in Mashhad, Iran. Genomic DNA was extracted from 5 ml fresh peripheral blood and the genotyping was performed by TaqMan allele discrimination method.

Results: Hardy–Weinberg test was done and samples were in equilibrium ($p<0.05$). Chi square test was used to investigate the association between rs6983267 and cancer development, however the results did not show any significant association and genotype frequencies were similar between control and case groups.

Discussion: In conclusion, rs6983267 did not show any significant association with esophageal cancer in these patients. This might be due to small sample size or the effect of interacting factors. Therefore, we suggest to study this SNP in combination with other SNPs and also in a larger sample size to confirm the results.

Keyword: Esophageal cancer, Single-nucleotide polymorphism, 8q24 region, rs6983267

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Anti–cancer effect of immobilized whey proteins on grapheme oxide Nano sheets on human breast cancer cell line MCF-7

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Objective: Breast cancer is one of the common malignancies in women worldwide. Due to the increasing incidence of cancer and toxicity of chemotherapeutic agents, development of an effective therapeutic method without side effects is an urgent need. Recently, protein immobilization has aroused much interest because it can improve protein efficiency. Therefore, the aim of this study was to evaluate of anti–cancer effect of immobilized whey proteins on graphene oxide.

Material and methods: Cytotoxicity and mechanism of cell death induced by the immobilized whey proteins were analyzed by MTT assay and flowcytometery method respectively.

Results: The results showed that immobilized whey proteins have potent cytotoxic activity against MCF–7 cells in a dose dependent

manner, while they did not have cytotoxicity against cell lines HTB–22. Immobilized forms of whey proteins inhibited the MCF–7 growth by 69 and 87% during 24, 36, and 48 h, respectively but did not have inhibitory effect on normal cell lines. The apoptosis level of MCF -7 in flow cytometry was 70 and 86% in 24 and 48 h, respectively.

Conclusion: Since anti–cancer potential of immobilized whey proteins on silver nanoparticles is more than native whey proteins, it can be taken as a cytotoxic agent on MCF–7 cells.

Keywords: Whey, Lyophilized, Immobilization, Breast cancer, Apoptosis

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ID:788

An anthropometric measurement is Conversely Correlated to LAMP-2 Gene Expression Level: A Predictor for diseases like atherosclerosis

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Objective: The nutritional assessments are merged with cellular events to understand the role of food on progression of nutrition-related diseases which can act as early predictors for atherosclerosis. The associations between anthropometric measurements and lipid profile may affect cholesterol homeostasis through lysosomal entrance system. Since lysosomal membrane LAMP-1 and LAMP-2 proteins are effectively involved in cholesterol transportation. The aim of this study was to investigate the relation between gene expression levels and anthropometric measurements.

Material and methods: The community-based survey was conducted with 126 healthy volunteers in the study. The LDL-C, HDL-C, and TC values were measured by routine laboratory techniques. The HC, WC, and WHR measures were calculated on the basis of current anthropometric material and methods. The LAMP-1 and LAMP-2 expression levels were measured by Real Time qPCR technique.

Results: The results indicated that the HC, WC, WHR measures are significantly related to BMI value (r 0.6, p 0.0001; r 0.6, p 0.0001; r 0.1, p 0.006, respectively). The LAMP-2 expression level was conversely related to LDL-C value, based on normal upper range (>130mg/dl, $p<0.005$). Furthermore, these results were studied between the gender groups which showed the LAMP-2 expression level was conversely correlated to WHR among males (r -0.37; $p<0.05$).

Conclusion: Our data showed that the LAMP-2 expression level is reduced when the serum LDL is above the normal range (>130mg/dl). In addition, we suggested that the increase of WHR may indiate the increase of intracellular cholesterol synthesis due to the decrease of cholesterol uptake.

Keywords: LAMP, Lipid, Anthropometric measurements, WHR, atherosclerosis

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Oxidative modifications of human hemoglobin during exposure to iron-catalyzed oxidation systems

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Objective: The main aim of this study was to describe the oxidative effects of of iron on human hemoglobin.

Material and methods: Oxidative changes in hemoglobin were studied by spectrophotometric analysis. Protein oxidation was estimated by carbonyl groups assay. Oxidative damage in erythrocyte membrane was investigated according to structural changes in cytoskeleton proteins by sodium dodecyl sulfate polyacrylamide gel electrophoresis and staining with Coomassie briliant blue G-250.

Results: Increase in optical density (OD) at 340 nm showed a significant change in globin and heme interaction, which predicted for low oxygen affinity. Formation of methemoglobin (metHb) was represented by an increase in optical density at 630 nm. Also there was a marked elevation in hemichrome content of erythrocytes in comparison to control groups. A decrease in OD420 showed a significant decrease in oxyHb concentration and conversion of oxygen hemoglobin to methemoglobin. Interestingly, elevated levels of carbonyl groups confirmed the oxidative damage in human erythrocytes. Also a positive correlation was observed between hemoglobin absorbance at 340 nm and iron concentration. Analysis of membrane proteins showed a slight decrease in the intensity of α-spectrin band and molecular aggregates in the range of 150 to 180 kD.

Conclusion: These findings may be helpful in evaluating the oxidative status of erythrocytes and structural changes in Hb and membrane proteins during iron administration in patients with iron deficiency or thalassemia.

Keywords: Hemoglobin, Iron-catalyzed oxidation system, Oxidative modifications

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ID:791

Evaluation of SEPP1 and SELS gene polymorphisms (rs7579 and rs34713741) in

relation to colorectal cancer susceptibility in subset of Iranian population

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Objective: Colorectal cancer is one of the most common cancers worldwide, and according to WHO in 2013, 45 of every 100000 people were develop this cancer. In studying genetic factors that cause this cancer, attention is focused on mutations. Nowadays, extensive and numerous studies are conducted on the relationship between genetic changes such as polymorphisms and the risk for developing various kinds of cancer. Research has shown that some of selenoproteins polymorphisms are also involved in the development of various types of cancer, among which the pivotal role of rs7579 is in the SEPPI and rs34713741 in the SELS genes.

Material and methods: In this research, peripheral blood samples were randomly taken from 60 colorectal cancer patients and 74 healthy people who were matched to the patients with respect to age and gender. The DNA genomes were extracted from the blood samples using kit, and the HRM technique was employed to study two polymorphisms.

Results: HRM diagrams related to the polymorphism were analyzed, the genotypes in the case and control groups were then compared, and a significant relationship was observed between frequency distributions A,G alleles of the rs7579 polymorphism (p value=0.03). In the SELS gene, no significant correlation was found between allele frequency and genotypic distribution in rs34713741 polymorphism and colorectal cancer. (pvalue=0.93).

Conclusion: Based on results of this study, we can suggest that there is a significant relationship between the rs7579 polymorphism of the SEPPI gene and increased risk for colorectal cancer development. In this study, there was not found any significant relationship between rs34713741 in the SELS gene and colorectal cance

Keywords: Colorectal cancer, SEPPI gene, SELS gene, Gene polymorphism, HRM

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ID:793

Investigating the activity of Arylesterase in patients with esophageal cancer

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Objective: Cancer has the highest disease-related mortality rate in Iran. Esophageal cancer is among the 10 most frequent cancers in the world. Iran is one of the known areas with a high incidence of esophageal cancer. The most fundamental cause of cancer is known to be oxidative stress. Low level of antioxidants increased free radical activities and significantly increases the risk of cancer. Reduction of antioxidant enzymes such as arylesterase plays an important role in the pathogenesis of esophageal cancer. So the aim of this study was to investigate ARE activities in esophageal cancer in comparison with healthy persons.

Material and Methods: During this case control study, 25 patients with esophageal cancer and 25 normal subjects were selected (considering the inclusion and exclusion criteria) by simple sampling. After obtaining written consent from them, blood samples were prepared. Arylesterase activity was measured with phenyl acetate (Fluka) according to the method proposed by Gan. Data analysis was done using SPSS software, version 22. The t-test was used to compare the groups and assess their difference.

Result: Upon matching of case and control groups, arylesterase activities in patients with esophageal cancer showed to be significantly lower than healthy subjects ($P<0.001$).

Conclusion: It was concluded that in patients with esophageal cancer, oxidative stress was raised by attenuation of arylesterase activities and oxidant levels rising.

Keywords: Arylesterase, esophageal cancer, oxidative stress

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ID:800

Evaluation of marker of lipid peroxidation (MDA) and its correlation with insulin resistancein women with polycystic ovary syndrome

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Objective: Polycystic ovary syndrome (PCOS) is common endocrinopathies which affects 15.2% Iranian women at the reproductive age. Insulin resistance is a common feature of this syndrome. PCOS is also associated with oxidative stress changes. Insulin resistance can augment oxidative stress in due to high levels ofglucose and free fatty acids. The goal behind present study was to evaluate the correlation between malonyldialdehyde (MDA)

serum and insulin resistancein PCOS and control groups.

Material and Methods: This case-control study was carried out 60 women with PCOS and 90 healthy women as control group. All women were 20-40 years old who referred to Fatimah Zahra Infertility and Reproductive Health Research center, Babol in 2015 and PCOS was diagnosed according to the Rotterdam criteria (2003). Insulin, MDA were measuredusing ELISA and TBARS methods respectively. Also homeostasis model assessment for insulin resistance (HOMA-IR) was calculated Correlations between MDA and HOMA-IR were evaluated by spearman correlation test.

Results: It was found that the mean of serum MDA, fasting insulin and HOMA-IR were significantly higher in the PCOS group compared with matched controls ($p<0.001$, $p=0.003$ and $p=0.008$ respectively), but no significant correlation was found between MDA and HOMA-IR in both group.

Conclusion: This study revealed that there is significant increase oxidative stress and insulin resistance in PCOS group compare with control group. Also, no correlation was found between the serum MDA and insulin resistance.

Keywords: Polycystic ovary syndrome, Insulin resistance, Oxidative stress, Malondialdehyde

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ID:801

Comparison of continuous and non-continuous aerobic exercise on serum vascular endothelial growth factor (VEGF) and Endostatin (ES) in male rats with coronary artery disease

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Objective: Cardiovascular diseases (CVD) are considered as the fatal diseases worldwide. Physical activities are associated with decreasing the risk of coronary heart disease (CHD) which is one of the widespread CVDs. The purpose of the presented study was to investigate the effect of discontinuous and continuous aerobic exercise on serum VEGF and ES in rats with coronary artery disease.

Material and Methods: A group of forty healthy rats were divided into different groups including discontinuous and continuous aerobic exercise group with coronary artery disease, control group with coronary artery disease and healthy control group. After rupturing the rats by isoproterenol, rats in the experimental group performed discontinuous and continuous aerobic exercise on a treadmill. Then blood samples were collected for serum VEGF and ES indices.

Results: From the gained results, it is proved that both types of continuous and non-continuous aerobic exercises could increase the blood VEGF in rats with coronary artery disease ($p=0.01$), while there was no difference in the level of endostatin in the experimental group compared with control groups ($p>0.05$).

Conclusion: As a conclusion, discontinuous and continuous aerobic exercises can be used in the rehabilitation of patients with coronary artery disease, additionally, these methods might be effective in the process of angiogenesis.

Keywords: coronary artery disease, discontinuous aerobic exercise, continuous aerobic exercise endostatin, vascular endothelial growth factor

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ID:804

Analysis of water and methanol extracts from a red alga Dichotomaria obtusata by GC-MS

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Objective: Marine algae have various biological and medicinal benefits such as anti-cancer, anti-inflammatory, antioxidant, antibacterial and antifungi effects. The aim of the present study was the analysis of water and methanol extracts from a red algae Dichotomaria obtusata to find the potent beneficial ingredients of the algae.

Material and Methods: Dichotomaria obtusata were collected in June 2017 from the coastal area of Bushehr City in Persian Gulf, Iran. The red algae was transported to the laboratory, cleaned and dried. The dried seaweed was ground to a fine powder for preparaton of methanol and aqueous extract. The analyses of the algae extracts was performed by gas chromatography-mass spectrometry (GC-MS).

Results: The GC-MS analyses of the algae extracts resulted in identification of twenty substances in the methanol and water extract

of D. obtusata. for the major ingradients were free fatty acids (FFAs) such as palmitic acid, Myristic acid, steroids (desmosterol, squalene), phenolics, indole, cyclobarbital and biphenyl.

Conclusion: FFAs from marine algae were reported as antibacterial against several test organisms. Therefor; it is suggested that D. obtusata extracts may have an antibacterial effect. Moreover, due to the presence of flavonoids, it may have favorable effects on bone metabolism especially on osteoporosis. This is the first report of the extract analysis of Dichotomaria obtusata from Persian Gulf using GC-MS which can clarify its beneficial effects in treatment and management of several disorders.

Keywords: Red algae, Dichotomaria obtusata, GC-MS

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Assessment of synthesis and absorption markers of cholesterol in type2 diabetes

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Objective: Type2 diabetes is a group of metabolic diseases that are associated with hyperglycemia, resulting from deficiency in the human body's ability to secretion or action of insulin. Several factors are involved in the pathogenesis of diabetes including the metabolic irregularities of cholesterol and non-cholesterol sterols. Themeasurement of serum noncholesterol sterols have been used as surrogate markers of cholesterol absorption and synthesis in clinical lipid research. Various studies have suggested that there is a relationship between this markers and type 2 diabetes mellitus (DM2). In this study, the concentration of sitosterol and lathosterol as absorption and synthesis marker was investigated.

Material and Methods: This cross-sectional study contained 155 male subjects divided into two groups as healthy controls (50 non-DM2 volunteers) and patients with DM2, (105 sample). The analytical method in this study for measuring the concentration of synthesis and absorption markers of cholesterol in blood plasma was gas chromatography and mass spectrometry (GC-MS).

Results: According to statistical analysis, Sitosterol level was significantly decreased in DM2 groups compared with controls ($p<0.006$) and also significant difference was shown in lathosterol level between DM2 groups with controls ($p<0.01$) and lathosterol level was higher than sitosterol level.

Conclusion: This study showed that cholesterol metabolism maybe altered in DM2 and is associated with high cholesterol synthesis and low absorption. This may contribute to the pathogenesis of DM2.

Keywords: Type 2 diabetes, synthesis and absorption markers of cholesterol, gas chromatography-mass spectrometry (GC-MS)

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Studies on paxillin expression in 4T1 mammary carcinoma tumors treated with an anti-VEGF receptor peptide

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Objective: The breast cancer is one of most common cancers among women worldwide. Tumor growth and metastasis depend on angiogenesis triggered by chemical signals from tumor cells. Angiogenesis, the formation of new blood vessels from pre-existing vessels, is a prerequisite for tumor growth to supply the proliferating tumor with oxygen and nutrients. Due to the important role of Vascular endothelial growth factor (VEGF) in the induction of angiogenesis, so prevention of this function must be effective way in inhibition of angiogenesis and proliferation of tumor cells. VEGF-binding molecules appear to regulate VEGFR1 and VEGFR2 mediated downstream signaling cascade several intermediary signalling molecules such as paxillin. Paxillin is a cytoskeletal protein that colocalizes at focal adhesion contacts. Currently, increasing evidence has demonstrated that the paxillin signaling pathway participates in the processes of cancer invasion and metastasis via different molecular mechanisms. Disrupting the paxillin pathway blocks the migration and invasion of cancer cells. Therefore paxillin pathway activation is recognized as a potential predictor of cancer metastasis. Increased paxillin expression have been observed in many malignant human tumors.

Materials and Methods: In this study, we assessed paxillin gene expression level in breast tumor-bearing Balb/c mice either treated with PBS or antagonistic peptide. Total RNA was isolated using Trizol reagent (Invitrogen) followed by cDNA synthesis. Real time PCR carried out using specific primers and relative expression of paxillin gene assessed, and analyzed by the SPSS software.

Results: Our Results indicated that the expression level of paxillin gene remarkably

reduced in the peptide-treated against of control groups.

Conclusion: This finding demonstrated that the sequesterated VEGFR-1 and VEGFR-2 followed by inhibition of activation of paxillin gene can caused to reduced the cell migrating of 4T1 breast cancer tumor model, suggesting that paxillin is a downstream signalling target of the antiangiogenic peptide.

Keyword: Tumor angiogenesis, Antagonistic peptide, Paxillin, Real time PCR

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The protective effect of Zataria multiflora Boiss essential oil on CCl4 induced liver fibrosis in rat via down-regulation of bFGF and IL-1β

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Objective: Hepatic stellate cells (HSCs) activation is an essential step in the development and progression of liver fibrosis. Many factors such as growth factors (FGFs) and inflammatory mediators (ctyokines) can attribute in HSCs activation. In other hand, Zataria Multiflora Boiss essential oil has anti-inflammatory effect and may had a preventive effect on the development of liver fibrosis. Thus, in the present study the protective effect of Zataria Multiflora Boiss essential oil on CCl4 induced liver fibrosis was evaluated with regard to the expression of bFGF and IL-1β.

Material and Methods: Male rats were divided into 5 groups, C: control rats; CO: vehicle control group; CE: rats that received essential oil (500µl/kg); F: fibrosis group that was given CCl4 (1mg/kg); FE: fibrosis rats that received both CCl4 and essential oil with mentioned dosages. At the end of the 11th week, liver tissues were collected for analysis of bFGF and IL-1β expression by real time RT-PCR and histopathological evaluations.

Results: The Results of histopathological study showed that the development of liver fibrosis with 5.35±1.34 score in F group, while in FE group fibrotic index was 3.1±0.73. Also, the expression of bFGF and IL-1β significantly were increased in F group compared to C group. But, Zataria Multiflora Boiss essential oil could significantly modulate their expression.

Conclusion: Zataria Multiflora Boiss essential oil could had a protective effect on CCl4-induced liver fibrosis with down-regulation of growth factor (bFGF) and inflammatory cytokine (IL-1β).

Keywords: Zataria Multiflora Boiss, essential oil, liver fibrosis, carbon tetrachloride, bFGF, IL-1β, Zataria Multiflora Boiss

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Investigation sitosterol and lathosterol in serum of patients with coronary artery disease

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Objective: Today, cardiovascular disease is one of the main causes of morbidity and death. One of the most important risk factors for developing cardiovascular disease is high blood cholesterol levels. Serum non-cholesterol sterols are considered as successor markers of cholesterol absorption and synthesis. Lathsterol is a precursor to cholesterol which is believed as a marker of cholesterol synthesis while, sitosterol is a marker of cholesterol absorption.

Material and Methods: The standard method for analyzing cholesterol serum markers in blood plasma is gas chromatography and mass spectrometry (GC-MS). In this method, sterols are extracted from physiological fluids and, after derivatisation, are analysed by gas chromatography mass spectrometry. The study population included 128 patients, undergoing clinically indicated coronary angiography. The severity of coronary stenosis was scored after coronary angiography, and patients were divided into 2 groups; the stenosis group (CAD patients, n = 74) had a significant stenosis indicated by coronary angiography and the second group, N-stenosis (control, n=54), had no significant coronary stenosis.

Results: The Results of the analysis show that the level of sitosterol in the group CAD patients (stenosis) decreased compared with patients without coronary artery (N-stenosis) ($P<0.18$), according to statistical analysis, there is no significant difference between the two groups. Also level of lathsterol in the group CAD patients (stenosis) increased compared with patients without coronary artery (N-stenosis) ($P<0.01$), according to statistical analysis, there is significant difference between the two groups.

Conclusion: Overall, various studies have shown that the concentrations of these markers will be different between the control and the patient group and the results of this

study indicate that in patients with coronary artery stenosis, cholesterol absorption is not significantly different, but cholesterol synhesis in patients with coronary artery disease decreased.

Keywords: Coronary artery disease, markers of cholesterol absorption and synthesis, G Chromatography-Mass Spectrometryas

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ID:819

Assessment of erythrocyte Na^+K^+-ATPase activity in type 2 diabetic patients

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Objective: Unfavorable alteration of erythrocyte membrane Na^+K^+-ATPase activity is thought to play an important role in pathophysiology of diabetic complications, but its relationship to glycemic status and other biochemical parameters is poorly understood. This study aims to evaluate erythrocyte membrane Na+K+-ATPase activity and its relationship to atherogenic and anti-atherogenic parameters in type 2 diabetic patients.

Material and Methods: This cross-sectional study comprised 90 type 2 diabetic patients and 40 non-diabetic control groups. Fasting plasma levels of glucose (FPG), total cholesterol, triglycerides, HDL-C, LDL-C and HbA1c were determined in the study subjects. Erythrocyte membrane were prepared for the estimation of Na^+K^+-ATPase activity by osmotic lysis in terms of inorganic phosphate released/mg protein/hour.

Results: Significant reduction in erythrocyte membrane Na^+K^+-ATPase activity was seen in diabetic patients compared to the control group (0.509±0.08 and 0.949±0.07 µM Pi/mg protein/h respectively) ($P<0.05$). Na^+K^+-ATPase activity was negatively correlated with FBS ($r= -0.18$, $P= 0.044$), HbA1c ($r= -0.214$, $P= 0.030$) and waist- hip ratio ($r= -0.183$, $P= 0.043$) and positively but non-significant, correlated with HDL-C ($r= 0.161$, $P= 0.072$) in diabetic patients. FBS, triglycerides, HbA1c, weight, waist and hip circumferences, waist-hip ratio and BMI were significantly higher and HDL-C was significantly lower in diabetic patients compared to control group.

Conclusion: The data indicates significant correlation between lower levels of erythrocyte Na+K+-ATPase activity and bad glycemic status in diabetic patients. Unfavorable changes of erythrocyte membrane Na+K+-ATPase activity and serum lipid profile, might explain some of the pathogenetic mechanisms of diabetic complications.

Keywords: Erythrocyte membrane, Na+K+-ATPase activity, Type 2 diabetic patients

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ID:824

Investigation of an isothermal amplification-based method for specific identification of Morganella morganii

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Objective: Morganella morganii is a gram-negative rod in the Enterobacteriaceae family. Although, it is mostly found as normal flora in the intestinal tracts of human mammals, however, M. morganii could serve as an opportunistic pathogen mainly causing nosocomial infections and hospital diseases mostly infecting urinary tract. Therefore, its timely and precise detection seems to be crucial.

Materials and Methods: The standard strain of M. morganii and nine other related bacteria was purchased. Briefly, the bacteria were cultured in nutrient broth and DNA was extracted from the cultured colonies. Nucleic acid content of the cells was subjected to isothermal amplification-based detection using specific primers of M. morganii. For specificity assessment, all strains were amplified separately using the designed primers. In addition, a mixture of all bacteria was prepared to analyze selectivity of the method. Amplicon detection was performed by agarose gel electrophoresis.

Results: According to the results, a ladder like pattern on the gel was supposed as positive presence and successful identification of M. morganii among other bacteria both in separate samples and the mixed sample. Therefore, specific detection of M. morganii was found to be possible by the designed method.

Conclusion: The designed method requires neither temperature alteration, nor high cost instrumentation and reagents. Therefore, it could be used as a point-of-care diagnostic approach for rapid detection of pathogens especially those causing secondary hospital infections.

Keywords: Morganella morganii, isothermal amplification, point-of-care diagnosis, infection

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Study on the effect of charged amino acids on thermal amorphous aggregation of human lysozyme with in vitro and in silico tools

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Objective: Misfolding and aggregation of proteins affects adversely their structure and function. These changes in proteins may result in the appearance of diseases in vivo, while causing serious problems in the half-life of proteins used or produced by food and pharmaceutical industries. Lysozyme is of significance in these industries, since it is used as natural food preservative, antimicrobial in cheese, antibiotic in chicken food and inhibitor of the growth of HIV virus in vitro. Since amino acids could preserve the stability of proteins, it would be beneficial to investigate the effect of their various structures on protein aggregation process.
Material and Methods: For in vitro experiments, we used UV-Vis spectrophotometer to and transmission electron microscopy (TEM) to generate and study the aggregation process of human lysozyme. For in silico experiments, docking was made by Autodock Vina softwares, and aggregation-prone regions of the enzyme were predicted by AGGRESCAN, and Tango programs.
Results: The result obtained from these experiments showed that between the tested amino acids, positively charged ones were the best in reducing heat-induced aggregation of human lysozyme.
Conclusion: Therefore, it is possible that these amino acids, by increasing protein solvability and stabilization of protein structure, could be effective in reducing protein aggregation problems in the medical, pharmaceutical and food industries, and even in the prevention of aggregation-related diseases caused by protein aggregation.
Keywords: Protein amorphous aggregation, Human Lysozyme, Heat-induced aggregation
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The effect of metformin and curcumin combination on high glucose-induced lipogenesis in HepG2 cells

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Objective: Control of type 2 diabetes and its associated lipid disorders are the medical challenges facing the world today. Metformin, as the first line of treatment, has potentially harmful side effects. Combination therapy is a novel approach to reduce these complications and increase the effectiveness of metformin. Since plant polyphenols, such as curcumin, have been reported to have hypolipidemic effects, we in this study aimed to study the combination effect of metformin and curcumin on lipogenesis in a model of hepatocyte, HepG2 cells.
Material and Methods: 33mM glucose was used to induce lipogenesis in HepG2 cells. MTT test was used to obtain non-lethal doses of metformin and curcumin. After treatment of the cells with different concentrations of metformin and curcumin, total lipids (Oil Red O-test), triglyceride levels, and the expression of genes involved in lipogenesis (FAS and SREBP-1c) was measured.
Results: Metformin and curcumin, both significantly decreased high glucose-induced lipogenesis by decreasing total lipids and triglyceride levels ($p<0.001$). The lowest effective dose of metformin and curcumin were 0.25mM and 5µM, respectively. The combination of these concentrations greatly enhanced this effect ($p<0.001$). The lowest effective doses of metformin and curcumin significantly reduced the expression of FAS and SREBP-1c in high-glucose treated cells. The combination of metformin and curcumin reinforced these effects.
Conclusion: Our findings suggest that curcumin can potentially increase the efficacy of metformin through enhancing the inhibition of FAS and SREBP-1c expression.
Keywords: lipogenesis, metformin, curcumin, HepG2
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ID:836

Combined application of lithium chloride and mitomycin C reduces metastasis and induces G2/M cell cycle arrest in MDA-MB-231 breast cancer cells

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Objective: Breast cancer is the main reason of cancer mortality in females. Mitomycin C (MMC), as a potent antitumor drug, is used for the treatment of various types of cancers, however, adverse toxic effects and resistance of cancer cells, have limited the application of MMC suggesting combination of MMC with novel biological agents. Recent studies indicate that lithium possesses antitumor and anti-metastasis activity in different types of malignancies. In the present study, we aimed to explore the effect of MMC combined with lithium chloride (LiCl) on cell death, metastasis and cell cycle arrest in MDA-MB-231 breast cancer cells.

Material and Methods: MDA-MB-231 breast cancer cells were exposed to various concentrations of mitomycin C alone and combined with LiCl and viability determined by MTT assay after 24 h incubation. To test if MMC plus LiCl inhibit metastasis, we assessed mRNA expression of MMP9 by RT-PCR and colony-forming assay. To determine whether the cell proliferation inhibition was because of cell cycle arrest, cell-cycle analysis performed using PI staining and flow cytometry analysis.

Results: LiCl synergistically promoted cytotoxicity induced by mitomycin C and IC50 value of MMC declined from 20 µM to 5 µM. LiCl combined with mitomycin C significantly down-regulated MMP9 gene expression as an important biomarker of metastasis. Also, combination of LiCl with MMC reduced the ability of cells to form colonies. Cell-cycle analysis revealed that an obvious accumulation of cells are in Go/G1 phase in the control, whereas in the cells treated with LiCl plus MMC, the fraction of cells in the G2/M phase is significantly increased indicating that LiCl enhanced MMC-induced apoptosis through arrest of MDA-MB-231 cells at G2/M phase.

Conclusion: Taking all together, these findings demonstrate that combination of LiCl with MMC represents potential anti-metastatic and anti-proliferative effects, and this combination could be a promising candidate therapy for the treatment of breast cancer.

Keywords: Lithium, Mitomycin C, Metastasis, Cell cycle arrest, Breast cancer cells

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Cofilin, a mediator of VEGF signaling, downregulated by blockade of VEGF receptors with an anti-angiogenic peptide in the breast cancer bearing Balb/c mice

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Objective: Angiogenesis is the main mechanism for the formation of new vessels in adults. VEGFs are important regulators of vascular development during health and disease which comprise of five members and acting on vascular endothelial cells through three VEGF receptors (VEGFRs), including VEGFR1, VEGFR2, and VEGFR3. Tumor angiogenesis plays a key role in metastasis. In tumor cells stimulated by growth factors, the activation of cofilin initiates actin polymerization, which leads to cell migration. Thus, cofilin pathway is essential for cell motility and metastasis. In this study, we investigated the cofilin expression in the breast cancer bearing model mice treated by a peptide that neutralizes VEGFR1 and VEGFR2.

Material and Methods: The breast cancer bearing model mice were divided into two groups, PBS and anti-angiogenic peptide-treated mice. Total RNA was extracted from tumor tissues using TRIzol reagent followed by cDNA synthesis. The level of cofilin expression was determined in breast tumor tissues by Real-time PCR using cofilin specific primers, and was evaluated the quantitative expression of cofilin against GAPDH as the reference.

Results: The treated mice showed less cofilin expression against control. Therefore, we found that decrease the level of cofilin expression by blockage of VEGFR was mediated by the antagonistic peptide. In other words, the VEGFR antagonist peptide leads to angiogenesis inhibition and reduces the tumor size.

Conclusion: These findings suggest that cofilin expression may be a useful strategy to address the downregulation of angiogenic signals and may be regarded as a novel target for drug design in cancer therapy.

Keywords: Breast cancer, anti-angiogenic peptide, cofilin, Real-time PCR

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Induction of Endoplasmic Reticulum Stress by Tunicamycin in ovarian cancer cell lines

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Objective: Recently, induction of apoptosis via ER stress is the strategy for cancer therapy especially in ovarian cancer. The aim of this study was to investigate ER stress induction in ovarian cancer cells by TM and confirm by quantitative real-time RT-PCR.

Material and Methods: Ovarian cancer cells (OVCAR-3 and SKOV-3) were used in this study. The cells were seeded into 15-cm diameter plate and were treated with Tunicamycin (2.5µM) and incubated for several times (0, 6, 12, and 18 hr). The mRNA

expression levels of the ER stress markers including XBP-1, sXBP1, Chop and ATF4 were determined by real-time RT-PCR and normalized by GAPDH expression.

Results: TM significantly increased the expression levels of XBP-1, sXBP1, Chop and ATF4 genes in time dependent manner. This effect was more obvious in expression of sXBP1 (5.5 fold in skov-3 and 2.5 fold in ovcar-3), XBP1 (8 fold in skov-3 and 4.5 fold in ovcar-3), and ATF4 (3fold in skov-3 and 1.5 fold in ovcar-3) than CHOP (5 fold in skov-3 and 3,5 fold in ovcar-3).

Conclusion: Our Results showed that Tunicamycin induced ER stress in ovarian cancer cell lines. Moreover, XBP1 is the best sensitive gene marker for determining activated UPR.

Keywords: ER stress, Tunicamycin, ovarian cancer, XBP1, UPR

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Supportive roles of fibrin scaffold in increasing of expression and cardiac protein markers during of differentiation of human adipose-derived stem cells

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Objective: Human adipose-derived stem cells (hADSCs) are potentially predisposing for clinical application of tissue engineering as like as cardiac tissue, because of its easy isolation from the patients and high capability of these cells to amplify and it's differentiation in culture is the most advantage for autologous transplanting to same patients. Suitable scaffold helps to protect, attachment and active orientation of the cells. The main purpose of this study focused on the possibility of better amplification and differentiation of hADSCs towards to the cardiac-like cells in fabricated fibrin scaffold, in comparison with culture plates, by checking the expression levels of cardiac protein markers.

Material and Methods: After approving the characteristics of hADSCs by flow cytometry and differentiation of hADSCs into adipocytes, osteocytes and chondrocytes, treated cells with trichostatin A (TSA) cultured in scaffold (3D) and plates (2D) were followed until 4 weeks. The morphology of the scaffold was characterized by Scanning Electron Microscopy. Immunochemistry assays and qRT-PCR were used to evaluate the expression of special cardiac proteins and genes such as NKX2.5, Cx43 and cTnI in treated hADSCs in 3D and 2D groups.

Results: Immunochemistry assay and qRT-PCR showed the significantly higher expression of special cardiac genes such as NKX2.5, Cx43 and cTnI in TSA treated hADSCs in the 3D group in comparison with 2D group ($P<0.05$).

Conclusion: The Results had shown that the fibrin scaffolds allow a higher and sooner differentiation of hADSCs into cardiomyocyte-like cells treated especially TSA and can lead to the expression of special cardiac genes in a shorter period of time in comparison to 2D.

Keywords: Human ADSCs, Cardiomyocyte-like cells, Fibrin scaffold

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Molecular Docking Studies of endonuclease inhibitors for IRE1

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Objective: ER stress is an important Causes of diseases especially developing cancer. Serine-threonine kinase/endonuclease depending Inositol-1 protein (IRE1) is an enzyme that possesses intrinsic endonuclease and protein kinase activity and is reactivated in ER stress network. Endonuclease activity lead to cell survive. IRE1 endonuclease Inhibitors have recently used as anti-cancer drug. In this study, the molecular docking studies of three different IRE1 endonuclease Inhibitors, MKC-3946, 4UC8 and STF-083010.

Material and Methods: The pdb file IRE1 and STD files of endonuclease inhibitors, MKC-3946, 4UC8 and STF-083010 were obtained from Protein Data Bank and Pub Chem respectively. For converting STD to pdb format, OpenBable GUI version 2.3.2a was used. AutoDock 1.5.6 was used for molecular docking.

Results: The Results have showed that the synthesized ligand STF-083010 favorably well with the standard ligands. The best binding affinity is in ligand STF with -5.97. Also, the Results: showed that the STF derivatives gave better binding interaction than ligand MKC and 4UC8. The S atom in the ring of STF derivative as the hydrophobic group and SO2 group as the acceptor band gave binding affinities values (-5.9797 Kcal/mol) for IRE1. This interaction in

STF have enhanced the binding affinity compare another ligands.

Conclusion: The sited ligands carry out binding energy in the selected receptor (IRE-1). STF-083010 was favorable affinity and have the best interaction for IRE1. Our Results: suggest STF as a suitable ligand for cancer therapy.

Keywords: Molecular docking, STF, IRE1, inhibitor, ER stress

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Immobilization of recombinant uricase on the Metal-Organic Framework (Ni-MOF) to improve enzyme stability

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Objective: Uricase (EC 1.7.3.3) converts uric acid to allantoin. This enzyme (34kDa) mainly used for therapeutic goals and diagnostic objectives. Despite having many applications, its low stability is one of the major problems for use in industry. So far many methods have been used to stabilize uricase, such as PEGylation and use of additives. In this study Metal-Organic Framework (Ni-MOF) is used as a support for immobilization of uricase.

Material and Methods: The strain BL21 includes pET28a-uricase vector was used. Recombinant uricase was expressed in the presence of 1 mM IPTG at 37°C for 5h and purified by Ni-NTA column. The quality of purified enzyme determined by SDS-PAGE. Then, Ni-MOF crystals washed twist with Tris/HCl (50 mM) and employed to immobilize uricase. The optimum time for incubation of uricase with Ni-MOF calculated by investigation of fluorescence spectra of protein. The activity of the naked and immobilized enzyme was assayed and compared to various conditions.

Results: The Results show that the best time for immobilization of uricase (0.15 mg/ml) on the Ni-MOF (0.5 mg) was 30 minutes. Comparing of the optimum temperature displays that binding of uricase to particle caused of remaining activity of the enzyme at 40 to 65 °C, while naked enzyme inactivated at the temperature above 35°C. Result belongs to calculating of activity in various pH solution shows that the optimum pH for activity of immobilized uricase increased 1.0 unit, relative to the naked enzyme. Also, the Results: of thermal inactivation indicated that the half-life of the immobilized enzyme was 15 min at 55°C, while free enzyme loses its activity within about 30 seconds.

Conclusion: The obtained Results indicate that Ni-MOF due to having Ni ion can bind to recombinant protein (including His-tag) with high affinity. These interactions between enzyme and support were formed in a way that protein folding was preserved. So that caused the increased stability of enzyme at high temperatures and pH.

Keywords: Recombinant uricase, Metal-Organic Framework, Immobilization, Stability

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Kinetic study of immobilized alcohol dehydrogenase: A comparison between physical adsorption and chemical immobilization

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Objective: The enzyme immobilization methods are identified either as chemical or physical procedures based on the nature of bonding. In this study, kinetic parameters of immobilized alcohol dehydrogenase and immobilization yield were investigated to evaluate the pros and cons of these two methods.

Material and Methods: For physical immobilization, 5 mg titania nanoparticles were dispersed in an alcohol dehydrogenase solution (1 mg/ml) in different pHs (5-9) for 5 minutes to 4 hours. For chemical immobilization, the nanoparticles were functionalized with (3-Aminopropyl) triethoxysilane; then crosslinked with Glutaraldehyde. Functionalized support dispersed in phosphate buffer and mixed with alcohol dehydrogenase solution (1 mg/ml) for 5 min to 4 h. kinetic parameters were investigated by using formaldehyde as a substrate and NADH as a cofactor.

Results: Unlike chemical immobilization, in covalent bonding, the immobilized enzyme was debonded after washing, since the driving force of immobilization in physical immobilization is electrostatic and

hydrophobic interaction. On the other hand, the Micaelis constant (Km) of immobilized enzyme in chemical and physical immobilization is about 23 mM and 11 mM, respectively, compared to the free enzyme (11.5 mM). Moreover, catalytic efficiency of the immobilized enzyme in chemical immobilization is a quarter of physical immobilization value.

Conclusion: The kinetic parameters of covalently immobilized enzyme are being degraded than those of physical adsorption due to a lower affinity of enzyme for substrate in the chemical immobilization. On the other hand, the strength bond in chemical bonding is very strong compared to the physical one.

Keywords: Alcohol dehydrogenase, physical and chemical immobilization, titania, kinetic parameters

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ID:861

Autophagy and DAPK1

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Objective: Autophagy consists of several sequential steps sequestration, transport to lysosomes, degradation, and utilization of degradation products. This process is quite distinct from endocytosis-mediated lysosomal degradation of extracellular and plasma membrane proteins. Autophagy has opposing, context dependent roles in cancer. It plays a complex dual role in tumorigenesis and can behave similarly as a tumor suppressor (acting to prevent tumor initiation) or as a tumor promoter to ensure tumor longevity via apoptosis inhibition. Reduced autophagy can contribute to tumor progression, whereas increased autophagy may be a mechanism for tumor survival under hypoxic, metabolic, or therapeutic stress conditions. The first studies in the 1990s pointed to the relationship between autophagy and tumorigenesis and showed that about 50% of prostate, breast, and ovarian cancers have an absence of one Beclin1 allele that codes for Beclin1, a key component in the autophagosome nucleation. A critical and important regulator of cell death and autophagy is Death-associated protein kinase 1 (DAPK1). DAPK1 belongs to a family of five serine/threonine (Ser/Thr) kinases that possess tumor suppressive function and also mediate a wide range of cellular processes, including apoptosis and autophagy. The loss and gain-of-function of DAPK1 is associated with various cancer and neurodegenerative diseases respectively. Recent research indicates communications between cellular organelles under cancerous and neurodegenerative conditions where in endoplasmic reticulum stress, inflammation, oxidative stress and autophagy are the signaling pathways. Both cancer and neurodegenerative disease have been linked with misregulated autophagy, and to loss and gain-of-function of DAPK1, respectively. Thus it will be interesting to determine DAPK1's autophagic functions contribute to its role in these pathologic conditions.

Keywords: autophagy, DAPK1, cancer

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Beta Boswellic Acid enhances spatial learning and memory by reduction of tau phosphorylation level and increase of Reelin expression in the hippocampus regions of adult male rats

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Objective: One of heterocyclic compounds that plays an inhibitory role on protein kinases, is beta boswellic acid (BBA). A few protein kinases induce hyperphosphorylation of tau protein and acts as a destructive factor on memory. To evaluate the effect of BBA on Reelin expression for regulation of hyperphosphorylated tau protein, acute and chronic dose of the herbal component were utilized.

Material and Methods: Four rat groups received different doses of BBA, intracerebroventricularly. Then, their spatial memory was assessed by behavioral tests like Morris Water Maze (MWM). Histological analysis was performed for various regions of hippocampal neurons. In addition, phosphorylation of tau protein at residues Ser396 and Ser404, and expression of Reelin protein were demonstrated by both western hybridization analysis and immunohistochemistry techniques. The alteration of astrocyte cells were evaluated using immunofluorescence.

Results: BBA (35g/kg of body weight) has a significant effect in the probe trial of MWM test. Dark neuron formation in CA1 and CA3 regions of hippocampus was reduced by BBA administration. The level of phosphorylated

tau in hippocampus was declined upon BBA injection. Astrocyte cells immigrated to the hippocampal regions to remove tau hyperphosphorylated. This component improves Reelin expression.

Conclusion: Reelin expression enhances spatial learning and memory in the presence of BBA, so it is an effective drug for reduction of hyperphosphorylated tau protein in the brain.

Keywords: Spatial Memory; Boswellic acid; Reellin; Hyperphosphorylated tau

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Inhibiting Notch Activity in liver cancer Stem Cells by Functionalized Gold Nanoparticles with SAHM1 and vitamin C

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Objective: Liver cancer is the sixth most frequent cancer and the second leading cause of cancer-related death worldwide. Hepatocellular carcinoma (HCC) accounts for over 80% of primary liver cancer cases and it is characterized by a high recurrence rate and heterogeneity. These pathological properties may flow from cancer stem cells (CSCs), which are capable of self-renewal and differentiation responsible for tumor progression, metastasis, and chemotherapy-resistance. Notch signaling has been implicated to regulate the CSC population, where it has been shown to be critical for maintenance and self-renewal of CSCs. Notch is linked to aggressive metastatic growth and therapy resistance. Notch-targeted therapy is thus an interesting treatment option. Another novel therapeutic strategy for HCC treatment is Vitamin C (VC). VC kills cancer cells and preferentially kills CSCs via SVCT-2. Utilizing these CSC features, after we made the GNPs suspension using a reference method, by adding 2 ml of trisodium citrate 1% to 50 ml of aqueous solution of 1% HAuCl4 we functionalized Au nanoparticles, carrying Notch inhibitor peptide, SAHM1, with VC to efficiently deliver Notch signaling inhibitors to CSCs via SVCT-2. The VC and peptide were co-immobilized on surface of gold nanoparticle. We aimed to enhance particle uptake in CSCs by utilizing the machinery for cellular import of VC. Our data reveal that specific CSC characteristics can be utilized in nanoparticle design to improve CSC targeted drug delivery and therapy.

Keywords: Notch inhibitor, Cancer Stem Cells, Gold nanoparticles, Vitamin C, Liver cancer

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Evaluation of galectin-9 on caspase-3 activity in two cell lines of Acute Lymphoblastic Leukemia

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Objective: Acute lymphoblastic leukemia (ALL) is a malignant of the bone marrow which it makes too many lymphocytes. Galectin-9 belong to a lectins superfamily, which are carbohydrate-binding proteins that has recently been revealed to use antitumor effects on various types of cancer cells. In general, the functions of galectin-9 in tumors include enhancing oncogenic signal pathways, regulating tumor cell growth or apoptosis, modulating cell migration, cell adhesion and suppressing immune responses. In cells undergoing apoptosis, two different mechanisms are operated: the intrinsic or extrinsic pathways. Galectin-9 plays an important role in these pathways by binding to various ligands. Anti-cancer dysregulation of apoptosis is a major hallmarks of cancer. Caspase-3 is one of the key regulators of the apoptotic response. In this study we investigated the clonogenic inhibitory capability of galectin-9 and caspase-3 activity in the induction of apoptosis by galectin-9 in Jurkat and KE-37 cell lines.

Material and Methods: The growth inhibitory effect of galectin-9 was determined by using Colony forming assay in Jurkat and KE-37 cell lines. Detection of galectin-9 on pro-apoptotic protein (Bax) and anti-apoptotic protein (Bcl-2) was conducted using Western blot in these two cell lines. To investigate caspase function in the induction of apoptosis by galectin-9, we examined the role of caspase-3 after treatment by galectin-9 in Jurkat and KE-37 cell lines.

Results: Our Results: showed that galectin-9 significantly reduced cellular colonies in a dose dependent manner (1-100 nM) in Jurkat and KE-37 cell lines. In addition, we found that galectin-9 also induced apoptosis by regulation of Bax/Bcl-2 ratio, and notable increase caspase-3 activity.

Conclusion: The present investigation introduced a possible mechanism for the control of acute lymphoblastic leukemia cell inhibition through galectin-9. Also galectin-9 can inhibit cell proliferation and induce apoptosis in Jurkat and KE-37 cell lines. Galectin-9 may be potential targets for developing novel cancer therapies.

Keywords: Acute lymphoblastic leukemia, galectin-9, apoptosis, caspase-3

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Association of Methylentetrahydrofolate Reducase (MTFR) Gene Polymorphism (C677T) with Homocysteine in Coronary Artery Disease (CAD)

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2 Cell and Molecular Research Center, Faculty of Medicine, Guilan university of Medical Sciences, Rasht, Iran***Objective:*** MTHFR is an essential enzyme for homocysteine, Metionine and Folate metabolism. The most common gene polymorphisim of MTHFR (C677T) is associate with labile enzyme and subsequently, Folate reduction and elevation of hcy level those are risk factor for cavdiovascular disease. The aim of this study was to investigate the association between genetic polymorphisim of MTHER (C677T) and coronary artery disease.

Material and Methods: This was case-control study consisted of 80 pateints with CAD documented with angiography and 80 normal controls. DNA was extracted with Rouch DNA extraction kit. Using ARMS_PCR, we studied the prevalence of MTHFR mutation (C677T) analyzed by agarose gel electrophoris and the effects of these polymorphisim on plasma level of Hcy, measured by EIA methods.

Results: The frequency of different genotype of C677T (CC, CT, TT) were determind in patient and control groups. it was (42.2%, 50% and 7.8%) in patients and (39.5%, 46.1% and 14.5%) in control groups, respectively. Also allele frequency for C and T in patients were 67.5% and 53.9% and in the controls were 62.5% and 53.3%.the mean plasma level of Hcy was 17.58 µmol/l and 13.59 µmol/l in patients and controls, respectively.

Conclusion: The polymorphism of C677T in patients are higher than control groups. But in the controversy with some other findings, especially in patients, TT genotype may be protective genetic marker for coronary artery disease. also the other biochemical risk factor for CAD is elevation of Homocysteine. The mean level of Hcy in patients is higher than controls. This may be return to mutation in 677C>T or deficiency of vit.B12 and folic acid in diet.

Keywords: Homocysteine Reductase, Coronary artery disease, C677T polymorphism, Homocysteine

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Detection of surface antigen of the hepatitis B virus based on WS2 nanoparticles by using ELISA method

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Objective: Hepatitis B virus (HBV) is one of the most common viruses that causes liver cirrhosis and acute and chronic infections. One of the main markers of viral replication in the serum of S1 proteins is the surface antigen of hepatitis B (HBs Ag) transmitted by infected hepatocytes. Given the fact that the ELISA method is capable of detecting low concentrations of specific antigens, labeled in this method can increase the sensitivity to be detectable at least as much as possible from the antigen. One of the metal nanoparticles is WS2 (IUPAC Name: bis sulfanylidene tungsten) that is used as a label for safety experiments that has high availability and, unlike enzymes, is more susceptible to pH and humidity and chemical stability than the enzymes themselves.

Material and Methods: Given that these nanoparticles have a high surface-to-volume ratio, they can be a good place to stabilize antibodies to construct the immunosensor. Also, the properties of WS2 nanoparticles, including low cost and the ability to magnetism, and the ability to bind molecules on the surface according to the absorption method by borate buffer, have led to consideration in this study.

Results: On the WS2 nanoparticles, antibodies are fixed against the surface antigen of hepatitis B and in the immunological sandwich model, the amount of surface antigen of hepatitis B is evaluated.

Conclusion: In this study, the WS2 nanoparticle stabilization is carried out on secondary antibodies to increase the susceptibility to surface antigens of hepatitis B, which leads to an enhanced qualitative detection of hepatitis B by ELISA.

Keywords: Hepatitis B virus, bis sulfanylidene tungsten, ELISA, immunosensor

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ID:914

Investigate of antioxidants status in coronary artery disease patients

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Objective: Cardiovascular disease (CVD), especially coronary artery disease (CAD), is the leading cause of death worldwide and responsible for the highest mortality rate in Iran (nearly 50% of all deaths each year). The known traditional risk factors for CAD are smoking, obesity, hypertension, a family history of CAD, diabetes mellitus, and hyperlipidemia. In addition to the traditional CAD risk factors, enhanced oxidative stress is a novel risk factor of CAD. The aim of present study was to investigate blood (enzymatic and non-enzymatic) antioxidants status with the occurrence and severity of CAD.

Material and Methods: Generally, 286 samples consisted of 141 men and 145 women aged 30–70 y who were classified as CAD cases and controls according to the results of coronary angiography. The severity of CAD was scored on the basis of the number and the extent of lesions at coronary arteries. Activity of the SOD, CAT, GPX and the concentrations of TAOC by using of FRAP as well as other risk factors were investigated. MDA also was measured in order to investigate of lipid peroxidation.

Results: The results showed a significant increase in SOD activity ($p=0.019$) and uric acid concentration ($p=0.000$) of CAD patients compared to control group. Although there were any change in GPX and CAT activity also in FRAP and MDA, a significant positive correlation were seen between GPX and SOD activity ($r=0.154$, $p=0.011$), and between levels of FRAP and uric acid ($r=0.749$, $p=0.000$).

Conclusion: The results suggest that some of antioxidants are associated with the occurrence and severity of CAD significantly, but the association is not independent and requires to more investigation.

Keywords: Cardiovascular disease, antioxidants

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Insulin Receptor in pancreatic ductal adenocarcinoma and In vitro Doxorubicin treatment

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Objective: The roles of the Insulin like growth factor (IGF) system in carcinogenesis have been established for various cancers. Recently it has been shown that IGF-1 is highly present in serum of patients with cancers. IGF-1 ligand also binds to Insulin receptor (IR) with equal affinity of IGF-1 receptor. Therefore the aim of this study was evaluate IR expression in pancreatic ductal adenocarcinoma (PDAC) tumors in compared to normal adjacent tissue, and In vitro study of Doxurubicin (DOX) treatment in AsPc-1 cells, as well.

Material and Methods: In this study first mRNA expression of IR in 27 cases of tumor tissues and matched adjacent non-tumorous tissues by quantitative real-time PCR were measured. In addition, the effects of Doxorubicin on its mRNA expression were evaluated in AsPc-1 cell lines and finally the data were analyzed using one way ANOVA.

Results: The result of the current study showed that average expression of IR in PDAC tumor was two fold of normal adjacent tissue ($P<0.001$). Moreover our study showed that IR expression was reduced in a dose dependent manner ($P<0.05$).

Conclusion: Overally the present study indicated that IR strongly involved in PDAC. This observation showed that IR was over-expressed in PDAC, and its expression was catastrophically reduced in response to DOX treatment.

Keywords: Insulin receptor, PDAC, Doxorubicin

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Evaluation of Copper level in the serum of hypo and hyperthyroidism patients in Urmia county.

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Objective: One of the largest endocrine glands of human body is thyroid gland, the normal actions of this gland depends on presence of trace element like as copper. The above element is needed for many metabolic and physiological activities in the human body. The present study investigated the alteration in copper levels, hypo and hyper thyroid patients.

Material and Methods: In this cross-sectional study, 120 members were selected randomly. The patients were 33 males and 47 females with average age of 38 ± 16 and healthy group included 40 persons 18 males and 22 females with average age of 40 ± 12. Patients were classified into 2 categories including hypothyroidism, hyperthyroidism and healthy group.3 milliliters of venous blood were drawn, sera were separated then TSH, T3, T4 were measured by ELISA assay and copper by spectrophotometric method. Statistical analysis was performed by using SPSS software

version 22 and after examining the normality of the data with Kolmogorov-Smirnov test, the results were analyzed by One-way ANOVA, and subsequently Tukey test. The level of significance was also determined (P<0.05).

Results: The findings indicated that there was significant increase in TSH (P<0.001) of hypothyroid patients, significant decrease in T4 and copper levels (P<0.01), but obvious change was not observed in the level of T3. Also there was significant decrease in TSH levels (P<0.001) of hyperthyroid patients and increase in T4, T3, copper (P<0.05).

Conclusion: According to the results of this study, it can be concluded that copper plays an essential role in production of thyroid hormones. The deficiency of copper may cause disorders during processes and functions related to thyroid hormones. Increasing in copper levels of hyperthyroid patients demonstrated disturbance in copper metabolism and its aggregation in patients body.

Keywords: Hypothyroidism, Hyperthyroidism, T4, T3, Copper

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ID:924

Effects of naringin on Liver Glutathione peroxidase activity in rats after swimming

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Objective: Stressful conditions induce physiological changes in a body to maintain the homeostasis. Acute stress exposure like swimming has effects on several cell functions. The present study was to investigate the influence of acute swimming stress and naringin on liver glutathione peroxidase (GPX) activity. Naringin belongs to the flavonoid family compounds which is found naturally in citrus fruits.

Material and Methods: Forty male wistar rats were randomly divided into 5 groups: 2 control groups containing non-exercised control without naringin supplements and normal control rats and three experimental groups with orally administration of 40, 80 and 160 mg/dl naringin. After 20 days, the rats were killed and the activity of GPX in the collected liver tissue was measured.

Results: Analysis of our data demonstrated that the statistically higher GPX activity in exercised rats in comparison to normal controls (p value=0.0028) naringin increased GPX activity in 80 and 160 groups in comparison to exercised controls (p value 160<0.001) although there was no significant difference between 40 groups in comparison to exercised control.

Conclusion: The findings d demonstrated that acute swimming would increase GPX activity in exercised rats. Also, naringin provided significant amelioration of GPX activity in exercised rats, however, the greatest effect of naringin was observed at 80 and 160 mg/kg body weight.

Keywords: Naringin, Swimming, Glutathione peroxidase

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ID: 926

Insulin Receptor can be used as therapeutic target in gastric cancer

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Objective: Insulin receptor (IR) is a tyrosine kinase receptor that has central role in glucose uptake and also can bind to IGF-II with high affinity. Recent investigation show that IR can involve in some disease like cancer. Following, by insulin binding to its receptors activating some signaling that involve in mediating cell growth and proliferation. Therefore, IR can play key role in metabolic and mitogenic biological actions.

Material and Methods: We used gastric cancer and normal adjacent tissue for this study (n=32). Gene expression levels were assessed by quantitative real-time (RT-PCR). mRNA expression were evaluated finally and analyzed using one way ANOVA test.

Results: The result of current study was showed that average expression of IR in gastric cancer tumor was increase 1.2 fold in compare with normal adjacent tissue (P<0.001).

Conclusion: Overally the present study indicated that IR involved in gastric cancer. This observation showed that IR was over-expressed in gastric cancer and in compare with normal adjacent tissue. By investigation in IR and its signaling can approach to new therapeutic strategies for some cancers.

Keywords: Insulin receptor, gastric cancer, therapeutic strategies
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ID:932

Evaluating of induction of apoptosis by Cornus mass L. extract in the gastric carcinoma cell line (AGS)

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Objective: Natural products and derivatives of medicinal plants can play an important role to cure cancer. Present study was aimed to determine the effect of Cornus mass L. extract on the induction of apoptosis in AGS gastric carcinoma cell line in compared to L929 cells.
Material and Methods: In this experimental study, AGS and L929 cells were cultured and treated with different concentrations (0–10 mg/ml) of Cornus mass L. extract for 48 and 72 hours. Cell proliferation was assessed by MTT assay. The percentage of apoptotic cells was determined by flow cytometry. Data were analyzed using one-way ANOVA. Differences with a p value less than 0.05 were considered significant.
Results: There was a significant difference among various concentrations of extract when cells were treated for 48, 72 h decreased cell viability in AGS cells compared to L929 cells in a dose and time-dependent manner ($P<0.05$). This extract also displayed approximately several-fold enhanced anti-cancer potency in AGS compared to L929 cells. The IC50 value in AGS cells (evaluated after 48,72h) of extract against AGS cells was 5/44, 2/44 mg/ml ($p\leq0.05$). Flow cytometry results exhibited an obviously significant augmentation in apoptotic AGS cells compared to L929 cells.
Conclusion: Our results implicate the fact that Cornus mass L. extract acts as a novel inhibitor of cancer proliferation in in vitro. This may results in developing a promising therapeutic agent for the treatment cancers.
Keywords: Apoptosis, Gastric cancer, Cornus mass L. extract, L929 cells, AGS cell line
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ID:939

Study of the association between blood androgen with perforin and geranzyme levels in PCOS women

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Objective: PCOS is one of the endocrinopathies among women. Hyperandrogenism is one of the indexes of PCOS diagnosis. It is said that androgens are involved in the regulation of perforin and geranzyme secretion from secretory granules of T cytotoxic lymphocytes. The aim of present study is to evaluate the association between blood androgen with perforin and geranzyme levels in PCOS women.
Material and Methods: 40 healthy and 40 PCOS women who were matched based on BMI and age and were verified by an endocrinologist and gynecologist were selected for this study. Biochemical factors including hormonal profile were measured using biochemical methods. Perforin and geranzyme levels were measured by ELISA.
Results: Patients had higher FAI, DHEA-S, free testosterone (FT), perforin and geranzyme than healthies while their SHBG levels were lower. There were significant correlations between perforin with FT and FAI and between geranzyme with FAI.
Conclusion: It is showed that T cytotoxic lymphocytes are higher in PCOS women than normals. Also, hyperandrogenemia was said to affect perforin and geranzyme secretion. So, based on that studies and current results, it could be concluded that change in androgen levels in PCOS can be associated with change in perforin and geranzyme levels by affecting T cytotoxic lymphocytes.
Keywords: Androgen, perforin, geranzyme, PCOS
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ID:941

Effects of 17-AAG in combination with Oxaliplatin and Capecitabine on the angiogenesis major indicator in HT-29 human colorectal cancer cell line

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Objective: Angiogenesis considered as a major determinant of tumor growth and development. One of the important mediators of this pathway, nitric oxide synthase (NOS) enzyme is directly linked to evaluated angiogenesis development. Numerous anti-cancer drugs qualified because of their angiogenesis effects. In this study, we aimed to investigate the effects of 17-AAG as a new treatment option in combination cases with oxaliplatin and capecitabine on NOS2 gene expression in HT-29 cells.
Material and Methods: Based on previous WST-1 (cell viability assessment) the lowest dose with high cytotoxicity which was 0.5×IC50 for double combination and 0.25×IC50 dose for triple combination selected for NOS2 gene (Real-Time PCR) expression assessments. The NOS2 gene expression levels selected with Real-time PCR examination.
Results: NOS2 level decreased in single treatment comparing control group and also in capecitabie/17-AAG group (in relation to single treatment), which are in line with WST-1 assay results. But in disagreement with WST-1 results, all of other double combinations (which were shown decreased viability), could not down-regulate NOS2 mRNA levels. Surprisingly in triple combination, NOS2 gene expression decreased, however decrease in viability was not significant comparing single treatment.
Conclusion: Our results indicate that 17-AAG in double combination with capecitabine can affect viability and angiogenesis. All other double combinations were shown significant anti proliferative effect but not anti-angiogenic effect. 17-AAG in triple combination with capecitabine and oxaliplatin inhibit angiogenesis more potent than viability. According to our results 17-AAG as a heat shock protein inhibitor had anti-angiogenic effect in single and especially in double combination cases on colorectal cancer cell lines.
Keywords: Angiogenesis, HT-29, NOS2, 17-AG
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ID:946

Assosiation of 12058T>C, HNF1β Nucleotide Transition with Benign Prostatic Hyperplasia: a Case-Control Study in Iranian Population

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Objective: Genome wide association studies (GWAS) have identified several non-coding genetic variants in associated with prostate cancer risk and benign prostatic hyperplasia (BPH). These SNPs could affect genes expression levels. HNF1β codes hepatocyte nuclear factor-1beta that binds to DNA as a homodimer or heterodimer. Recently have been reported that expression of HNF1β is associated with cancer risk in various organs such as prostate gland. So, HNF1β variants could increase the risk of BPH and prostate cancer.
Material and Methods: To investigate the correlation of rs4430769 which is located on intron 2 of HNF1β and BPH, the Boiling DNA extraction and the PCR-RFLP methods have been used for the blood sample of 30 patients and 30 normal controls participants. The PCR product has been 397bp which has been cut by BpmI restriction enzyme in C allele. For visualizing the PCR-RFLP bonds, the 1.5% gel agarose electrophoresis has been used.
Results: There could be 3 types of bonds with 246bp, 151bp, and 397bp that for CC the first and 2nd bond, for CT all of 3 bonds, and for TT just the 3rd bond have been visualized on gel agarose from PCR-product with 397bp length. The frequency of allele A rs4430796 was almost Significant different (Pvalue = 0/09) in case and control groups.
Conclusion: In spite of what our study showed, the frequency of allele A rs4430796 might be more different in case and control groups if the number of sample increase.
Keywords: Hepatocyte Nuclear Factor-1beta, Polymorphism, Benign Prostatic Hyperplasia
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ID:951

17-AAG in double combination with capecitabine and irinotecan inhibits cell migration and metastasis

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Objective: The purpose of this study was to assess anti-metastatic effect of newly presented anticancer agent (17-AAG), an HSP-90 inhibitor, alone and in combination with capecitabine and irinotecan (common chemotherapy agents) on HT-29 human colorectal carcinoma.
Material and Methods: According to our previous study on cytotoxic effect of 17-AAG, capecitabine and irinotecan, in this study, HT-29 human colorectal cancer cells treated with IC50 dose of every single drug, 0.5×IC50 in double combination groups and 0.25×IC50 in triple combination group. We accomplished wound scratch and Real-time PCR assays to assess migration and MMP-9 gene expression, respectively.
Results: Wound scratch assay showed that 17-AAG when used in double combination with capecitabine and irinotecan was effective anti-metastatic agent in HT-29 cells. However, we observed significantly increased cell migration capacity in our triple combination group, that is in line with our previous study which showed this combination's antagonistic effect .17-AAG, capecitabine and irinotecan single treatments and 17-AAG/capecitabine and 17-AAG/irinotecan double treatments were significantly decreased MMP-9 mRNA expression, but triple comination had no significant effect on mmp-9 mRNA expression.
Conclusion: In conclusion both wound scratch assay and MMP-9 mRNA expression analysis indicated that 17-AAG acts as an anti-metastatic agent in combination with capecitabine and irinotecan against HT-29 cells, but triple combination could not be a suitable candidate for colorectal cancer treatment, because it couldn't inhibit cell migration and MMP-9 gene expression significantly. So 17-AAG could be a suitable choise for colorectal cancer therapy in double combination with common chemotherapy agents.
Keywords: HT-29, migration, metastasis, MMP-9, 17-AAG
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ID:952

Antitelomerase activity of blackberry extract in human colorectal cancer cells

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Objective: Berries have attracted considerable attention because of their antineoplastic activities demonstrated in both preclinical and clinical studies. Several mechanisms have been proposed to explain berry anti-tumor effects, which include inhibition of angiogenesis and induction of cell cycle arrest and apoptosis. However, no previously published studies have investigated the antitelomerase activity of berry in cancer cells. The aim of this research was to examine the antitelomerase effect of blackberry in human colorectal cancer (CRC) cells.
Material and Methods: Anti-telomerase activity of blackberry juice was analyzed in 6 human CRC cells, both in cell-free systems and intact cells by TRAP assay. The effect of blackberry on the expression of human telomerase catalytic subunit, hTERT mRNA and methylation status of its promoter was also examined by quantitative RT-PCR and MSP analysis, respectively.
Results: Blackberry extract significantly inhibited the growth of 6 CRC cells in a dose-dependent manner. Telomerase activity of CRC cells incubated with IC50 concentration of berry extract for 48 and 72 h decreased by 15-37.5% and 43.23-62.5% ($p<0.05$), respectively. Berry treatment caused a significant reduction of hTERT expression in SW480, HT29/219, LS180, and HCT116 cells ($p<0.01$) and a non-significant reduction in other 2 cell lines. Berry treatment partially induced hypomethylation of hTERT promoter in these cells.
Conclusion: Our data indicate that telomerase inhibition is a key mechanism by which blackberry exert its anticancer effect in CRC cells.
Keywords: Blackberry, colorectal cancer, anti-telomerase, hTERT expression, promoter methylation
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ID:961

Antioxidant effect of taraxasterol on ethylene glycol-induced kidney stone in rats

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Objective: Taraxasterol is one of the important constituents of Taraxacum officinale L. (Compositae) with antioxidant potential.
Material and Methods: The present study was designed to evaluate the antioxidant effect of taraxasterol on ethylene glycol induced urolithiatic rat. Urolithiasis was induced by oral treatments of ammonium chloride and ethylene glycol in adult male rats. Taraxasterol (2, 4 and 8 mg/kg) was treated for 33 days by gavage. Then, the animals were anesthetized and blood, liver and kidney sampling were done. Serum alanine aminotransferase, aspartate aminotransferase and lactate dehydrogenase activities, superoxide dismutase and glutathione peroxidase activities in serum, kidney and liver were evaluated.
Results: The Results showed that taraxasterol decreased serum alanine aminotransferase ($p<0.001$), aspartate aminotransferase ($p<0.001$), lactate dehydrogenase ($p<0.05$) activities, while increased superoxide dismutase and glutathione peroxidase in serum ($p<0.01$), kidney ($p<0.05$ and $p<0.001$, respectively) and liver ($p<0.01$ and $p<0.001$, respectively) tissue homogenates in treated urolithiatic rats in comparison to the control urolithiatic rats.
Conclusion: In conclusion, the Results showed that acute exposure to ethylene glycol decreased the endogenous antioxidant defense system of liver and kidney tissue rats, suggesting an important role of oxidative stress in the pathogenesis of ethylene glycol-induced cellular toxicity. potential antioxidant may prevent crystal deposition in renal tissue. Taraxasterol treatment effectively ameliorates reactive oxygen species production by promoting antioxidants SOD and GPx.
Keywords: Kidney stone, Antioxidant, taraxasterol, Rat
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ID 976

The association of rs2241766 polymorphism in adiponectin gene with liver enzymes, fasting blood glucose and adiponectin in patients with non-alcoholic fatty liver

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Objective: The adipose tissue, as a microorganism, produces substances called adipokines, one of which is the adiponectin hormone, which is effective on the metabolism of glucose and preventing damage to liver cells. In this study, the association of single-nucleotide polymorphism rs2241766 or (+ 45T> G) with liver enzymes, fasting blood glucose and adiponectin in patients with non-alcoholic fatty liver was investigated.
Material and Methods: This case-control study was performed on 80 patients with non-alcoholic fatty liver and 80 healthy controls as control. Fasting blood glucose, aspartate aminotransferase (AST) and alanine aminotransferase (ALT) enzymes were measured by standard methods using the kits of Pars Azmoon company and Adiponectin levels with using the Eliza kits of Sweden Merdodia company. Determination of genotypes was determined using PCR-RFLP method. Data were analyzed by SPSS software version 20.
Results: The two groups were significantly different in terms of age, ALT, AST, adiponectin and fasting blood sugar. In this study, there was no significant difference in genotypes or alleles in two groups. There were no significant differences in rs2241766 polymorphism genotypes in any of the variables in the healthy group, but in patient individuals, the liver enzymes AST ($P=0.09$) and ALT ($P=0.09$) differed significantly in genotypes.
Conclusion: It seems that there is no meaningful relationship between rs2241766 polymorphism in adiponectin gene and non-alcoholic fatty liver disease. The level of adiponectin in patients with liver enzymes has a significant but reversible relationship.
Keywords: Non-alcoholic fatty liver, Adiponectin, polymorphism, Liver Enzyme
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ID:982

Effect of Atorvastatin with and without vitamin E supplementation on PPARγ gene expression in type 2 diabetic patients with hyperlipidemia

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Objective: The peroxisome proliferation-activated receptor γ (PPARγ) plays an important role in lipid and glucose homeostasis. The highest expression of PPARγ is at the adipocytes which affects on signaling pathways of insulin and endothelial dysfunction. Type 2 diabetes increases the risk of cardiovascular diseases which is more related to dyslipidemia. Statins, as a lipid lowering drugs, activate PPARγ gene expression via 15-deoxy-delta-12-14PGJ2

production. Moreover, studies have shown that vitamin E induces PPARγ expression, as well as improves glycemic control. Then, co-supplementation of atorvastatin with vitamin E may have more beneficial effects in hyperlipidemic patients.

Material and Methods: Twenty-four type 2 diabetic women with hyperlipidemia enrolled at the present study. They were randomly assigned to receive 20mg/day atorvastatin alone and/or in combination with 400IU/day vitamin E for 12 weeks. Fasting blood samples were gathered at the baseline and end. PBMC was extracted and PPARγ gene expression was measured by the real time PCR.

Results: Results showed that PPARγ mRNA level was significantly higher in the atorvastatin plus vitamin E supplemented group than atorvastatin alone (4.9±1.77 vs 3.12±0.93, P≤0.05).

Conclusion: The present study showed that vitamin E supplementation with atorvastatin has a synergistic effect on PPARγ gene expression which may has beneficial effects on dyslipidemia to reduce risk of cardiovascular disease in diabetes.

Keywords: Atorvastatin, Vitamin E, PPARγ, Diabetes Mellitus, hyperlipidemia

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ID:987

Serum immunoglobulin levels in splenectomized and non-splenectomized patients with major beta-thalassemia in Zahedan

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Objective: Major Thalassemia is the most common hemoglobin disorder in the world. This disease results in clinical side effects in the affected persons and these patients need blood transfusion. This study was conducted with the aim of investigation of serum immunoglobulin levels in splenectomized and non-splenectomized patients with major beta-thalassemia in Zahedan.

Material and Methods: The study sample included 60 beta-thalassemia patients were splenectomized and non-splenectomized and also 20 healthy subjects who were enrolled by accessible method. IgA, IgM and IgG immunoglobulin levels evaluated in all group using Eliza method.

Results: Mean serum level of IgM in splenectomized patients was lower in non-splenectomized group. Mean serum level of IgA and IgG were not statistically different in splenectomized and non-splenectomized patients.

Conclusion: The results of this study showed that only serum level of IgM was statistically different in splenectomized and non-splenectomized patients and IgA level was significantly lower in the control group compared to both splenectomized and non-splenectomized groups. These are due to the effects of the disease on the immune system.

Keywords: Major Beta-thalassemia, Immunoglobulin, Splenectomy

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ID:988

Some markers of autophagy are too important to investigate neurodegenerative diseases under the influence of herbal component

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Objective: Alzheimer's disease is an advanced neurodegenerative disorder. It is the most common cause of dementia. Nowadays the use of herbal medicines to prevent and slow down the progression of Alzheimer's disease is very important. One of the suggested natural products to control neurodegenerative diseases is saffron. In order to investigate the neuroprotective role of saffron compounds, we studied the effect of crocin on a PC12 model of Alzheimer's disease. Understanding the signaling pathways involved in the regulation of autophagy is crucial to the development of strategies for therapy. In this regard, we studied the expression of some autophagic markers (LC3-II/ LC3-I, Beclin-1) in PC12 model of Alzheimer's disease.

Material and Methods: The differentiated neuron-like PC12 cells were incubated with the aggregated amyloid beta (Aβ) to induce an Alzheimer's model. Fluorimetric methods like thioflavin-T, circular dichroism and electron microscopic Images were applied to confirm the aggregated Aβ. Then PC12 was treated to the effective dose of crocin to assess the role of the mentioned herbal reagent as prevention or treatment of Alzheimer's disease. Finally, the alterations of apoptosis in treated cells were examined through flow cytometry method. The expression of Beclin-1 and LC3II protein were evaluated using Real time and western blotting analysis to survey autophagy examination.

Results: The results show that crocin increase the expression of Beclin-1 and LC3II protein accumulation.
Conclusion: We concluded that crocin through autophagy activation could improve the biochemical process of Alzheimer. So we can introduce crocin as potential drug for improvement of Alzheimer disease.
Keywords: Alzheimer's disease, Crocin, Amyloid Beta, Autophagy, PC12
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ID:990

Imidazoquinolines induce apoptosis via ROS production in U-87MG glioblastoma cells

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Objective: Glioblastoma multiform, one of the most common and aggressive malignant brain tumors, is highly resistant to therapy. We aimed to determine the effect of 5 new derivate of Imidazoquinolines on the U-87MG glioblastoma cells.
Material and Methods: U87MG glioblastoma and AGO1522 normal fibroblast were treated with 5 derivate of Imidazoquinolines. We analyzed cell viability by MTT assay and the induction of apoptosis using annexin V-PI staining via flow cytometry. Additionally, caspas-3 activity and ROS production were measured by fluorometric assays.
Results: U-87MG cells treated with 5 derivate of Imidazoquinolines demonstrated reduced viability, and an increase in annexin V- and annexin V/PI-positive cells. A dose dependent decrease in cell viability was observed in U-87MG treated by 5 derivate of Imidazoquinolines compared with AGO1522 normal fibroblast cells. In addition this derivate significantly induce caspase-3 activity and ROS generation.
Conclusion: These findings indicate that Imidazoquinolines that have potent direct activity against Glioblastoma cells, inhibits cell growth of U-87MG cells by inducing apoptosis and generation of ROS.
Keywords: Glioblastoma, Iimidazoquinolines, Apoptosis
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ID:993

Hematological Parameters in Newborns of Mothers with and without Hypertension

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Objective: Pregnancy induced hypertension (PIH), preeclampsia and eclampsia syndrome is a multi system disorder associated with adaptive changes in the fetal circulation and causes a marked imbalance in the haemostatic system of the mother and the neonate. The aim of this study was Comparison of hematological parameters in newborns of mothers with and without hypertension.
Material and Methods: This case–control study included 30 newborns of mothers with PIH and 30 newborns with normotensive mothers matched for age and sex as a control group. The ombelical cord blood samples were collected from all newborn and complete blood count and ferritin levels were estimated
Results: The mean corpuscular volume, mean corpuscular hemoglobin, red cell distribution width, mean platelet volume and platelet distribution width were higher in the newborns of hypertensive mothers compared to the control group, and total white cell counts, thrombocyte counts and ferritin level were lower. The mean of red blood cell count, hemoglobin and hematocrit was higher in newborns of hypertensive mothers compared to the control group, but the difference was not significant.
Conclusion: Newborns of hypertensive mothers should be carefully evaluated and monitored in terms of hematologic abnormalities. Complete blood counts can be used as significant parameters for early diagnosis of possible complications.
Keywords: Infant, Hypertension, Blood Parameters, Pregnancy
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ID:994

Cisplatin-modified SiO2 and SiOC nanocomposites: A smart nanocomposite system for controlled drug loading and release

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Objective: Ovarian cancer is the 8th common cancer in women and is the 5th leading cause of mortality from cancer among women in the United States of America. In this research, surface modified SiO2 and SiOC nanoparticles were characterized for cisplatin (CP) loading.
Material and Methods: SiOC nanoparticle was made by using sol-gel method and SiO2 was

made by using Thermal decomposition and were surface-modified with N-(3-dimethyl aminopropyl)-N'ethylcarboimide hydrochloride (EDC) and 1,1'carbonyl diimadazole (CDI) for better drug entrapment. Cisplatin loading on nanocomposites was carried out by oil-in-water emulsion method. The copolymers were evaluated by FTIR, UV-Vis absorption by Nanodrop, and electron microscopy. Human epithelial ovarian cancer cells of A2780 type were cultured in RPMI with 10% FBS and treated with synthesized copolymer system.

Results: The dialysis-based UV-Vis absorbance results fort cisplatin release from SiO2 and SiOC nanoparticles at 37°C and pH 7.4 (body's physiologic temperature and pH) and, 42°C and pH 6.5 (temperature and pH of cancer microenvironment) have shown that SiOC-CDI with 1 mg CP showed 91.18% drug release at pH 6.5 after 6 h 42 oC, SiO2-CDI (1 mg CP) exhibited 97.3% drug release at pH 6.5 and 42 oC after 48 and 72 h, respectively, which shows that this nanocomposite could have the ability of controlled drug release after 48-72 h, which is a good property for a nanocomposite based drug carrier system.

Conclusion: The present results show that the CP-loaded polymer modified SiO2 and SiOC nanocomposite systems showed effective drug loading and controlled-release capacities, which can be exploited in the drug delivery of cisplatin for cancer treatment, which is the next aim of this project.

Keywords: SiO2, SiOC, Controlled release, Biodegradable nanoparticles, EDC

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ID:1008

Evaluation the effects of pyrazole with new substitutes on the proliferation of MDA-MB-468 breast cancer cells

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Objective: Triple negative breast cancer is an aggressive form of breast cancer with limited treatment options and is without proven targeted therapy. Pyrazole moiety represents an important category of heterocyclic compound in pharmaceutical and medicinal chemistry. A navel series of 11 different pyrazole substitutes have been evaluated for their potential anti-proliferative activity against human breast tumor cell line, MDA-MB-468.

Material and Methods: MTT assay, apoptosis assay by Annexin V-PI staining via flowcytometry, caspase-3 activity and generation of ROS using fluorometric assay were carried out to determine anticancer effects of the compounds on MDA-MB-468 breast cancer cell line.

Results: Some of the compounds, specifically 12 and 18, showed potent growth inhibition against MDA-MB-468 cells in a dose-dependent manner compared with AGO-1522 normal fibroblast cells, with IC50 values in the range of 8.36 and 13.25 µM, and an increase in annexin V- and annexin V/PI-positive cells. Moreover, the compounds led to increased levels of reactive oxygen species (ROS) and caspase-3 activity.

Conclusion: Our data indicate that these derivatives may present promising chemotherapeutic agents, via targeting apoptosis by ROS production.

Keywords: Triple Negative Breast Cancer; New Pyrazole Substituts; Apoptosis; ROS

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ID:1012

Effects of P-coumaric acid in presence of low level laser irradiation on human melanoma skin cancer cells

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Objective: Melanoma is malignant form of skin cancer and is associated with a high mortality rate. Therefore, early diagnosis and surgical intervention play a key role in treatment. One of the significant strategies for the prevention and treatment of various cancers is the use of plant compounds. Phenolic compounds are important category of natural antioxidants in plants that have important biological activities, such as antioxidant and anticancer effects. In this study, the effect of P-coumaric acid as phenolic compound along with low level laser therapy was investigated on human melanoma cell line A375.

Material and Methods: Human melanoma cancer cell line A375 was exposed to irradiated with a red laser source (660 nm; power density: 30 mW cm-2) and another was kept in the dark for 90 sec. After treatment with laser, the cells were treated with different concentrations of P-coumaric acid (0-1000 µg/mL) for overnight. The MTT assay was used to determine the cell viability. The

morphology of cells was studied using inverted light microscopy.

Results: The results showed that early treatment with low level laser and then P-coumaric acid reduced the survival of the melanoma cancer cells more than the early treatment with P-coumaric acid and then low level laser irradiation.

***Conclusion*:** This study showed that low level laser therapy alone is not able to kill melanoma skin cancer cells. However, application of low level laser therapy along with P-coumaric acid, reduced the cell viability. The morphology study of the cells has confirmed the MTT results.

Keywords: Human Melanoma Skin Cancer, P-Coumaric Acid, Low Level Laser Therapy (LLLT), Cell viability

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D: 1016

Assessment the structural model of antiEGFR-ZZ-PE38 under analogous of physiological condition

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Objective: Expansion the cancer therapy methods has leading to development a range of monoclonal antibodies and immunotoxins. In this regard, anti-GFR-ZZ-PE38 immunotoxin was introduced since 2008 up to 2013. So, structural and functional assay of this drug at physiological like condition, could be confirm the literature sequence of it for optimization, which are considered in this study based on advanced computing methods.

Material and Methods: NCBI, Uniprot and RCSB were subjected for achievement to the sequences and structures of proteins. Modeller was used for antigen modeling and assembling of the fragments of drug. ERRAT, Verify 3D and RAMPAGE were employed to determine the quality of protein structure. Stability assay of drug was performed by Gromacs via Gromos force field at 310 K during 20 ns. Functionality properties of drug was evaluated via its affinity to corresponding antigens and epitope mapping by HADDOCK and IDEB, respectively.

Results: Literature review led to obvious a sequence with 744 amino acid in the length of anti-GFR-ZZ-PE38 including scfv-cetuximab part, ZZ sequence with penetrance capacity, and modified toxin of exotoxin A of the Pseudomonas which are conjugate with flexible linkers. On the other hand, modeling led to represented structures of fragments with suitable quality. Fragments assembling led to the appearance of 10 structures of the drug. Nonetheless, one model among them showed appropriate stability and immunogenicity at physiological like condition. Moreover, functional assay of the drug based on affinity of it to corresponding antigens showed significantly affinity to EGFR related to other antigens.

Conclusion: Generally, the results of this study led to the presentation of a model of antiEGFR-ZZ-PE38 with is suitable in the structure and function. So, this model can be used in the experimental state. Moreover, this model is provide opportunity for its optimization, which are considered in our group.

Keywords: Cancer, Monoclonal antibody, Immunotoxin, antiEGFR-ZZ-PE38, Simulation

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ID: 1017

Structure-function relationship of RHO kinase I

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***Objective*:** The serine/threonine Rho-associated protein kinases (RHO kinases I/II), which are key determinants in many fundamental cellular functions, serve as distinguished therapeutic targets in the treatment of a wide variety of diseases, particularly cardiovascular diseases. In contrast to the terminal globular kinase domain and the PH-C1 tandem little is known about the sequence-structure-function relationship of the central amphipathic α-helical segment of the RHO kinase proteins. Thus, a major aim of this study was to elucidate the structural basis of the entire segment of RHO-kinase I by using multiple biophysical platforms, including multi-angle light scattering (MALS), analytical ultracentrifugation (AUC), small-angle X-ray scattering (SAXS), negative stain electron microscopy (EM), and X-ray crystallography. The obtained results together with structural reconstitution of full-length RHO kinase I

revealed that a highly elongated coiled-coil structure may switch between a dimeric and a tetrameric state. These and unexpected data obtained from measurements of enzymatic activity of full-length RHO-kinase I about the role of RHOA as a RHO kinase activator will be presented and discussed.

Keywords: Rho kinase, ROCK, Serine/threonine kinase, Coiled-coil, Structure function relationship

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D: 1023

Role of pancreatic duct cell in beta cell neogenesis

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Objective: Diabetes mellitus is known as main threatening for health society. Main characteristic of type 2 diabetes is hyperglycemia, which is associated with the selective destruction of pancreatic beta cells, these cells as the main center of blood glucose preservation at normal level. Proliferation and neogenesis are two factors for preservation of beta cell mass. Continues production of beta cell is a therapeutic strategy to keep normal blood glucose and pancreatic duct cell can be one of the sources of new beta cells.

Material and methods: Review method for better access to relevant articles, we searched keywords such as beta cell neogenesis; diabetes mellitus; duct cell and compensatory mechanisms in databases of Wiley; Scopus; Science Direct and PubMed. Then obtained papers from 1990 to now according to the year publication were classified. Indeed; our goal was evaluation of articles based on chronological order.

Results: In the study, reviewed the role of pancreatic duct cell in the production of beta cell based on a chronological. Reviewed show one of the sources of beta cell production is pancreatic duct cells. They have the ability to convert beta cells in the postnatal period and even adulthood. Pancreatic duct-derived cells can be a potential source for the production of beta cells. Indeed they acquire mesenchymal characteristics and then differentiate into cells with potential of insulin secretion.

Conclusion: In final, we concluded given that in obese people and patients with diabetes there are probability of duct cell replication and beta cell neogenesis under obesity and diabetes especially in the early stages of diabetes.

Keyword: Diabetes, Pancreatic duct cell, Beta-cell, neogenesis

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ID: 1034

Fumigant properties of nano-encapsulated essential oil form of essential oils of Artemisia haussknechtii as Biopesticides in Insect-pest Managemen

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Objective: The Artemisia species are one of the most popular plants, which are used for the management of diseases such as hepatitis, malaria, cancer, inflammation and infections by fungi, bacteria, and viruses. Nano-capsules containing pesticides could provide more precise, controlled and effective use of pesticides and therefore potentially reduce the overall quantities of pesticide used. In this study, the insecticidal activity of nano-encapsulated form from Artemisia Haussknechtii essential oils was investigated.

Material and methods: Interfacial compression polymerization method was investigated for nano-capsules preparation. The effects of emulsifier composition, co-emulsifier, and temperature on the properties of the nano-capsules were investigated. The scanning electron microscopy of particles proved the preparation of nanoparticles. Fumigant toxicity of Nano-encapsulated form of Artemisia Haussknechtii essential oils was evaluated against Tribolium castaneum and Sitophilus oryzae.

Results: It was demonstrated a mortality of 100 percent of Sitophilus oryzae in the concentration of 166 ppm. With the alteration of concentrations of the oil and extracts and exposure time, the variety of fumigant toxicity had shown due to the volatility of extract. The results demonstrated that A. haussknechtii essential oil and its nano-encapsulated form could play a significant role in the formulation of essential oil-based insecticides for the management of stored-grain insects.

Conclusion: New formulation and techniques such as nano-encapsulated form of essential oils and controlled release technique were applied to overcome the rapid degradation of essential oils for using as pesticides.

Keywords: Artemisia Haussknechtii; Essential oil; Extract; Fumigant toxicity; Nano-encapsulated

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ID: 1035

Coenzyme Q10 increases SIRT1 gene expression in the liver of STZ induced diabetic rats

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Objective: Oxidative stress, through the production of reactive oxygen species (ROS), has been proposed as the root cause underlying the development of diabetes complications. Various factors, such as sirtuins (silent information regulators or SIRTs) are associated with these complications. Antioxidant therapy may be effective in decreasing the risk of diabetic complications. This study was carried out to investigate the effects of Coenzyme Q10 on the expressions of SIRT1 gene in the liver of STZ-induced diabetic rats.

Material and methods: A total of 30 male rats were randomly divided into five groups; groups 1 and 2 as control received saline or Sesame Oil respectively (as vehicle), group 3 received CoQ10 (10 mg/kg), group 4 was diabetic rats (induced with STZ:55 mg/kg) and group 5 diabetic rats that received CoQ10 (10 mg/kg) for 5 weeks. At the end of experiments, liver tissue was collected from all rats. The SIRT1 gene expression was determined by qRT-PCR. In addition, liver malondialdehyde (MDA), as an index for lipid peroxidation, was estimated by colorimetric method.

Results: Results of qRT-PCR showed that gene expression of SIRT1 significantly decreased in the liver tissue of diabetic rats compared to control groups. Our data revealed that treatment with CoQ10 significantly increased levels of SIRT1 mRNA compared with the diabetic rats. The treatment of diabetic rats with CoQ10 also showed a significant decrease in the MDA level.

Conclusion: The present data illustrated that diabetes-induced oxidative stress may be causally related to the downregulation of SIRT1 mRNA. Thus, it is possible that CoQ10 with its effect on gene expression can have antioxidant effects, thus decreasing diabetic complications.

Keywords: Coenzyme Q10, Diabetes mellitus, Gene expression, SIRT1, liver

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ID: 1036

Association between Growth Hormone and Insulin-Like Growth Factor-1 Axis in two age groups

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Objective: Human growth hormone (GH) is an endocrine hormone, secreted from the anterior pituitary. GH/GHR interaction stimulate production of peptide insulin-like growth factor-I (IGF-I) from liver. IGF-I synthesized by other extrahepatic tissues in small amounts. The IGF-I is key for developmental and postnatal growth. Serum Growth hormone (GH) and IGF-I levels are utilized as diagnosis biomarkers in GH-related disorders. The aim of the study was to investigate the relationship between serum levels of GH and IGF-I in two age groups.

Material and methods: A total of 108 persons entered in this study. Serum GH and IGF-I levels were measured using chemiluminescence technique on MAGLUMI 800 analyzer.

Result: The results indicated that the mean concentrations of GH and IGF-I were 1.88 ng/ml and 86.77 ng/ml. We also found that there was a negative correlation between GH levels and IGF-I levels (P-value 0.076) for ≤ 20 years age group and a significant positive correlation between GH levels and IGF-I levels (P-value 0.004) For ≥ 20 years age group.

Conclution: This data suggested that Serum GH levels did not predict serum IGF-I level in ≤ 20 years age group, but Serum GH levels was useful to predict serum IGF-I level in ≥ 20 year age group.

Keywords: GH, IGF-I, chemiluminescence

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ID: 1037

Sequence analysis of the outer membrane cytochrome c from UV induced Thiobacillus ferrooxidans

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Objective: This paper studies the effects of ultraviolet irradiation (UV) on the outer membrane cytochrome c (Cyc2) sequence in the mutated Thiobacillus ferrooxidans (T.

ferrooxidans) which can affect the iron oxidation activity of the bacteria. Several membrane and soluble c-type cytochromes such as Cyc2, proposed to be involved in the respiratory pathway of FeII oxidation in T. ferrooxidans.

Material and methods: The bacteria irradiated with UV light for 180s and oxidation experiment was carried out with 5% pulp density ore powder. Then, DNA samples were obtained from original bacteria and mutated bacteria. cyc2 gene was amplified by using specific primers using HotStar HiFidelity PCR. Then, cyc2 fragments were extracted from agarose gel (1%) using gel purification kit and PCR products were sequenced.

Results: The results showed that the Eh of UV mutated bacteria and original bacteria reached to 586, 487 mV respectively at the first 8h of the bioleaching process, while, the Eh value of negative control was 332 mV. These results indicated that the oxidative activity of T. ferrooxidans is greatly improved by mutation. However, the UV irradiation has no significant effects on DNA sequence of cyc2 gene from mutated bacteria.

Conclusion: The improved oxidation rate of the mutant bacteria may be attributed to changes in regulatory regions or other carriers in the Fe2+ oxidation respiratory pathway, which need more detailed research to arrive at a solid conclusion.

Keywords: Thiobacillus ferrooxidans, Ultraviolet irradiation, mutation, cytochrome c

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ID: 1038

Associations between serum paraoxonase activity and APO-A and APO-B in subjects with different levels of HDL

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Objective: There is a strong inverse relationship between plasma high density lipoprotein (HDL) level and the risk of developing coronary artery disease (CAD). Serum concentration of HDL is inversely related to the development of Atherosclerosis. Paraoxonase-1 (PON1) is a HDL associated enzyme that plays a vital role in reduction of low density lipoprotein (LDL) oxidation. The aim of this study was to investigate the associations between paraoxonase activity (PON1) with APO-A and APO-B levels in subject with different levels of HDL cholesterol (HDL-C) levels.

Material and methods: 135 subjects, 20–60 years old, contributed to this study. The subjects were divided into three groups (45 in each group) with different level of HDL (High, Normal and Low). For each group, the activity of PON1 was measured using paraoxon as a substrate. Moreover, the serum level of APO-A and APO-B were measured. The statistical analysis was performed using SPSS software.

Results: PON-1 activity and APO-A levels were decreased in subject with lower levels of HDL ($P<0.001$). APO- B levels were higher in subject with lower levels of HDL ($P<0.001$). Serum PON-1 activity was positively correlated with TC, TG, apo A-B, and LDL-C levels ($P<0.01$).

Conclusions: In conclusion, determination of serum PON1 activity and lipoproteins may play important roles in the earlier prediction of CAD and design of therapeutic in treatment of CAD toward PON1 activity regulation.

Keywords: High density lipoprotein, Coronary artery disease, Paraoxonase-1, lipoproteins

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ID: 1040

Bioinformatic analysis of Aspartyl/asparaginyl β-hydroxylase protein

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Objective: Membrane Protein Human Aspartyl/Asparaginyl beta-hydroxylase (ASPH) play an important role in calcium homeostasis. The gene is expressed from two promoters and undergoes extensive alternative splicing. The encoded set of proteins share varying amounts of overlap near their N-terminal but have substantial variations in their C-terminal domains resulting in distinct functional properties. The longest isoforms (a and f) include a C-terminal ASPH domain that hydroxylates aspartic acid or asparagine residues in the epidermal growth factor (EGF)-like domains of some proteins, including protein C, coagulation factors VII, IX, and X, and the complement factors C1R and C1S. In human tumorous cells expression of this enzyme can be elevated, which is associated with progression of tumor. Serum level of ASPH served as indicator for different carcinomas.

Materials and methods: In this article we study the structure and some aspects of bioinformatics in ASPH using different bioinformatics methods and sites. The amino acid sequence of the enzyme was taken from the NCBI site. One part of the study was carried out with bioinformatics tools that are available on the NCBI and Expasy and was done online. Another part was performed via Pdb Viewer-Swiss.

Results: There are several isoforms of this enzyme in different organisms, so we draw its phylogenetic trees using the blast review software on NCBI. In addition to drawing phylogenetic tree, we determined the amino acid sequence. Also we identified the main physico-chemical properties of a protein, predicted primary, secondary, tertiary structure analysis, looked for transmembrane segments and coiled-coil regions, of ASPH. Finally we used the hydrophobicity to identify the groups with hydrophobic characterization of ASPH.

Conclusion: Owing to the bioinformatics knowledge, ASPH can be considered as an ideal target in cancer studies, such as cancer detection and therapy.

KeyWords: Bioinformatics, ASPH, Isoform, Hydroxylase

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ID:1053

The Effects of Ginger Extracts and Vitamin K on Serum levels of enzymes ALT, AST or ALP in Mice NMRI with Non-Alcoholic Fatty Liver

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Objective: Non-alcoholic fatty liver is a liver inflammation caused by excessive accumulation of fat in the liver tissue. The objective of this study was to investigate the effects of ginger extracts and vitamin k on Serum levels of enzymes Alanine Transaminase (ALT), Aspartate Aminotransferase (AST) or Alkaline Phosphatase (ALP) in mice NMRI with a non-alcoholic fatty liver.

Materials and Methods: In this study, mice NMRI were randomly divided into control) standard diet (Sham (High-fat diet), Silymarins received, hydroalcoholic Zingiber extract (200 mg/kg/body weight), vitamin K received, Zingiber extract and vitamin K received of 5 mice in each. After the experiences blood samples were collected using a cardiac puncture method and the serum proteins levels were measured. Data were compared between groups using ANOVA.

Results: Serum AST or ALP level significantly increased in the ginger extract, vitamin K groups compared to control group ($p<0.001$); But The serum levels of ALT was significantly decreased($p<0.001$).

Conclusion: The results of this study showed that ginger extract with vitamin K protects the damage induced by the non-alcoholic fatty liver in the liver tissue.

Keywords: Ginger extract, Vitamin K, ALT, ALP, AST

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ID:1063

Synthesis and evaluation of the antileishmanial activity of antimony (V)-complexes of hydroxypyranone and hydroxypyridinone ligands

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Objective: Most of antimony (Sb) compounds including N-methylglucamine Sb (V), which have been widely used for the treatment of leishmaniasis are less effectve and toxic. Attempts have been made to synthesize safer and more effective Sb-complexes as antileishmanial drugs in the last decades. In the present study, we report the synthesis and antileishmanial activity of five novel complexes of Sb (V) with hydroxypyranones (HPs) and hydroxypyridinones (HPOs) ligands.

Material and Methods: The complexes were synthesized from related ligands and $SbCl_5$ in water at 60°C and pH 8. Identification and structural elucidation of complexes were achieved by FTIR, 1HNMR, electron spin ionization mass spectroscopic (ESI-MS) technique, elemental analysis and through physical constants. All compounds were evaluated for in vitro activities against the amastigote and promastigote forms of Leishmania major.

Results: Most of the synthesized compounds exhibited good antileishmanial activity against both forms of the Leishmania major. The IC50 value of the most active compound after 24, 48 and 72 h against amastigote model was 30, 24 and 16 µg/mL, respectively. However, the most potent complex inhibited the promastigote form of parasite after 24, 48 and 72 h with IC50 values of 20, 15 and 8 µg/mL, respectively.

Conclusion: These results indicated that antimony (V)-complexes of HPs and HPOs ligands would be a good candidate for treatment of Leishmania major.

Keywords: Hydroxypyranones, Hydroxypyridinones, Antimony (V)-complexes, antileishmanial, activity

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ID: 1072

Combination of Metformin and Phenformin inhibits synergistically proliferation and

hTERT expression in human breast cancer cells

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Objective: Emerging evidence has revealed the potent anti-cancer effects of biguanides, Metformin (MET) and Phenformin (PHE). Thus, to explore an efficient chemopreventive strategy for breast cancer, the antiproliferative effects of the combination of MET and PHE against breast cancer cells were assessed in this work.

Material and Methods: Cytotoxicity of the drugs individually and in combination against T47D and MDA-MB-231 breast cancer cells were assessed using MTT assay and the median-effect method was used to analyze the precise nature of the interaction between MET and PHE. Besides, the expression levels of hTERT after 48 h drug exposure was determined using qRT-PCR.

Results: Based on the cytotoxicity assay, both MET and PHE further inhibited the growth of MDA-MB-231 cells compared with T47D cells. It was found that MET+PHE drastically reduced the IC50s of MET and PHE in both cells than the single treatments in synergistic manner. Importantly, MET+PHE showed higher antiproliferative effect with smaller IC50 values against MDA-MB-231 cells than T47D cells. Real-time PCR results revealed that hTERT expression was significantly reduced in both breast cancer cell lines treated with MET+PHE than the single treatments. In comparison between two types of breast cancer cells, it was detected that MET+PHE could further decline hTERT expression in MDA-MB-231cells than T47D cells ($p<0.001$).

Conclusion: It is speculated that the combination of MET and PHE may be a promising and convenient approach to improve the efficiency of breast cancer treatment.

Keywords: Metformin, Phenformin, Combination therapy, Synergistic effects, Breast cancer

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ID: 1077

Quercetin attenuates high glucose-induced lipotoxicity and lipid droplet accumulation in RAW264.7, involvement of suppression of skew RAW264.7 toward M1

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Objective: Macrophages are flexible cells and able play multiple functions in inflammatory conditions. These major components of innate immunity cells secrete various cytokines and a vast number of mediators molecules and CD markers. These process tightly regulated and these molecules have both beneficial and detrimental outcome in health. macrophages can acquire specialized phenotypes; M1 (pro-inflammatory phenotype) and M2 (anti-inflammatory phenotype). M1 subset secreted inflammatory mediators such as iNOS, TNF, MCP1, IL-6, and have CD11-c surface marker. But, M2 markers are CD206, CD163, TGFβ, Arginase. M1/M2 balance has a critical role in inflammation. Diabetes Mellitus is an inflammatory condition and polarization pattern of macrophage is going toward to M1. Quercetin is a flavonol, one of the six subclasses of flavonoid compounds. This polyphenol possesses strong anti-inflammatory capacities; through an increase of antioxidative activities, reduction of lipogenesis and macrophage polarization regulation.

Material and Methods: RAW 264.7 macrophages were stimulated by high glucose concentration, then we have studied effects of Quercetin (25μM) on high glucose-induced lipotoxicity and macrophage polarization. we have measured high glucose-induced lipogenesis by oil-red O staining. For investigating macrophage polarization, we assessment M1 marker, CD11c, as an inflammatory factor via flow cytometry. Also, inflammatory genes expression include: iNOS, arginase, and MCP1 were assayed by Real-time PCR.

Results: This study suggests that high glucose induce RAW264.7 lipogenesis. Flow cytometry analyses showed that high glucose skew RAW264.7 toward M1 subset, whereas Quercetin attenuated M1 marker up to about 70%. RT-PCR confirmed the anti-inflammatory effect of Quercetin through attenuation of inflammatory genes expression ($P<0.05$).

Conclusion: Reduction of lipogenesis, M1 surface marker and above inflammatory genes approve that Quercetin can be used as a therapeutic drug in inflammatory diseases.

Keyword: RAW624.7 cell line, Quercetin, High Glucose, Macrophage polarization

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ID:1088

Development of CRISPR System for Editing of Parkinson Disease Genes in prokaryotic cells

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Objective: CRISPR as a restriction endonuclease enzymatic system is a simple powerful tool for different genomes editing purposes. It enables researchers to easily alter DNA sequences and modify gene expression. This technique has many potential applications in correcting genetic defects, treating and preventing the spread of diseases and improving crops. CRISPR consists of two key molecules, an enzyme, called Cas9 and a piece of RNA, called guide RNA (gRNA) causing alterations in DNA molecules.

Material and Methods: By current study, LRRK2 Parkinson disease gene gRNA was designed with high score using of crispr.mit.edu webserver. gRNA oligonucleotides were then ligated into PX459-Puro expression vector using of T4 DNA ligase and then transformed into DH5α host bacterial cells via heat-shock procedure. After 24 hrs and using of ampicillin antibiotic screening well-grown colonies were selected and plasmid extraction performed using of alkaline lysis method.

Results: Successful cloning of gRNA segment was verified using of colony PCR and DNA sequencing analysis.

Conclusion: Primary results found by this work can enable us to more develop systems for editing, regulation, mutation and other manipulations in some bacterial genes.

Keywords: CRISPR system; Parkinson Disease; prokaryotic cells

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ID:1092

Assessment of association of circulating BDNF levels and its gene promoter methylation status with coronary artery disease

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Objective: New evidences show an important role of brain-derived neurotrophic factor (BDNF) in cardiovascular homeostasis. The aim of present study was to investigate the association of BDNF methylation status and its serum level with coronary artery disease (CAD) risk.

Material and Methods: According to angiography report 128 CAD patients with at least 50% stenosis in one major coronary artery were selected and divided into 1 vessel disease (1VD=48), 2 vessel disease (2VD=40) and 3 vessel disease (3VD=40) groups. For comparison, 73 angiographically proven non CAD participants were recruited as control. Genomic DNA was isolated from blood sample and methylation status of exon 2 BDNF gene promoter was determined using MS-PCR method. Serum BDNF levels were measured by ELISA. Data were analyzed using SPSS v16.0.

Results: BDNF gene promoter was methylated in 76.7%, 79.2%, 82.5% and 90.0% of the control, 1VD, 2VD and 3VD groups, respectively. The results indicate that hypermethylation of BDNF gene can increase the risk of CAD. However, the association was marginally significant (p=0.087) (1VD vs control group: OR=1.154;95% CI,0.477-2.790; 2VD vs control group: OR=1.431;95% CI,0.537-3.812 and 3VD vs control group: OR=2.732;95% CI, 0.851-8.776). Serum BDNF level was not statistically different between groups.

Conclusion: Our findings indicate that patients with severe CAD have a higher percentage of BDNF gene methylation compared to control group. Serum BDNF level was not statistically different between studied groups. Additionally, hypermethylation of BDNF gene could increase the risk of CAD. Although, this association was marginally significant.

Keywords: DNA methylation, Coronary Artery Disease, Brain-derived neurotrophic factor

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ID:1099

Study of Cytotoxic Effects of Tamoxifen-PLA Polymer Nanocapsules on Breast Cancer Cell Line MCF-7

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Objective: Breast cancer is an uncontrolled growth of abnormal cells which occurs in various breast tissues, such as the transmitter ducts, or the milk gland or in non-glandular tissue. A combination of chemotherapy,

radiation therapy and surgery are usually prescribed. Nowadays, nanocomposites are a successful tool to improving the quality of the drug delivery system in cancer patients, as well as reducing the complications of chemotherapy drugs on healthy cells. PLA Polymer Polymers are biocompatible biodegradable materials which are used as drug carrier. These materials turn to neutral lactic acid monomers during carbohydrate metabolism. In this study, the effect of cytotoxic nanosilver tamoxifen-encapsulated with PLA polymers on MCF-7 cell line (breast cancer) was investigated.

Material and Methods: The anticancer effects of nano-tamoxifen on the MCF-7 cell line were investigated using MTT assay at 48 and 72 hours. In this assay, tetrazolium (MTT) is converted by mitochondrial enzymes into furmasan purple crystals in the living cells. The amount of furmasan was calculated by spectrophotometric colorimetric method in a wavelength of 570 nm which, represents the percentage of cell biomass.

Results: With increasing drug exposure time from 48 to 72 hours and increasing drug concentration from 10 to 200µg/ml, the cytotoxic effect of the drug on the MCF-7 cell line was increased.

Conclusion: Finally, treatments of 200µg/ml for 72 hours lead to the highest mortality rate and decreased 6.57% to 5.35% cell viability.

Keywords: Poly lactic acid PLA, Tamoxifen, Nanodrugs, MCF-7

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ID:1100

Nitric Oxide concentrations changes in the plasma of patients with trigeminal neuralgia during different pain states

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Objective: Trigeminal neuralgia (TN), with exclusive severe pain, is a chronic neuropathic pain disorder in cranial nerves. Since involved mechanisms in pain pathway sensitization during TN is not understood completely, the results of the treatments are not satisfactory all the times. Regarding nitric oxide (NO) fundamental role in neuropathic pain, it is a candidate molecule involved in the pain pathway during TN.

Material and Methods: Thirteen healthy individuals, as a control group, and thirteen patients undergoing microvascular decompression (MVD) for treatment of purely paroxysmal TN, were included in the study. In order to evaluate NO in plasma of control group and patients before and after MVD, we used commercial calorimetric nitrate/nitrite (NO) assay Kit. Based on manufacturers' instructions, absorption of samples at 540 nm was read by the microplate reader and the level of total NO, including both nitrite and nitrate, was measured. McGill pain questionnaire was used to assess Pain Rating Index (PRI) in patients before and after MVD.

Results: NO concentration was 38.53±1.45, 47.61±1.261 and 44.23±2.948 µM in the control group, and patients before and after MVD, respectively. Statistical analyses of NO concentrations revealed a significant decrease ($P<0.01$) after MVD. In addition, it was significantly higher in patients (before and after surgery, $P<0.01$), in comparison with the control group. Moreover, assessment of pain severity in patients showed significant decrease after surgery ($P<0.01$).

Conclusion: Regarding elevated NO and PRI, in patients compared to healthy individuals and their decrease after MVD, it is suggested that No plays important role in pain pathway sensitization during TN.

Keywords: Trigeminal neuralgia, Nitric oxide, Pain pathway, Pain rating index

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ID:1101

Promoter methylation status of ABCA1 gene and its association with the severity of coronary artery occlusion

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Objective: Recent findings suggest that aberrant DNA methylation may have an important role in the pathogenesis of coronary artery disease (CAD). The aim of present study was to investigate the promoter methylation status of ABCA1, as an important gene in HDL metabolism, and its association with the severity of coronary artery occlusion.

Material and Methods: In this study 146 subjects based on the results of angiography were classified into four groups including normal group (n=42), patients with 1 coronary artery occlusion (1VD=40), patients with 2 coronary artery occlusion (2VD=33) and patients with 3 coronary artery occlusion (3VD=31). Blood sample was collected before angiography and used for genomic DNA

isolation. Methylation-specific PCR was used to examine gene promoter methylation status.

Results: ABCA1 gene promoter were methylated in 61.9% of the control group and 77.4, 54.5 and 77.7% of patients with 1VD, 2VD and 3VD, respectively. Promoter hypermethylation of the ABCA1 gene could not significantly increase the risk of CAD. Additionally, no significant association was observed between methylation status of ABCA1 gene and clinical risk factors of CAD.

Conclusion: Our findings demonstrate that the promoter methylation pattern of ABCA1 gene were not markedly different in patient groups compared to control. Additionally, changes in methylation status of this gene could not significantly increase the risk of CAD.

Keywords: DNA methylation, Coronary artery disease, ABCA1 gene

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ID:1106

CRISPR Development of Parkin gene in N2A eukaryotic cells

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Objective: Clustered Regularly Interspaced Short Palindromic Repeats-associated nuclease (CRISPR-Cas) system which is consist of a gRNA and an endonuclease protein called Cas that this protein can be conducted by single guide RNAs in order to disrupt genes in cells. Although the originates comeback to a microbial adaptive immune system, but nowadays it has become beneficial versatile achievement which provide a very efficient method for targeted gene disruption and any other genetic manipulations. Parkinson's disease (PD) cause involuntary shaking, muscle rigidity and also progressive loss of dopaminergic neurons. It is the second most incurable and common neurodegenerative disease in population until now. Parkin gene has an important role in incidence of Parkinson disease since some study reported which delete mutations can be causes PD severity.

Material and Methods: By this work, Desire gRNAs were ligated into Pguide-it vector which was modified by TAKARA Company then exist of gRNA was demonstrated by cloning PCR and sequencing analysis then recombinant vector containing gRNA of parkin gene was successfully transfected in N2A eukaryotic cells using of lipofectamine material.

Results: Florescence microscopy analysis and also PCR experiments verified successful cloning procedure.

Conclusion: Results found in this work could help us to modify different genes using of CRIPR endonuclease system and the result show mutation with exon 4 deletion which is common in people suffering of heritable form of PD.

Keywords: Genetic Manipulation, CRISPR System, Parkin Gene, Parkinson Disease

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ID:1108

Genetic manipulation of the ZNF543 as a guilty gene in Parkinson disease (PD)

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Objective: RNA-guided platform technology based on CRISPR (Cluster Regularly Interspaced, Palindromic Repeat) open a new avenue toward DNA manipulation which consisted of two major parts: guide RNA and Cas9 endonuclease. Collaboration between these components form a RNA-protein complex which cause DSB (double strand break). Cell repair mechanisms consist of NHEJ (non-homologous end-joining) and HDR (Homology-Directed Repair) can detect break in genome and repair it. Inspired by these nature mechanism, scientists were able to precise manipulate cells enome. Given a recent study, ZNF543 gene mutation acts as one of the Parkinson disease reasons, so we decide to establish a cell model with mutation in promoter region of ZNF543 as a guilty gene in Parkinson disease.

Material and Methods: A general analysis to finding conserved region throughout the ZNF543 gene using UCSC genome browser were done, then the dsDNA for desire guide RNA with highest score offered by crispr.mit.edu site was ligated into linear (Pguide-it) vector and recombinant vectors were then transformed into DH5α) E. coli), then we use of SH-SY5Y cell line for vector transfection and transfect were done with lipofectamine2000, for mutations detect in promoter region conventional PCR were done.

Results: Transfection efficiency was determining by fluorescence microscopy and mutations were demonstrate with conventional PCR.

Conclusion: Crispr system as a new method for genome editing were used in this study, and we create some indel mutation in ZNF543 gene as a guilty gene in Parkinson disease. It was demonstrated which delete mutation in this gene is related to PD.

Keywords: Crispr System, ZNF543, Parkinson Disease, Mutation, Cell Model
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ID:1109

α-Lipoic Acid: A Multifunctional antioxidant that improves lipid profile in patients with gestational diabetes

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Objective: The importance of gestational diabetes (GDM) is due to its harmful effects on the fetus and the long-term prediction of NIDDM in the mother. Increasing serum levels of TG and LDL are risk factors for high blood lipids and cardiovascular disease in the future for women with GDM. GDM are associated with an increased level of oxidative. Data has shown that ALA is effective due to its antioxidant properties to prevent or treat diabetes complications and prevents excessive production of reactive species of oxygen and nitrogen. The aim of this study was to investigate the effect of lipoic acid on lipid profile in women with gestational diabetes mellitus.

Material and Methods: Sixty women with GDM enrolled in this study. Thirty of them were randomized in the drug group (receiving 100 mg/day of ALA) and 30 women were randomized in placebo group. Intervention was continued for 12 weeks. In both groups all subjects finished the study and were included in the analysis. Serum levels of the variables were measured before and after supplementation.

Results: Serum value of TG (P = 0.006) decreased significantly in the drug group Also, the mean serum triglyceride level before the study was not statistically significant, but the mean serum triglyceride level after the study was statistically significant. However, did not show significant differences in TC, HDL-C and LDL-C.

Conclusion: The results of the current study had shown that after supplementation with 100 mg/day of ALA for 12 weeks, serum value of TG in women with gestational diabetes mellitus decreased.

Keywords: Alpha lipoic acid, Gestational diabetes, oxidative stress
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ID:1112

Targeting Cancer Stem Cells by Exosome-Madiated Drug Delivery

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Objective: High prevalence and mortality of cancer have made this disease a major health concern worldwide. Late diagnosis, resistance to conventional therapies and metastasis are challenges that need to be overcome by novel anticancer approaches. Since cancer stem cells (CSCs) are associated with undesired properties such as failure of chemoradiotherapy, specific targeting of these cells will lead to much more promising clinical outcomes.

Material and Methods: To review novel targeting strategies against CSCs, recent papers including key words cancer stem cells, exosome and drug delivery were extracted from databases PubMed, Scopus, and Web of Science.

Results: Exosomes are very small vesicles derived from intracellular late endosomes, presented in cell conditional medium and body fluids. They can be isolated by special surface markers, and carry different biomolecules, such as proteins, lipids, mRNAs and micro RNAs, which protect them from degradation. Due to their biocompatibility, stability and ease of production by most cell types, exosomes are good candidates for precise delivery of therapeutic molecules to CSCs. Recent studies reported that doxorubicin-loaded exosomes induced considerable anticancer effects in vivo, similar to exosome-encapsulated paclitaxel that can directly target drug resistant CSCs. Other anticancer drugs that showed improved efficacy upon exosome-mediated delivery are withaferin A, celastrol and curcumin. Since CSCs express surface markers such as CD44, CD24 and CD133, exosomes coated with such antibodies could specifically deliver their therapeutic cargo to improve CSC targeting efficiency.

Conclusion: Exosomes are natural nanocarriers with great potential to be used in future CSC-targeted therapies, although more research is necessary to optimize their cargo loading capacity.

Keywords: Exosome, Cancer stem cell, Targeted therapy

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ID:1113

Synthesize, characterizing and study of the cytotoxicity of nioliposomal nanocarrier containing ginger extract

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Objective: Today, Cancer is the most common cause of mortality in human societies. Treatment on different types of cancer is very complex and the discovery of new anticancer drugs along with high efficiency, low cytotoxicity that is able to affect the cells selectively with a low price, is one of the major concerns of the pharmaceutical community in the world. Recently, it has been proven that nanoscience can increase the effectiveness of treatment while reducing the side effects. Nioliposomes is one of these nanocarriers for drug delivery. The aim of this paper was to synthesize Nioliposomes containing ginger extract and investigate its cytotoxicity on healthy and cancerous cells.

Material and Methods: Ethanolic extract of Ginger root was prepared using soxhlet apparatus. Nioliposomes containing ginger extract were synthesized by thin-film hydration method. In order to reduce nanocarrier particles size probe sonication was applied. Nanoparticle's size, zeta potential, encapsulation efficiency, and release profile of extract form carriers were assayed. Blank nanocarrier, nanocarrier containing ginger extract and the extract alone cellular cytotoxicity were evaluated by MTT assay on Human foreskin fibroblast (HFF) cell line, as a normal and typical cell line.

Results: The Nioliposomes showed the mean diameter of 87 nm and the loading efficiency of 48.5%. The release profile of extract from nanocarrier showed to be controlled and time-dependent. Although nioliposome containing ginger extract showed no cytotoxicity in healthy cell lines, it was toxic to cancer cell lines.

Conclusion: Given the fact that nioliposomal form of ginger has cytotoxic properties in cancerous cells and has no cytotoxic effect in normal cells proves the carrier to be a potent therapeutic option in cancer treatment.

Keywords: Ginger, nioliposome, cancer

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ID:1114

The role of Retinoic Acid in pathogenesis of Craniosynostosis

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Objective: The aim of present perusal was to perform a systematic review for revealing the impact of Retinoic acid in pathogenesis of Craniosynostosis. The condition in which cranial sutures are fused prematurely is predicated Craniosynostosis. Increased intracranial pressure, conversions of the pattern of cranial growth, the maladaptive shape of the head and mental delay are caused by this. Skeleton organ s development is affected by retinoic acid witch the most active metabolite of vitamin A.

Material and Methods: An electronic search using the databases PubMed, Cochrane Library and Scopus until March 2018 was carried out. Literatures that performed the PICO (Patients, Interventions, Controls and Outcome) criteria, were selected. PRISMA checklist were used to appraise the quality of included studies. There was language restriction.

Results: A whole of 311 abstracts were matched by key words in the literature search, extracted. Nine studies met the inclusion PICO criteria. Four studies were about pathophysiological conditions that caused craniosynostosis. Four studies were about signaling pathway of retinoic acid in craniosynostosis development. And finally one study proceeded to metabolism of retinoic acid and mutagen role of it.

Conclusion: These finding have ascertained that retinoic acid altered osteoblast-to-preosteocyte transitioning. Development of cranial suture at different phase affected by activity of functional module. Moreover, cranial suture patency maintains by retinoic acid. Based on this study, if key signaling molecules in these pathways are recognized, probably can use of pharmacological approaches to therapy.

Keywords: Craniosynostosis, Retinoic acid, vitamin A, Signalling pathway

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ID:1116

The investigation obscure degree of reticulation in breast cancer management;

providing new pliable network for molecular targeted therapy

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Objective: Breast cancer (BC) is a heterogeneous disease and different interlinked molecular platforms are implicated in the various developmental stages of complex entity. In particular, some signaling pathways, inflammatory factors and immune system related- lattice are drastically coordinated with tumor mass to introduce more flexible and destructive progression in BC.

Material and Methods: Our analysis through studying some articles and several well done Meta analyses is exerted a newly designed hypothesis that is implied a concrete risk factor assessment for obtaining more precise evaluation of therapy regimens.

Results: Generally, C-MYC, PGE2, IL-6, TNF-α, some stromal cells specially tumor- associated macrophages (TAMs), adipokine and psoriasin are provided a tenacious and feasible schemata of tumor growth and progression in both early stage management of breast cancer and therapy implication periods.

Conclusion: The mentioned interlinked molecular mechanisms can be abnormally regulated in different stages of breast cancer similar to that of impaired molecular interactions based on cell-type, the degree of drug metabolism as well as the stress and immune response level whose can contribute to tumor viability. In a way that, IL-6, IL-10 and psoriasin can be considered as external influential switches for mesenchymal transition of cognate interlinked lattice to manifest more pliable gowth type. Finally, the therapeutic implications of this molecular interactome might be play a key role in the early diagnosis of targeted therapy risks.

Keywords: Breast cancer, molecular interaction, targeted therapy

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ID:1119

Long-Term Effects of Prenatal Stress and Protective effects of Nano-curcumin on Dopamine and Glutamate Receptors in Adult Mice Brain

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Objective: Prenatal stress is so common but its significant effects on development and life time of fetus is unknown. In this study, we assessed the protective effects of Nano-curcumin and prenatal stress on the expression of selective dopamine and glutamate receptor subtypes in the adult offspring's of mice subjected to repeated restraint stress during the last week of pregnancy.

Material and Methods: Virgin female mice (25±30 g) were obtained from a highly inbred rats from our own animal facility at the Shiraz University of Medical science. On the day of proestrus, sexually experienced male mice (25±30 g) were introduced for mating. At the end of the test, the pregnant females were randomly assigned to prenatal stress, nano-curcumin and control group. After 90 days, the adult mice were sacrificed and brains removed and Dopamine D2-like receptors and Glutamate NMDA receptors in dorsal frontal cortex (DFC), medial prefrontal cortex (MPC), hippocampal CA1 region and core region of nucleus accumbens (NAc) were measured.

Results: These results indicate that stress during the gestational period has long lasting effects that extend into the adulthood of prenatally stressed offsprings Changes in dopamine and glutamate receptor subtype levels in different forebrain regions of adult mice in prenatal stress was significant compare with control group.

Conclusion: Our research concludes that Maldevelopment of these pathways may provide a neurobiological substrate for the development of schizophrenia and other idiopathic psychotic disorders and Nano-curcumin has a protective impact on these complications.

Keywords: Dopamine D2-like receptors, Glutamate receptors NMDA, Nano-curcumin, Prenatal restraint stress

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ID:1121

The Effect of high intensity intermittent trainings on brain-derived neurotrophic factor and glial cell linederived neurotrophic factor levels in brain of rats

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Objective: Researches have showed that exercise trainings increase the brain-derived neurotrophic (BDNF) and glial cellderived neurotrophic factor (GDNF) in the brain. In addition, hydrogen peroxide (H_2O_2) and tumor necrosis factor alpha (TNFα) increase protein content of BDNF and GDNF in vitro. However, there is insufficient information about the interactive effects of high intensity exercise training, H_2O_2, and TNFα on neurotrophins. Hence, in the present study, we investigated the effect of high intensity intermittent training on the content of BDNF, GDNF, H_2O_2 and TNFα in the brain of albino wistar rats.

Material and Methods: Sixteen albino wistar rats divided into control and high intensity intermittent training groups. High intensity intermittent training has carried out for 6 weeks with 95 to 100% of maximum oxygen consumption on treadmill. BDNF, GDNF and TNFα contents have measured by sandwich ELISA method and H_2O_2 concentration by colorimetric method by commercial kits. Data analyzed using Student's t-test, and $p \leq 0.05$ considered as statistically significant.

Results: High intensity intermittent training resulted in 75 and 143 percent increased in H_2O_2 ($p<0.0001$) and TNFα ($p<0.0001$) levels, which accordance with 149 and 170 percent increase in BDNF ($p<0.0001$) and GDNF ($p<0.0001$) content in the brain, respectively.

Conclusion: Overall, performance of training sessions as interval with maximum capacity resulting in increase of BDNF and GDNF content in brain of albino wistar rat and it seems H_2O_2 and TNFα influence on neurotrophins adaptation induced by high intensity intermittent training.

Keywords: Rat, BDNG, GDNF, TNF-A, H_2O_2

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ID:1124

Diagnostic Aptamer for Cancer Detection: Recent Advances

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Objective: Aptamers, single-stranded oligonucleotides (generally less than 100 nucleotides), bind to broad variety of cancer specific targets with same binding affinity to antibodies (nano or picomolar range); However, there are several advantages of using aptamer in comparison with antibodies, for instance more convenient in vitro selection, lack of aggregation problems, simple chemical synthesis methods and inexpensive process of selection and production. In addition, after identification of specific aptamers during different selection process, they can be easily modified and improved for diagnostic applications. In general, each round of SELEX, the systematic evolution of ligands by exponential enrichment, contains three main steps: Binding, Partitioning and Amplification. About cancer detection, there are some SELEX technologies, such as protein-based SELEX, Whole Cell-Based SELEX, Live-Animal-Based SELEX and High-Throughput SELEX, using them aptamers are developed against different types of cancers. In the field of cancer specific biosensor, aptamers are ideal bioreceptors. There are some aptasensor methods in cancer detection such as Fluorescent, colorimetric and electrochemical strategies. Aptamers are developed against a wide variety of tumor specific biomarkers, such as those of early detection, metastatic detection and etc. Some of aptamers are designed to target multiple cancers. In addition, aptamer are appropriate tools for tumor marker discovery. Aptamers are becoming common as promising diagnostic agents, as of last decades, there were substantial advances developing aptamers detecting a variety of tumors, such as lung, ovarian, colorectal, prostatic, osteosarcoma, hepatocellular, bladder and breast cancers.

Keywords: Aptamer, Cancer, Aptasensor, diagnosis

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ID:1126

Theranostic application of aptamers in cardiovascular diseases

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Objective: Aptamers are biomolecular ligands made of single-stranded DNA or RNA oligonucleotides selected by a method known as Systematic Evolution of Ligands by Exponential Enrichment (SELEX) based on affinity and specifity for target molecules. Whereas aptamers have many advantages versus monoclonal antibodies, such as fast detection method, high affinity and specificity, flexible modification and stability, and low toxicity and immunogenicity, they are hopeful novel diagnostic and therapeutic approaches. To date, aptamers have been selected against a various of targets such as proteins, sugars, phospholipids, metal ions, chemical compounds, as well as whole cells. A notably active field of aptamer research in the last decade was development of aptamers against various molecular targets involved in

cardiovascular diseases. Aptamers were also applied to cancer diseases, infectious diseases, inflammatory diseases, and eye diseases. Until now, therapeutic applications of synthetic nucleic acid aptamers for cardiovascular diseases include aptamers that were selected against thrombin, von Willebrand factor (vWF), factor IX, factor XII, P-selectin, VEGF as potential anticoagulants, antithrombotics, and anti-angiogenic. Also, aptamers that were selected against troponin T and I, C-reactive protein (CRP), CK-MB, myoglobin, and brain natriuretic peptide(BNP) used to diagnostic applications for cardiovascular diseases. With the developments of SELEX technology and further preclinical and clinical trials, aptamers are promising to replace conventional anticoagulants or antithrombotics in treating cardiovascular diseases. Furthermore, this highly sensitive and selective aptamers provides a novel method for clinical diagnostics that predict risk for cardiovascular disease.

Keywords: Aptamers, Cardiovascular diseases, SELEX, Anticoagulants

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ID:1134

Molecular cloning and expression of the oxalyl-coenzyme a decarboxylase in E. coli

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Objective: Oxalic acid is found in nutritional sources or is produced by the intestinal microflora. Enzyme oxalyl-coenzyme a decarboxylase from the bacterium Oxalobacter formigenes can degrades oxalic acid. Oxalic acid is catabolized by an activation-decarboxylation reaction which yields formate and CO2. Oxalyl-coenzyme a decarboxylase is a 568-amino-acid protein with a molecular weight of 60,691. In this study, we report the heterologus over-expression of Oxalyl-coenzyme a decarboxylase in E. coli BL21 (DE3).

Material and Methods: Escherichia coli is the most commonly used host for producing of recombinant protein. Using BL21 derived strain can reduce proteolyses of hetrologous protein. In this study for over-expression of oxalyl-coenzyme a decarboxylase we design a synthetic gene and clone in pET28a using NdeI and EcoRI sites. To express oxalyl-coenzyme a decarboxylase from pET28a, transformed BL21 (DE3) and different medium like LB and TB was applied. The results of experiments were analyzed by SDS-PAGE, western blotting and cell growth and recombinant protein production kinetics.

Results: The optimal expression of oxalyl-coenzyme a decarboxylase in E. coli can be easily achieved when the growth conditions are properly controlled. Media components and IPTG concentration have profound effects on the way in which recombinant protein is produced. In this study the maximum expression was obtained from TB medium at 28°C with IPTG concentration of 0.1mM. The final yield was 35 % of total soluble proteins, which is a significant rate for oxalyl-coenzyme a decarboxylase expression in Escherichia coli.

Conclusion: In conclusion, the studies presented here establish that high-level expression of oxalyl-coenzyme a decarboxylase. Using rich medium likes TB and decrease temperatures can improve the amount of protein considerably.

Keywords: Oxalyl-coenzyme a decarboxylase, Oxalobacter formigenes, Escherichia coli, Over-expression

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ID:1143

The association of SNP rs1870634 in LINC00841 with CAD: A GWAS-Replication Study in an Iranian Population

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Objective: Recent genome-wide association studies (GWAS) identified a list of single-nucleotide polymorphisms (SNPs) associated with coronary artery disease (CAD). Replication of GWAS findings in different population corroborated the observed association in the parent GWAS. In this study, we aimed to replicate the association of rs1870634, a GWAS identified SNP, to CAD in an Iranian population.

Material and Methods: The study population consisted of 267 subjects undergoing coronary angiography coronary angiography including 155 CAD patients and 112 non CAD age- and gender-matched controls. The genotype determination of rs1870634 SNP performed using high-resolution melting analysis (HRM) technique.

Results: Our results revealed that the GG genotype frequency was significantly higher in CAD patients compared with controls (P =0.03). The results of binary logistic regression suggested that this genotype was significantly associated with CAD risk adjustment for age, BMI, sex, TC, and LDL-C

lipid levels (OR of 2.78, 95% CI (1.10–7.01), P=0.03).

Conclusion: Moreover, our results showed that the GG+TG genotypes were 2.52 times more likely to develop CAD (95% CI 1.05–6.03) than TT genotype carriers after adjusting for age, sex, and lipid profiles (P=0.037). These data showed that the GG genotype could be associated with increased risk of CAD in a sample of Iranian population.

Keywords: Coronary artery disease, Long intergenic non-protein coding RNA841, Single-nucleotide polymorphisms

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ID:1146

Coffee could halve breast cancer recurrence in tamoxifen-treated BALB/c mice

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Objective: Breast cancer is the biggest health threat to women. The current common treatments include surgery, chemotherapy, and radiotherapy. In most cancers, metastasis is the primary cause of treatment failure. Surgery and radiotherapy are effective on local tumors, but they cannot affect metastatic cancers. Tamoxifen is a non-steroidal anti-estrogen that is widely used to treat breast cancer. Combination therapies are one of the therapeutic strategies that can help enhance the performance, reduce the dose, and shorten the consumption period of tamoxifen. This study aimed to investigate the synergistic effect of tamoxifen and coffee on the 4T1 into BALB/c mice.

Material and Methods: Methods Female Balb/c mice (5-7 weeks old) were used in this study. Tumors were established using 4T1 tumor transplantation method. Treatment began after two weeks, when tumors reached an appropriate size, the first, second, and third groups of BALB/c mice were injected with 17beta-estradiol and tamoxifen dissolved in dimethyl sulfoxide (DMSO) at doses of 5.1, 10, and 20 µM, aged coffee and tamoxifen at doses of 10, 30, and 60 mg/kg, and PBS over a 14-day period respectively. Then, the tumor volume was measured using a caliper. TUNEL assay kit was used to detect apoptosis. Results Data were analyzed using the one-way analysis of variance (ANOVA).

Results: The results showed a significant difference between the negative control group and tamoxifen-treated group in terms of the simultaneous injection of coffee extract and tamoxifen ($P<0.05$). The results also showed increased apoptosis in this synergy.

Conclusion: Tamoxifen prevents estrogen from binding to cancer cells, thus stopping cancer cell growth. This study aimed to investigate the synergistic effect of tamoxifen and coffee. The results of this study are consistent with this finding and apoptosis has increased.

Keywords: Hormonotherapy, Tamoxifen, coffee, Breast Cancer

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ID: 1149

Serum ferritin is correlated with the Thyroid stimulation hormone level

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Objective: Iron is one of the key factors necessary for the normal thyroid function. In most of the human tissues, iron is mainly stored in form of Ferritin. It has been reported that Serum ferritin level is dys-regulated in thyroid disease and ferritin level in circulation is associated with thyroid hormone function. Indeed, many studies have indicated the relationship between serum ferritin levels and Thyroid stimulating hormone (TSH). The purpose of this study was to measure serum ferritin levels in relation to concentration of TSH in Iranian population of Ahvaz city, Iran during 2016-2017.

Material and Methods: The number of 130 individuals (female=99 and male=31) were requited in this cross sectional study. The serum ferritin level and TSH were evaluated using chemiluminescence method. The data was analyzed using SPSS v.16 and the p-value≤0.05 was considered as significant.

Results: The results of our findings showed that most of the included individuals were in normal range for serum ferritin (73.76±78.75) and TSH level (2.63±9.56). The person's correlation test revealed that the ferritin level is significantly correlated with the measured TSH hormone (R=0.213, p value=0.015).

Conclusion: Altogether, we found that the serum ferritin and TSH levels are significantly co-related. Our results suggest that, measurement of the serum ferritin can be helpful in monitoring the thyroid hormone dysfunction.

Keywords: Ferritin, Thyroid hormone, TSH

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ID:1150

Synergistic effects of A2B adenosine receptors agonist with docetaxel in esophageal cancer cells

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Objective: The function of A2B adenosine receptors has been evaluated in various human cancer cells, but currently, there has been no study about the role of A2B adenosine receptors in esophageal cancer. The aim of current study was to evaluate the effect of A2B adenosine receptors agonist on cell growth of YM-1 esophageal cancer cells in presence of a chemotherapy drugs.
Material and Methods: The YM-1 human esophageal cancer cells were seeded in 96-well plates. The cells then were treated with various concentrations of A2B adenosine receptors agonist (BAY606583) in the absence or in the presence of the docetaxel for 48 h and cell viability determined by MTT assay.
Results: A2B adenosine receptor agonist induced cell cytotoxicity in YM-1 cancer cells in a dose dependent manner. Combination of A2B adenosine receptor agonist with docetaxel had a synergic effect on the reduction of cell proliferation.
Conclusion: A2B Adenosines receptors agonist can sensitize esophageal cancer cells to the chemotherapeutic drug with prolonger effect and thus it can be considered for designing of novel anticancer therapies.
Keywords: A2B Adenosines receptors, esophageal cancer cells, BAY606583, Docetaxel
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ID:1151

Correlation between β1-Integrin Expression and different stages of Colorectal Cancer in Iranian Patients

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Objective: Colorectal cancer (CRC) is a preventable and potentially curable disease if high risk adenomas and early stage tumors are removed. For early diagnosis, validated biomarkers are an urgent need. Beta 1 integrin not only is a membrane receptor that plays a role in ECM formation, but also contribute in proliferation, migration, invasion, survival in transformed cancer cells. In this study, correlation between different stages of CRC and expression level of β1-Integrin at protein level was investigated.
Material and Methods: Formalin-fixed, paraffin-embedded (FFPE) tumor samples of 45 patients who were operated because of colorectal cancer without any neoadjuvant therapy were obtained. β1 integrin expression was evaluated using Immunohistochemistry by a monoclonal antibody. Image J software was used to semi-quantify the intensity of colour within cells. The Relationship of colour intensity in different stages of CRC was assessed using statistical anylysis.
Results: In normal and primary stage tissues of CRC, weak reaction was observed in immunohistochemistry indicating that expression of β1 integrin does not work well for discrimination of early stages from normal tissues of CRC. Significantly higher β1 integrin expression was found in advanced stages of CRC compared with that of normal ones (p=0.01), showing that this biomarker could be able to diagnose higher stages from normal subjects.
Conclusion: β1 expression in CRC represents a reliable diagnostic factor regarding the staging of CRC and our findings imply that β1 integrin expression profiles may have further potential in identifying stages of colorectal cancer.
Keywords: Colorectal cancer, β1 integrin, biomarker, immunohistochemistry
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ID:1154

Synthesis, characterization and application of nano-liposome for co-delivery of cisplatin, cinnamaldehyde and al-trans retinoic acid to circumvent the drug resistance in MDA-MB-231 breast cancer cells

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Objective: Combination therapy-based on nano-carriers is an emerging technology in order to overcome the drug resistance in cancer treatment.
Material and Methods: Here co-encapsulation of cisplatin, all-trans retinoic acid (ATRA) and cinnamaldehyde (CA) was carried out in a single nano-liposome to investigate the CA and ATRA's synergistic effects to overcome cisplatin resistance in MDA-MB-231 breast cancer cells. In this way, liposomes containing drugs were prepared by thin film hydration

technique. The formulation characterized for particle size, zeta potential, scanning electron microscope (SEM) and Fourier transforms infrared spectroscopy (FTIR). In order to evaluate apoptotic rate, molecular mechanism and cell cycle arrest; MTT, flow cytometric assay and DAPI staining was performed.

Results: The co-loaded liposome demonstrated average size of 45±2nm with encapsulation efficiencies of >80%. CA as a natural product and ATRA exhibited significant synergetic efficacy in improvement of MDA-MB-231 cancer cells sensitivity to cisplatin as a cytotoxic agent. The IC50 values for free drugs were estimated 20µM for cisplatin, 130µM for CA and 50µM for ATRA. Our results showed that encapsulation of cisplatin, CA and ATRA increases the IC50 values to 16µM for cisplatin, 96µM for CA and 35µM for ATRA. Also, treating the cells with drugs IC50 combination significantly increases the cytotoxic effect compared with single treatments and the IC50 value for combination was 10µM. Remarkably, the composite liposome lead to increase in the apoptosis percentage.

Conclusion: This study suggests that co-delivery of ATRA, CA and cisplatin potentially affects the drug-resistant of tumor cells to chemotherapy.

Keywords: ATRA, Cisplatin, Co-delivery, Cinnamaldehyde, Liposome

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ID:1158

The Correlation between urinary catecholamine metabolites levels together in hypertensive patients

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Objective: Hypertension is defined as increased blood pressure of the arteries. It has been reported that in hypertension condition, levels of the epinephrine and norepinephrine secretion are increased. Measurement of these metabolites including Vanillylmandelic acid (VMA), Metanephrine (MN), Normetanephrine (NMN) in urine can be considered as a non-invasive method for monitoring different diseases such as cardiovascular complications. The aim of this study was to compare these metabolites levels in urine of the hypertensive patients according the gender.

Material and Methods: The 24H urine samples from hypertension patients (number=51, female=30 and male=21; aged of mean=40.49±2.32) were collected. All the individuals had systolic blood pressure level higher than 140 mmHg. The uVMA was measure with HPLC and for detection of the uMN and uNMN ELISA was used. The measured variables were compared with the normal range defined by the kit supplier. For statistical analysis, SPSS v25 was used.

Results: Our findings indicated that the mean levels of the Catecholamine metabolite in urine (uVMA=5.2±0.45, MN=157±21 and NMN=300±34) are in normal range. The level of the uNMN and uVMA was more in male (mean-difference= 27.68 and 1.62 respectively), however the female showed higher level of the uNMN (mean-difference=12.12, p value=0.01). We observed a significant correlation between uNMN and uMN (RS=0.624, P<0.0001), but there was no correlation between VMA and other metabolites.

Conclusion: Altogether our findings suggest that urinary Catecholamine metabolites can be associated with gender in hypertensive individuals.

Keywords: Hypertension, Catecholamine metabolites, Urine

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ID:1159

The role of CXCL 12 in pathogenesis of astrocytoma

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Objective: The purpose of this study was to appraise a competent systematic review of CXCL12 role in contribution and development of astrocytoma. Background Common language between tumor and microenvironment is chemokine. Microenvironment next the tumor, trace entire process of tumor. CXCL 12 is subset of chemokines and component of Immunological factors has significant figure in pathogenesis of astrocytoma. As a result, present study was designed for investigate the

communication of tumor cell proliferation and CXCL12 in tumor surrounding microenvironment Methods an electronic search in databases PubMed, EMBASE and Scopus was carried out until March 2018. Literatures that performed the PICO (Patients, Interventions, Controls and Outcome) criteria, were selected. There was no language restriction. Results of the 467 articles were found in initial search, 6 studies set by the PICO criteria. 3 studies were about axis of CXCL12 and its receptors CXCR4-CXCR7 in Tumor microenvironment. 3 studies were about pathogenesis role of CXCL12 in central nervous system (CNS) tumors specially astrocytoma. Conclusion these finding have ascertained that CXCL12 has cardinal character in neurogenesis happened in astrocytoma. For improving cancer remedies, interactions between tumor and Microenvironment have to qualify well. Based on this study, probably can use of CXCL12/CXCR4 axis in chemical therapy. Microenvironment is influenced by different biochemical factors so well -designed studies are need in future.

***Keywords*:** CXCL12, Astrocytoma, Microenvironment, Signalling pathway

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ID:1165

Evaluation Level of Total Antioxidant Status (TAS), Total Oxidant Status (TOS) and Thiol Disulfide Between Non-Obese And Obese İndividuals

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Objective: Obesity is an energy intake more than the energy consumed and the increase in body fat mass relative to lean body mass. It is a chronic disease causes hormonal disorders together; this makes various diseases in many systems. Obesity has been common in the worldwide increasingly and is associated with adverse health problems such as hypertension, coronary heart disease, diabetes, some types of cancer. The aim of this study is to investigate the role of thiol-disulfide balance as an oxidative stress formed in obesity.

Material and Methods: The study was conducted with 45 obese and 45 healthy (non-obese) control groups. TG, Total cholesterol, HDL, LDL were measured by the enzymatic colorimetric method in serum with Cobas Roche 6000 autoanalyzer. TAS, TOS and thiol-disulfide balance were measured with Erel method in the serum that is taken for routine triggers from the individuals who applied to the IMU Biochemistry Laboratory.

Results: In this study, obese group weight (kg), BMI, TG, TOS and OSI level compared to the control group was significantly increased ($p<0.001$), while HDL and TAS levels were significantly lower ($p<0.001$). In obese group compare to control group, disulfide, disulfide/native thiol, disulfide/total thiol concentration were significantly increased ($p<0.01$).

Conclusion: The results obtained of this study will benefit for further studies. A significant change in thiol-disulfide balance has been suggested that it is important parameter can calculate in future studies of obesity. Understand the molecular basis of obesity-related disease development; it will be useful in developing new approaches to prevent or treatment of these diseases.

Keywords: Disulfide, Disulfide/thiol ratio, Obesity, Oxidative stress, Thiol

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ID:1166

Evaluation of the silencing effect of miR-105 on Tim3 expression in Aml cell line

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Objective: Acute myeloid leukemia is a myeloid stem cell disease in which differentiation of cells is impaired. In AML, Stem cells consist of hematopoietic and leukemic ones. Treatments of cancers such as chemotherapy just targets leukemic cells, but does not affect on LSCs. Tim3 is a marker on the surface of LSCs that could be a subject for targeting. Tim3 just is expressed on LSCs and could be silenced by miRNAs. Some bioinformatic programs indicate that miR-105 can target Tim3. In this study the role of miR-105 in silencing of Tim3 was evaluated experimentally.

Material and Methods: HL-60 cell line was cultured and induced by PMA to express Tim3. On the next day, expression of Tim3 was measured by flow cytometry. Then PMA threated cells were cultured in 24 cell culture plate in four groups and transfected by miR-105-5p mimic, scramble FITC, transfection reagent and cell culture medium as negative control. After a day, scramble FITC group was observed by Fluorescent microscope and the next day the expression of Tim3 was evaluated by flow cytometery in all groups. Finally, the mRNAs of Tim3 were quantified by qPCR.

Results: Our results showed miR-105-5p can reduce Tim3 protein but can not affect on quantity of its mRNA significantly.
Conclusion: We concluded that miR-105 can target Tim3. Therefore, bioinformatic prediction data were confirmed by experiment and Targeting of Tim3 could be considered as a therapeutic methods.
Keywords: Tim3, Hl60, miR-105
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ID:1172

Visfatin induces gene expression of extracellular matrix components in pre-adipocytes and differentiated adipocytes

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Objective: Adipose tissue (AT) can respond rapidly to excess caloric intake and insufficient energy expenditure. Adipocytes and pre-adipocytes are enclosed by a three dimensional network of extracellular matrix (ECM) proteins which serve as mechanical support and allow AT to extend normally. Adipose tissue fibrosis is a condition in which ECM increases aberrantly, which restrict adipocytes and leads to immune cell infiltration and cytokine production. Visfatin is a multi-functional molecule that acts as an adipokine, cytokine and enzyme. Secretion of this cytokine in adipose tissue increases during obesity. The major objective of this study was to investigate the effect of visfatin on gene expression of collagen VI and osteopontin as major constituents of ECM family.
Material and Methods: 3T3-L1 cells were cultured in DMEM supplemented with 10% FBS and 1% antibiotic at 37℃in 5% CO2. To induce differentiation, confluent 3T3-L1 pre-adipocytes were further cultured in DMEM containing 10% FBS, 1% antibiotic, 0.5 mmol/L isobutylmethylxanthine, 0.25 µmol/L dexamethasone, and 1 µg/mL insulin. Cells were treated with 200 ng recombinant visfatin for 24, 48 and 72 h. Total cellular RNA was extracted and cDNA was synthesized from 1µg total RNA. Real-time quantitative RT-PCR analyses were performed using SYBR green method.
Results: Our results showed that visfatin significantly increased osteopontin gene expression in pre-adipocytes as well as differentiated adipocytes, 24 and 48 h after treatment. Although, the expression of collagen VI genes in pre-adipocytes was not affected by visfatin, it was increased in adipocytes.
Conclusion: Visfatin increases extracellular matrix proteins in pre-adipocytes and adipocytes and thus might be a contributing factor in adipose tissue fibrosis.
Keywords: Obesity, Adipose Tissue Fibrosis, Visfatin, Collagen VI, Osteopontin
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ID:1175

Evaluation of the Analytical Performances of Five Different Hemoglobin A1c Methods due to Significance of HbA1c Test in Diagnosis and Prognosis of Diabetic Patients

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Objective: Diabetes Mellitus is a global endemic disease and also considered as one of the biggest public health problems with rapidly increasing prevalence in both developing and developed countries. Glycated hemoglobin (HbA1c) is considered the gold standard test to evaluate the degree of glycemic control in patients with diabetes Mellitus disease. The American Diabetes Association has recommended HbA1c as a substitute test to fasting blood glucose (FBS) for diagnosis of this disease. Several laboratory methods have been developed to measure the levels of blood HbA1c in the clinical Laboratory. The aim of this study was to evaluate the clinical performance of different assays for categorizing patients into healthy, controlled and uncontrolled diabetes mellitus according to ADA's suggestion.
Material and Methods: In this study, HbA1c levels of 55 samples were analyzed by six commercially methods; microcapillary electrophoresis (Sebia), enzymatic method (Pishtaz Teb), immunoturbidometry (Pars Azmoon), boronate affinity (Nycocard), immunofluorescence (i-chroma) and Tosoh G8 HPLC. SPSS version 15 packages were used for computation and analysis of the data.
Results: Sensitivity of microcapillary electrophoresis, enzymatic method,

immunoturbidometry, boronate affinity, and immunofluorescence at HbA1c level of 6.5% were 97.5%, 100%, 77.5%, 77.5%, and 67.5%, respectively. The Specificity results of all methods at HbA1c level of 6.5% were 100%, 86.7%, 100%, 100%, and 93.3%, respectively. Positive (and negative) predictive values of all methods at HbA1c level of 6.5% were 100%(93.8%), 95.2%(100%), 100%(62.5%), 100%(62.5%), and 96.4%(51.9%), respectively.

Conclusion: The results show that some methods for measuring HbA1c for the classification of diabetic patients based on HbA1c levels are still not acceptable.

Keywords: Diabetes Mellitus, HbA1c, Analytical Performance, HbA1c measurement methods

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ID:1177

A Genetic Association Study of MTHFR C677T Polymorphism with Risk of Metabolic Syndrome: A Meta-Analysis

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Objective: Methylenetetrahydrofolate Reductase (MTHFR) is an enzyme that plays a crucial role as a methyl-group donor in demethylation of homocysteine. Due to the incidence of C677T mutation in the MTHFR gene, thymine is replaced by cytosine, followed by the translation of valine instead of alanine in the structure of the produced enzyme, resulting in the formation of a temperature-sensitive enzyme and thus reducing its activity. The aim of this systematic review and meta-analysis was to study the relationship between MTHFR gene polymorphism and metabolic syndrome (MS).

Material and Methods: We used search engines and databases such as Science Direct, Google Scholar, and PubMed to identify eligible studies up to 2018. The articles were studied based on keywords including MTHFR, mutation, variant, and polymorphism in combination with metabolic syndrome. Data were analyzed using Comprehensive Meta-Analysis version 2.2.064 software.

Results: After extracting the data from seven articles, the total number of subjects was 1280 in the patient group and 1374 in the control group. The odds ratio was estimated to be 1.078 for the allele model of T vs. C (95% confidence interval: 1.626-0.715), 1.157 for the allele model of CC vs. CT (95% confidence interval: 0.829-1.615), 1.020 for the allele model of CT + TT vs. CC (95% confidence interval: 1.611-0.646) and 0.799 for the allele model of TT vs. CC + CT (confidence interval 95%: 1.185-0.539). As well, the results showed no statistically significant correlation between polymorphism genotypes of MTHFR gene and metabolic syndrome ($P<0.05$).

Conclusion: In general, this study showed that the presence of a C677T polymorphism in the MTHFR gene has no effect on the incidence of metabolic syndrome.

Keywords: MTHFR Gene, Metabolic Syndrome, Polymorphism, Variant, Meta-Analysis

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ID:1178

Evaluation of Different Genotypes at Codons 72 and 248 of p53 Gene in Samples of Endometriosis

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Objective: Endometriosis is a prevalent gynecological disorder among women which is diagnosed by the growth of endometrial tissue outside of uterus and is mainly accompanied by severe pelvic pain and infertility. P53 also known as cellular tumor antigen P53 inside codons 72 and 248 are contained with single nucleotide changes in which tends to be nearly rampant. This will probably be increasing the chances of endometriosis infection to some great extent. Our aim was to evaluate the connection between endometriosis and polymorphism inside the codons 72 and 248 of P53 gene.

Material and Methods: In this study, single nucleotide changes in codons 72 and 284 of TP53 gene among 44 persons infected with endometriosis and the same studying population for non-infected group have been examined. After primer design and amplification of polymorphic sequences by PCR, the polymorphisms of related codons have been evaluated by the digestion method (RFLP).

Results: In this study on the codon 72, there were seen differences in the distribution of genotype frequencies of normal polymorphic subjects and control subjects with endometriosis. At codons 248, it was observed no significant correlations polymorphic and normal genotypes of endometriosis and non-endometriosis groups.

Conclusion: According to the results, we can say that probably polymorphism of codon 72 of p53 gene is one of the predisposing factors of endometriosis.

Keywords: Endometriosis, polymorphisms, tumor suppressor genes
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ID:1184

Prediction of insulin resistance with atherogenic index of plasma in type 2 diabetes patients

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Objective: Insulin resistance (IR) is a key factor in the pathogenesis of the type 2 diabetes mellitus (T2DM). Abnormal atherogenic index of plasma (AIP) and TG/HDL-C ratio, as two atherogenic indices, indicate an atherogenic lipid profile and may predict IR in T2DM. The purpose of this study is to examine the relationships of TG/HDL-C ratio and AIP to IR, esteamated by homeostatic model assessment of insulin resistance (HOMA-IR), in T2DM and healthy subjects.

Material and Methods: This cross-sectional study comprised 130 male subjects divided into two groups: 40 healthy subjects and: 90 T2DM patients. After recording age, anthropometric factors and blood pressure, fasting blood samples was taken for measurement of blood glucose, insulin, Hb A1c, high-sensitivity C-reactive protein and lipid profile. TG/HDL-C ratio, AIP and HOMA-IR were calculated. Kolmogorov Smirnov test, independent samples T-Tests, Mann–Whitney U test and correlation tests were used in this study.

Results: Compared to healthy subjects, T2DM patients showed significantly higher weight, waist circumference, hip circumference, waist-hip ratio, body mass index, fasting blood glucose, insulin, Hb A1C, triglycerides, HDL-C, TG/HDL-C ratio, AIP, hs-CRP and HOMA-IR. There were no significante differences in total cholesterol, LDL-C, systolic blood pressure and diastolic blood pressure between groups. AIP was significantly correlated with insulin, HOMA-IR, triglycerides, total cholesterol, TG/HDL-C ratio and inversely correlated with HDL-C in T2DM patients. In healthy subjects, AIP was significantly correlated with triglycerides, waist circumference and body mass index and inversely correlated with HDL-C and LDL-C. TG/HDL-C ratio didn't show any correlation with HOMA-IR in both groups.

Conclusion: The elevation of AIP is powerful predictor of IR in T2DM patients among all the lipid variables examined. AIP serve as a simple and clinically useful approach to identify IR in T2DM patients in daily practice, while TG/HDL-C ratio does not predict IR in T2DM.

Keywords: Type 2 Diabetes Mellitus, Insulin Resistance, HOMA-IR, AIP, TG/HDL-C ratio
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ID:1190

Comparison of pET23a and pQE30 vectors in expression of Heat shock protein 27

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Objective: Heat shock protein 27 (HSP27) is a multidimensional protein which acts as a protein chaperone and an antioxidant and plays a role in the inhibition of apoptosis and actin cytoskeletal remodeling. Heat shock proteins (HSPs) can be severed as the endogenous adjuvants to improve the efficiency of vaccines. In this study, we compared the two vectors for expression of Hsp27 in different strains of E.coli.

Material and methods: Hsp27 gene (Accession No: NM_013560) was synthesized in two prokaryotic expression vectors (pET23a and pQE30-Hsp27). The BL21 and Rosetta expression strains were transformed by these constructs. The hsp protein was purified by affinity chromatography using Ni-NTA resin and identified with SDS-PAGE and His-tag antibody Western blot technics.

Results: The detection of Hsp27 gene in pQE30 and pET23a vectors was confirmed by gel electrophoresis bond on ~720 bp site using 1KB DNA ladder. The HSP27expression was detected in the pET23a-Rossetta strain and Hsp27 was efficiently purified by affinity chromatography under both denaturing and native conditions. While the expression of hsp27 protein was not performed in bacterial strain pQE30-m15.

Conclusion: The considering new research on these vectors and Regarding pET23a-Rosetta's vectors superiority to other vectors of Hsp27, Use this vector to achieve the highest yield of expression, this recombinant protein can be used in vaccine design in future.

Keywords: HSP27, Expression vector, pQE30, pET23a, recombinant protein
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ID:1191

The effects of resveratrol on apoptosis of peripheral blood mononuclear cells in patients with type 2 diabetes: a randomized, double-blind, placebo-controlled clinical trial

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Objective: Type 2 diabetes (T2D) is one of the most common metabolic disorders that is now considered as a major public healthcare problem all around the world. The aim of this study was to determine whether resveratrol, a natural polyphenol with anti-carcinogenic, anti-inflammatory, anti-proliferative and antioxidant properties, affects apoptosis of peripheral blood mononuclear cells (PBMCs) in a randomized, placebo-controlled, double-blind clinical trial.
Material and methods: A total of 48 patients with T2D randomly were assigned to receive 800 mg/day resveratrol or placebo for 2 months. At the baseline and at the trial end, the apoptosis of fresh PBMCs was measured by Invitrogen Kit, using a double-stain YO-PRO 1 and PI by flow cytometry. We also measured metabolic and anthropometric parameters at the baseline and at the end of the study.
Results: Our results revealed that compared with the placebo group, consumption of resveratrol for two months significantly induced apoptosis in PBMCs. Furthermore, resveratrol resulted in a significant reduction in weight, body mass index, and blood pressure levels. Resveratrol was well tolerated, and no serious adverse event was occurred.
Conclusion: Our study demonstrated that 8 weeks of supplementation with 800 mg/day resveratrol can induce apoptosis in PBMCs of patients with T2D.
Keywords: Type 2 diabetes, Resveratrol, Apoptosis, PBMC
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ID:1198

Effect of Biochanin A on Serum Chemerin in Diabetic Rats

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Objective: Bioflavonoids are shown to have many biological activities, such as anti-diabetic effects, insulin-like effects, and stimulation of insulin secretion. Chemerin is an important hormone that secretes from adipocytes and is associated with insulin resistance. In this study, the effects of Biochanin A (a flavonoid) on serum levels of Chemerin, insulin and Fasting blood glucose were measured in diabetic rats.
Material and Methods: The Wistar rats were randomly divided into four groups of 6 members. The first group was selected as the healthy control group and in three other groups, diabetes was induced by streptozotocin (35 mg/kg intraperitoneally). The second group was selected as diabetic control, and the third and fourth groups were treated with Biochanin A with doses of 10 mg/kg and 15 mg/kg for 30 days, respectively. After the study, the biochemical parameters including Chemerin, insulin and fasting blood glucose were measured.
Results: There was no significant association between Biochanin A and the level of serum Chemerin in diabetic rats. However, the level of insulin and fasting blood glucose in these groups showed a significant difference compared to the diabetic control group ($p<0.05$).
Conclusion: In this study, Biochanin A did not show a significant effect on Chemerin levels in diabetic rats, which may be due to dose or duration of treatment. However, it showed that Biochanin A had hypoglycemic effects and therefore has beneficial effects in the treatment of diabetes.
eywords: Biochanin A, Chemerin, Diabetes, Insulin, Rat
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ID:1199

Histamine and Food Allergy

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Objective: Histamine is synthesized by histidine decarboxylase (HDC) in wide types of immune cells and is involved in abundant physiologic and pathologic processes. Histamine is a mediator released during inflammatory reactions, such as food allergy. Food allergy is immunological reactions to 'fight off' specific allergens within food in susceptible individuals. The Aim of this study is investigation of the histamine hemostasis and food allergy to discover the relationship between them.
Material and Methods: Analysis of data from multiple electronic databases such as Scopus,

PubMed, Google Scholar and Science Direct were performed. Various criteria were applied to select the articles for inclusion.

Results: Food allergy reaction is divided to 4 types of the immune response. These reactions with different mechanisms cause increased concentrations of histamine. Histamine does various action in different tissue.

Conclusion: The correct and timely diagnosis of food allergy can lead to reduction of the chemicals release and inhibit of abnormal reaction of the body. According to some studies, Measurement of N-methylhistamine (NMH) as the major metabolite of histamine may help to diagnose patients with food-allergen induced clinical symptoms.

***Keywords*:** Histamine, food allergy, histidine decarboxylase

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ID:1201

Effect of Biochanin A on Vaspin Hormone in Diabetic Rats

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Objective: Bioflavonoids have anti-diabetic effects. They can also stimulate insulin secretion or create insulin-like effects. Vaspin is a hormone from the adipose tissue that is associated with insulin sensitivity. In this study, the effects of Biochanin A, as a flavonoid, on vaspin, fasting blood sugar and glycated hemoglobin, have been measured in diabetic rats.

Material and Methods: 24 adult male Wistar rats were randomly divided into four groups and each group consisted of six rats. The first group was named as a healthy control group, and in the other three groups, diabetes was induced by intraperitoneal injection of streptozotocin (35 mg/kg). The second group was designated as diabetic control. The third and fourth groups received 10 and 15 mg/kg body weight of Biochanin A, respectively, for 30 days. Finally, biochemical parameters including vaspin, fasting blood sugar and glycated hemoglobin were measured.

Results: There was a significant difference in the level of vaspin in the healthy control group and diabetic control group ($p<0.05$), but the effect of Biochanin A on the level of vaspin in the third and fourth diabetic groups was not significant compared to the diabetic control group. The level of fasting blood sugar and glycated hemoglobin in rats treated with Biochanin A showed a significant decrease ($p<0.05$) in comparison with the second group.

Conclusion: Biochanin A may not have a significant effect on vaspin levels due to the duration of the study period or the use of prescribed concentrations, but showed beneficial effects in reducing blood sugar and glycated hemoglobin. This indicates the therapeutic potential of this bioflavonoid to improve diabetes.

Keywords: Biochanin A, Diabetes, Glycated hemoglobin, Vaspin, Rat

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Author index

Name		ID	ID	ID	ID	ID	ID	ID	ID
Abarghooi Kahaki	Fatemeh	1134							
Abbasbeigi	Sirvan	127							
Abbasifard	Anahita	558							
Abbaspour	Mohammadreza	616							
Abbaspour	Soheil	1154							
Abbaszadeh	Saber	366	612						
Abdali	Hossein	1114							
Abdizadeh	Hossein	859							
Abdollahi Teimourlouei	Mohammad	769							
Abdolmohammadi	Mohammad hossein	752	756						
Abdolrezaie	Alieh	499							
Abedi	Daryoush	38							
Abtahi-Eivary	Seyed-Hosein	1121							
Adibhesami	Glavizh	462							
Adibi	Hadi	127							
Afshar	Saeedeh	247							
Afshar	M.	1149							
Afshari	Mohsen	613	614						
Afsharmanesh	Mohammadreza	1036	1175						
Aghadavod	Esmat	23							
Aghaei	Mahmoud	752	756	850	886				
Aghajanpour	Mohsen	772							
Aghajany-Nasab	Monireh	388							
Aghakhani	Sara	66							
Aghazadeh Ghadim	Behrad	192							
Aghazadeh Ghadim	Mir Behrad	256							
Aghelan	Zahra	301							
Ahmadian	Reza	1017							
Ahmadvand	Hassan	366							
Akbari	Vajihe	415							
Akbari-Birgani	Shiva	270	496						
Akbartabar	Mehdi	397							
Akbarzadeh	Najmeh	80							
Akbarzadeh	Samad	558							
Akbarzadeh	Mohammad	1017							
Alamdari	Yasaman	1099							
Aldhaif	Saja	824							
Aliakbari	Fatemeh	939							

Azarmehr	Nahid	589				
Azimi Anaraki	Pegah	344				
Azimi Nezhad	Mohsen	739				
Azizi	Arsalan	397				
Azizi	Reza	777	1044	1198	1199	1201
Azizi	Soheil	1177				
Azizidoost	Shirin	79				
B. Rassouli	Fatemeh	577	578			
Baazm	Maryam	1035				
Babaei	Zeinab	30				
Babaei	Esmaeil	483				
Babaei	Reyhaneh	828				
Babaei Khorzoughi	Reyhaneh	1077				
Baghabane Slaminejad	Mohamadreza	220				
Bagheri	Shahrokh	366				
Bagheri	Babak	914				
Bagheri	Zohreh	952				
Bagherifar	Faeze	593				
Bagheri-Hosseinabadi	Zahra	851				
Bahabadi	Majid	691				
Bahrami	Gholamreza	584				
Bahramikia	Seifollah	492	570			
Bakhtiari	Hadi	1040	1124	1126		
Banan Khojasteh	Seyed Mahdi	135				
Bandehpour	Mojgan	1134				
Barahouie	Ahmad	1149				
Barangi	Samira	288				
Barati	Vahid	397				
Baratieh	Zohreh	449	450			
Barbast	Arash	606				
Barghi	Maryam	813				
Basati	Gholam	637				
Bathaie	Seyed Zahra	375	988	1100		
Bayati	Vahid	616				
Baziyar	Payam	35				
Bazzaz Dehkharghani	Roya	606				
Bazzaz Dehkharghani	Sattar	606				
Behbahani	Sara Edalat	256				
Beheshti	Maryam	37	38			
Behnampour	Nasser	1158				
Beitollahi	Hadi	724				
Bidram	Maryam	841				

Bikhof-Torbati	Maryam	1099			
Bolhasani	Azam	1190			
Bolhassani	Azam	158			
Boroumandnia	Nasrin	658	714		
Bouzary	Zaineb Alsadat	122			
Buchholzer	Marcel	1017			
Chadegani	Rabbani	62			
Chashmniam	Saeed	658	701	739	703
Chehrei	Ali	247			
Cheraghzadeh	Maryam	79			
Dadashpour	Mehdi	1072			
Dahim	Hajar	1178			
Dahmardeh	Fatemeh	987	993		
Danaei	Nazanin	417	455	589	
Danesh Dost	Danial	123			
Dargahi Abbasabad	Ghader	135			
Dastghaib	Sanaz	243			
Davoodian	Nahid	260			
Dayer	Dian	609			
Deemeh	Mohammad Reza	497			
Dehabeh	Maryam	739			
Dehghan	Elham	801			
Dehghan	Gholam-Reza	1154			
Dehghan Shasaltaneh	Marzieh	862			
Delattre	Cédric	17			
Delavar	Mostafa	1109			
Delkhosh	Soheil	910			
Dianatinasab	Aria	594			
Dianatinasab	Mostafa	594			
Didehdar	Reza	741			
Dinarvand	Negar	44	914	1199	
Divsalar	Adeleh	428			
Dolatkhah	Homayun	32	769		
Dorostkar	Hamidreza	1198	1201		
Doustimotlagh	Amir Hossein	229	589		
Dvorsky	Radovan	1017			
Ebadollahi	Shima	772			
Ebrahim Khamseh	Mohammad	701			
Ebrahim Pour	Anahita	123			
Ebrahim-Habibi	Azadeh	825			
Ebrahimi	Mehdi	170			
Ebrahimi	Marzieh	657			

Ebrahimi	Esmaeel	1023		
Ebrahimzadeh	Aillin	123		
Eftekhar	Ebrahim	484	1092	1101
Ehsani	Raheleh	1113		
Eidi	Akram	40		
Eidi	Maryam	961		
Ekhlasi	Zahra	415		
Elyaspour	Zahra	780		
Emadi-Baygi	Modjtaba	449	450	
Emami Aref	Parisa	329		
Emami Razavi	Amirnader	637		
Emekli	Nesrin	1165		
Entezari	Mohammad H.	281		
Esfahani	Maryam	213		
Esfahani	Homa	286		
Eshaghi	Ali	1016		
Eslami	Habib	522	523	
Eslami Muhammadi	Fatemeh	282	304	
Esmaeili	Sajad	214		
Esmaeili	Fataneh	1092	1101	
Esmaeili Mahani	Saeed	1108		
Esmaeilzadeh	Sedigheh	800		
Esmaeli Tarzi	Mojdeh	507		
Esnaashari	Omid	951		
Ezzati Mobasser	Samira	1172		
Faezi	Sobhan	17		
Fahmidehkar	Mohammad Ali	329		
Fahmidekar	Mohamadali	78		
Falavand	Masoume	295	296	
Fallah	Soudabeh	698		
Fallah	Hossein	729		
Fallahian	Faranak	752	756	
Farahani	Heydar	536		
Farajzadeh	Asghar	1100		
Faramarzi Nasab	Masoumeh	570		
Farimani	Azam Rezaei	399		
Goudarzi	Farjam	691		
Farshidi	Hossain	1101		
Farsi	Giti	781	924	
Farzaneh	Zahra	793		
Fassihi	Afshin	1063		
Shams	Seyyede Fatemeh	593		

Fatemi	Mohsen	406			
Fathi	Mojtaba	1151			
Fathi Azarbayjani	Anahita	941			
Fathi Chesli	Marziyeh	748			
Fattahpour	Shirin	1114	1159		
Fattahpour	Shohre	1159			
Fazaeli	Monire Sadat	78			
Fazel	Alireza	282	304		
Fazilati	Mohammad	95			
Ferizni	Fatemeh Sadat	1112			
Gaeini	AA.	801			
Galehdari	Hamid	734			
Ganjalikhany	Mohamad Reza	176	190		
Ghadirian	Shahrzad	1146			
Ghaedi	Kamran	1166			
Ghaedjhi	Hamid	1143			
Ghaemi	Nasser	961			
Ghaffari-Cherati	Maryam	257			
Ghanbari	Saba	723	724		
Ghanbari	Maryam	864			
Ghanei	Amin	1114			
Ghannadi	Saber	859			
Gharesi-Fard	Behrouz	80			
Ghasemi	Saeid Malek	1106			
Ghasemi Shahri	Seyyedeh Razieh	578			
Ghavami	Saeid	243			
Gheisarzadeh	Ali	1040	915	926	
Ghobadi	Sirous	127			
Ghobeh	Maryam	170			
Ghodrati	Sara	282	304		
Gholami Rad	Farah	584			
Gholampour Faroji	Nazanin	1016			
Gholizadeh Pasha	Abdulrahim	123			
Ghorbaninejad	Mahsa	220			
Ghorbaninia	Maryam	176			
Gilany	Kambiz	703			
Gohari	Minoo	282			
Gohari	Sepideh	304			
Gol Fakhrabadi	Hoda	174			
Golkar	Majid	359			
Golpour	Monireh	772			
Goodarzi	Mohammad Taghi	213	399	691	1035

Gremer	Lothar	1017				
Haddad Mashadrizeh	Aliakbar	1016				
Hadizadeh	Farzin	368				
Haghaniat	Vahid R	781	924			
Haghaniat	Saeed	924				
Haghi	Boshra	1158				
Haghighi	Arezoo	63				
Haghighi	Shirin	123				
Haghiralsadat	Bibi Fatemeh	1113				
Haji-Allahverdipoor	Kaveh	522	523			
Hajian-Tilaky	Karimollah	119				
Hajihosseini	Reza	252				
Hajipour	Hamed	135				
Hajizade	Mohamadreza	78				
Hajizadeh	Mohammad Reza	329	587	781	924	932
Hamidavi	Azin	648				
Hamidi	Masoud	17				
Hamidi	Asma	521				
Hamishehkar	Hamed	1154				
Hamzeloo-Moghadam	Maryam	752	756			
Harirchi	Iraj	648				
Hasanian Mehr	Seyed Mahdi	372				
Hasanvand	Zahra	1198	1201			
Hasanzadeh	Mohammad	51				
Hashemabadi	Mohammad	1108				
Hashemi	Zahra	23				
Hashemi	Seyed Ali	375				
Hashemi	Mohammad	688				
Hashemi Madani	Nahid	701				
Hashemi Niasari	Fatemeh	698				
Hashemi Tabar	Mahmoud	609				
Hashemi-Niasari	Fatemeh	836				
Hashemi-Soteh	Mohammad Bagher	257				
Hashemitabar	Mahmoud	616				
Hassanian	Seyed Mahdi	241				
Hassanzarei	Shekoufeh	688				
Hatami	Maryam	628				
Hayatmoghadam	Bentolhoda	808	816			
Hedayati	Mehdi	976				
Hejazi	Hossein	63				
Hemati	Mahdie	298				
Hemati	Mahdieh	307				

Hemati Azandaryani	Abbas	1034	
Hemmati	Mina	214	726
Hemmati	Mohsen	333	
Hemmati Dinarvand	Farshad	333	
Hiedarian	Esfandiar	140	
Honardoost	Mohammad-Amin	450	
Hoseinzadeh	Safoura	140	
Hosseini	Samaneh	220	
Hosseini	Farzaneh Sadat	932	
Hosseini Beheshti	Farnaz	187	325
Hosseini-Sharifabad	Ali	727	782
Hosseinpourfeizi	Mohammad-Ali	1154	
Hosseinzadeh Colagar	Abasalt	946	
Iranmanesh	Moein	1016	
Iranpak	Forough	25	
Iranpour	Daryoush	780	
Iranshahi	Mehrdad	577	
Izadi	Azadeh	281	
Jaberi	Hajar	558	
Jafari	Hanyeh	1053	
Jafari	Seyyed Mehdi	1150	
Jafari Dinani	Narges	499	
Jafarian	Amir Hossein	593	
Jafari-Gharabaghlou	Davoud	1072	
Jafarpour	Hamed	1177	
Jafary	Farzaneh	190	
Jahanbazi	Fatemeh	229	
Jahani	Mehrnaz	449	
Jahani Moghadam	Aria	282	304
Jalali	Mohammad Taha	1175	
Jalali Mashayekhi	Farideh	1035	
Jalili	Vahideh	784	
Jamilian	Mehri	1109	
Javadi Aghjeh Kohal	Meisam	769	
Javadi-Zarnaghi	Fatemeh	176	
Javanshir	Reyhane	726	
Joshaghani	Hamidreza	1036	1158
Jozaghkar	Fereshte	946	
K. Ardestani	Sussan	293	
Kabodanian Ardestani	Susan	335	
Kaboudanian Ardestani	Susan	405	
Kaeidi	Ayat	587	

Kakavandi	Naser	186		
Kalantari	Shiva	658	714	
Kamali	Kasra	641		
Kamali	Mahsa	1119		
Kanafchian	Maryam	800		
Kardani	Kimia	158		
Karimi	Masomeh	123		
Karimi	Gholamreza	288		
Karimi	Gilda	748		
Karimi	Farzaneh	785		
Karimitabar	Fatemeh	17		
Karimkhani	Hadi	1165		
Kashifard	Mehrdad	119		
Kassaee	Seyed Mehrdad	889		
Kazemi	Bahram	1134		
Kazerouni	Faranak	861	990	1008
Keradmand	Fatemeh	951		
Keramati	Mohammad Reza	593		
Ketabchi	Fatemeh	325		
Khadem	Fatemeh	584		
Khademi	Fatemeh	583		
Khademi Shirvan	Maliheh	220		
Khademolhoseini	Fatemeh	1016		
Khaki-Khatibi	Fatemeh	60		
Khakzad	Mohammad Reza	514		
Khalaj	Zahra	450		
Khalil Moghaddam	Shiva	81		
Khalili Yazdi	Aliakbar	723	724	
Khan Ahmad	Hossein	450	1166	
Khanahmadi	Masumeh	1034		
Khanaki	Korosh	17		
Khani	Behnaz	23		
Khasayesi	Mina	397	417	
Khatibi Shahidi	Fedora	335		
Khavari Nejad	Ramezan Ali	961		
Khavari-Nejad	Sarah	748		
Khayatian	Mahmoud	66	1101	
Khayatzadeh	Jina	282	304	
Khazaei	Sedigheh	461		
Khazaei	Mozafar	461		
Khazai	Majid	372		
Kheirollah	Alireza	79		

Kheradmand	Fatemeh	941				
Khodabandehloo	Hadi	1191				
Khodadadi	Iraj	691				
Khodaii	Zohreh	728				
Khodarahmi	Reza	127	301			
Khodarahmi	Ameneh	307				
Khojasteh	Sepideh	723	724			
Khooyi	Alireza	282	304			
Khorsandi	Khatereh	1012				
Khoshakhlagh	Mahdieh	372				
Khoshbin	Mobin	205				
Khoshdel	Alireza	78				
Khoshdel	Zahra	256				
Khoshdel	Alireza	329	781	924		
Khoshnevis Zade	Rabee	81				
Khosravi	Peyman	366				
Khosrowbeygi	Ali	1109				
Kianmehr	Zahra	1012				
Koolivand	Mohsen	47	48			
Koolivand	Ali	476				
Lashkari	Ali	405				
Latifi	Seied Amirhossein	626				
Lohrasbi Nejad	Azadeh	724	853			
Lotfi	Safa	628				
Lotfi	Abbas	781				
M. Matin	Maryam	577	785			
Maftoon	Houman	641				
Mahani	Mohammad	723				
Mahboob	Soltanali	51				
Mahdavi	Majid	483				
Mahjoub	Soleiman	800				
Mahmodi	Mehdi	924				
Mahmoodi	Mehdi	78	329	587	781	932
Mahmoodzadeh	Yavar	793				
Mahmoudi	Elham	635				
Mahmoudi	Minoo	889				
Mahrooz	Abdolkarim	257				
Mahrooz	Abdolkarim	447				
Malekhosseini	Saeed	95				
Malekinejad	Hassan	951				
Malekpour Dehkordi	Zahra	1172				
Malekpouri	Pedram	344				

Malekzadeh	Keyanoosh	48		
Manafi	Farideh	793		
Mansoori	Roghiah	388		
Mansoori	Elahe	1101		
Mansour Samaei	Nader	643		
Mansouri	Elahe	1092		
Mansourian	Azadreza	939		
Maryamabadi	Ammar	804		
Mashhadi Akbar Boojar	Masoud	40	748	
Masoumi	Parisa	447		
Mazani	Mohammad	793		
Mazloomi	Sahar	252		
Mazoochian	Leila	274		
Mehdipour	Samihe	1114		
Mehraban	Fouad	397		
Mehrabani	Mehrzad	507		
Mehrabani Natanzi	Mahboobeh	728		
Mehrabi	Mohammadreza	613	614	
Mehrad-Majd	Hassan	656		
Meknatkhah	Sogol	128	159	
Mervenur		1165		
Mesbah-Namin	Seyed Alireza	851		
Meshkani	Reza	14	828	1191
Meshkini	Azadeh	281		
Meshkini	Fatemeh	914		
Mir Mohammad Sadeghi	Hamid	38	274	
Mirbolouk	Fardin	889		
Mirhafez	Seyed Reza	739		
Miri	Saba	1037		
Miri-Aliabad	Ghasem	987	993	
Mirian	Mina	285		
Mirzaee	Mohsen	613	614	
Mirzaei	Rasool	17		
Mirzaei	Mohammad Reza	329		
Mirzaei	Mahmoud	777	852	
Mirzajani	Ebrahim	889		
Mirzamohammadi	Solmaz	507		
Moazeni-Roodi	Abdolkarim	648		
Mofid	Mohamad Reza	915	926	1040
Moghadam Ahmadi	Amir	781		
Moghadasi	Mona	366		

Mostafaie	Ali	583	584	
Mostafavi	Hossein	483		
Mostafavi	Fatemeh	990		
Mostafazade	Mostafa	397		
Motamedi	Neda	593	853	
Motemed	Niloufar	780		
Motlag	Behrooz	1151		
Moudi	Emaduddin	946		
Mousavi	Monireh-Sadat	128	159	
Mousavi Dehmordi	Rohollah	1175		
Mousavi-Fard	Seyed Hossein	229		
Moussavi-Torshizi	Seyed-Erfan	264		
Movahed	Ali	780		
Movahedian	Ahmad	200		
Movahedpour	Afsaneh Alsadat	1113		
Movahhed Abbasabad	Parvaneh	861		
Nabatchian	Fariba	156		
Nabi Afijadi	Mohsen	92		
Nabipour	Iraj	804		
Naderi	Nadereh	65	66	
Nafar	Mohsen	658	714	
Naghdi	Nasser	862		
Naghiaee	Yousof	741		
Naghibalhossaini	Fakhraddin	952		
Najafi	Leila	95		
Najafi	Mohammad	186		
Najafi	Rezvan	213		
Najafi	Mohammad	788	1146	
Naji	Hadi Eskandari	135		
Naji	Mohammad	714		
Namazi	Gholamreza	659		
Namazi	Fateme	813		
Namvarjah	Fatemeh	828		
Nasiri	Abolfazl	301		
Nasoohi	Nikoo	1146		
Nasrnezhad Nesheli	Reza	744		
Nath Dubey	Badri	1017		
Navidpour	Latifeh	825		
Nayeri	Hashem	5	499	1038
Nazarian	Atefeh	812		
Nazeri	Zahra	79		
Nazifi	Saeed	813		

Nejaddehbashi	Fereshteh	616							
Nejat Pishkenar	Fatemeh	119							
Nekooei	Maryam	801	804						
Nematollahi	Mohammad Hadi	507							
Neysi	Asma	192							
Nezhadali	Masoumeh	976							
Niazi Vahdati	Saeed	405							
Nikibakhsh	Ali	784							
Niknam	Maryam	185	228	333					
Niknia	Seddighe	329							
Nikpour	Parvaneh	449	450	739	701				
Nobakht M. Gh	B. Fatemeh	703							
Noroozi	Mojgan	932							
Nourbakhsh	Mitra	1172							
Nourooz-Zadeh	Jaffar	784							
Nuri	Reza	801							
Ollah Hajian–Tilaki	Karim	123							
Omidifar	Navid	229	589						
Omidifar	Abolfazl	700							
Orazizadeh	Mahmoud	616							
Pahlevani Gazi	Elham	42							
Pajouhi	Naser	366							
Pak	Marzieh	417							
Pakravan	Parvaneh	1034							
Panahi Kokhdan	Esmaeil	229	417	455					
Panjehfouladgaran	Flora	131							
Parsian	Hadi	30							
Parvaneh	Shahram	584							
Paryan	Mahdi	1116							
Pasham	Fariba	428							
Pestechian	Nader	1063							
Pilehvar-Soltanahmadi	Younes	1072							
Piri	Hossein	233							
Pouraminaei	Mehdi	329							
Pouramir	Mahdi	772							
Pouresmaeil	Vahid	514							
Pourfarzam	Morteza	44	274	746	808	816	819	1184	
Pourteimoor	Vida	1116							
Poustchi	Hossein	700							
Qujeq	Durdi	119	122	123	744				
Rabbani	Mohammad	782							
Rabbani-Chadegani	Azra	174	216	254	283	284	286	698	836

Rabiee	Samaneh	976		
Raeisi	Elham	140		
Raeisi Shahrak	Hadi	183		
Rahimi	Hossein	593		
Rahimzade	Mahsa	65	66	
Rahmani	Farzad	241	372	
Rahmati-Yamchi	Mohammad	32		
Rahsepar	Maryam	800		
Raissi	Heidar	585		
Rajaie Nejad	Athena	729		
Ranjbar	Monireh	131		
Rasmi	Yousef	941		
Rasooli	Azadeh	1037		
Rasoul Zadeh	Reza	35		
Rasouli	Mehdi	914		
Rassouli	Fatemeh B.	1112		
Rastegar	Shahdokht	1023		
Rasuli	Maryam	228		
Ravan	Hadi	1088	1108	
Ravasi	AA.	801		
Razaghi	Roghaye	233		
Razmi	Narsin	51		
Razmi	Mahdieh	698	836	
Razmkhah	Fatemeh	589		
Rezaee	Esmael	594		
Rezaee Vandchali	Nushin	476		
Rezaei	Marzieh	587		
Rezaei Adariani	Soheila	1017		
Rezaeifar	Alireza	987	993	
Rezaei-Zarchi	Saeed	994		
Rezaie	Shima	186		
Rezghi Barez	Shekufe	850	852	
Rezvannejad	Elham	628		
Riahi-Madvar	Ali	853		
Riazi	Gholamhossein	128	159	862
Rohban	Mohadese	78		
Roozi	Hanie	40		
Rostaei Rad	Niko	200		
Rostampour	Saeedeh	483		
Rouzbehan	Sahere	260		
Saadati-Eskandari	Naghmeh	825		
Sabaghzadeh	Reyhane	672		

Saberi	Sedigheh	1063				
Saboori	Masih	1159				
Saboury	Ali Akbar	859				
Sadat Hosseini	Bita	788				
Sadat Sotudeh	Fatemeh	514				
Sadat Tabaei	Banafsheh	982				
Sadeghi	Asie	14				
Sadeghi	Heibatollah	229				
Sadeghi	Hossein	229	397	417	455	589
Sadeghi	Heibatollah	397	417	455		
Sadeghi	Masoumeh	499	746			
Sadeghian	Mohammad Hadi	593				
Sadrayi	Seyed Mahdi	388				
Saeidi	Hamed	1190				
Safari-Alighiarloo	Nahid	701				
Safataj	Neda	325				
Safavi	Malihe	405				
Saghaeian Jazi	Marie	643	1158			
Saghaie	Lotfollah	1063				
Saghravanian	Javad	514				
Saidijam	Masoud	213				
Sajadimajd	Soraya	461				
Sajjadi	Seyed Ebrahim	727				
Salar Amoli	Sanaz	1158				
Salari Moghaddam	Roya	922				
Salarian	Maryam	254				
Salary	Hamide	577				
Salehi	Ehsan	247				
Salehi	Mansoor	325	450			
Salehi	Rasoul	791				
Salemi	Zahra	1198	1199	1201		
Samadi	Nasser	333				
Samareh	Azadeh	1088				
Sameni	Safoura	80	183			
Samimi	Fatemeh	1035				
Samsamshariat	Saed Ziaaldin	787				
Sanjary Pour	Maryam	988				
Sargolzaei	Javad	62				
Sasan	Hosseinali	1088	1106	1108		
Sattarifard	Hedieh	688				
Sattary	Roohollah	1124	1126			
Sepiani	Bahar	79				

Serati-Nouri	Hamed	135		
Seyyedebrahimi	Shadisadat	1191		
Shaban Sarbandi	Farzane	81		
Shabani	Zahra	260		
Shabani	Maryam	1077		
Shabanizade	Ahmad	1178		
Shabanzadeh	Masud	1099		
Shadjou	Nasrin	51		
Shafeezadeh	Zohreh	156		
Shafiee	Sayed Mohammad	185	228	804
Shafiei	Afsaneh	1036		
Shafiepour	Mohamadreza	78		
Shahbazian	Hajie Bibi	1175		
Shahhoseini	Maryam	220		
Shahrokhi	Seyedeh Zahra	497		
Shahsavari	Gholamreza	462		
Shahsavari	Zahra	990	1008	
Shakeri	Sepideh	593		
Shakori	Hajar	828		
Shamshirian	Amir	1177		
Shamsi	Maryam	32		
Shanaki	Mehrnosh	700		
Shanaki	Mehrnoosh	1143		
Sharif Dashti	Pouya	159		
Sharifi	Give	123		
Sharifi	Faranak	252		
Sheikh Darani	Ali	782		
Sheikhi	Maryam	593		
Shojaei	Mohammad	727		
Shokri	Zahra	366		
Shourian	Mostafa	864	910	
Siavoshinia	Leila	340		
Soleimani	Atena	241		
Soleymanifard	Shokouhozaman	577		
Soltanian	Sara	1106		
Soukhtanloo	Mohammad	288		
Tabandeh	Mohammad Reza	609		
Taghi Khani	Adeleh	657		
Taheri	Salman	990		
Taheri Chadorneshin	Hossein	1121		
Tahsiri	Behnaz	787		
Takhshid	Mohammad Ali	25		

Tamtaji	Omid Reza	1177			
Tarakameh Samani	Sulmaz	1119			
Taravati	Ali	641			
Tarighi	Shahriar	1143			
Tatar	Mohsen	952			
Tavakoli	Parisa	1053			
Tavakoly	Ramin	1023			
Tavassoli	Manoochehr	176			
Teimouri	Maryam	1038			
Tohidi	Fatemeh	641			
Torkzade Mahani	Masoud	724	853	723	
Ülfer	Gözde	1165			
Vafaeinezhad	Nasrin	1151			
Vafajouy-Jamshidi	Soheila	1072			
Vahabpour	Rouhollah	861			
Vahabzadeh	Zakaria	280			
Vakili	Mohsen	123			
Vakili	Omid	131	185		
Vakili	Mahmood	200			
Vakilpour	Hossein	455	589		
Valinezhadi	Nassim	1154			
Varedi	Masoumeh	952			
Varsee	Malihe	1151			
Vaseghi	Golnaz	156			
Vatanara	Alireza	359			
Vaziri	Mohammadsadegh	1177			
Vessal	Mahmoud	25			
Vessal	Soheila	48			
Yaghmaei	Parichehreh	825			
Yaghmaye	Parichehreh	1053			
Yazdani	Hootan	714			
Yazdanparast	Raziye	92			
Yazdanparast	Razieh	221	224	264	734
Yiğitbası	Türkan	1165			
Younesian	Ommolbanin	1036			
Yousef	Tooba	123			
Yousefi Ghale Salimi	Mahboubeh	961			
Zabihi	Ebrahim	772			
Zadhoush	Fouzieh	746	819	1184	
Zahedi	Abdollah	366			
Zahiri	Zahra	183			
Zahiri	Maria	804			

Zal	Fatemeh	192	
Zamani	Mohammad Reza	135	
Zamanian	Mohammad	924	
Zare	Elaheh	293	
Zare	Mojgan	994	
Zare Shehneh	Masoud	1113	
Zarei	Sadegh	399	
Zarei	Elham	939	
Zargar	Parisa	484	
Zargar Balajam	Narges	886	
Zargari	Mehryar	914	
Zarghami	Nosratollah	1072	
Zarrabi	Zeynab	1063	
Zavar-Reza	Javad	200	
Zeinali	Majid	335	
Zentilin	Lorena	643	
Zeynali Moghaddam	Shima	941	951
Zia	Aliabbas	62	
Zia Jahromi	Noosha	63	