POU5F1 Protein Expression Analysis in the Differentiation of Spermatogonia Stem Cells into Neurons by In-silico Analysis

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ABSTRACT

Spermatogonia Stem Cells (SSCs) might be used for reprogramming, therapeutic neuronal repair, and regeneration. Recent research has shown that by overexpressing a collection of pluripotent transcription factors, differentiated cells may be returned to a pluripotent state. POU5F1, a POU transcription factor family member, is required for the potential that governs pluripotency. It is highly expressed in pluripotent stem cells, but its expression decreases or is reduced following differentiation. In this study, we looked at POU5F1 expression in SSCs, Embryonic Stem Cell-like (ES-like), Embryonic Bodies (EBs), and Neurons in vivo and in vitro using immunocytochemistry (ICC), immunohistochemistry (IMH), and PCR. Furthermore, we employ databases such as STRING to predict protein interactions and enrichment analysis. We examined POU5F1 expression in this process and discovered that it is expressed in SSCs, ES-like cells, and EBs during the differentiation of spermatogonia stem cells into adult neurons. We demonstrate that adding RA to EBs reduces POU5F1 expression and prevents it from being expressed in neuron cells. We discovered that POU5F1 expression is connected to and interacts with the development of spermatogonia stem cells into neuron cells, and it has been shown to have biological functions such as stem cell maintenance and somatic cell reprogramming. Our results may help us better understand the process of spermatogonia stem cell differentiation into neurons, and they can be useful in developing novel and more efficient therapies for neurogenesis and neuron repair. Furthermore, this research might help to understand the unique POU5F1 reprogramming mechanism for clinical and therapeutic applications.

Keywords: Spermatogonia Stem Cells, POU5F1, Neuron, Reprogramming, Pluripotency

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DNA Interaction, Anticancer Activities and in Silico Molecular Docking Studies of Adenine- Based Carboxamide Ligand

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ABSTRACT

The interaction of drugs with DNA is the most important aspects of biological studies in drug discovery and pharmaceutical development processes. Many studies demonstrate that DNA is the primary intracellular target of antitumor drugs, because the interaction between small molecules and DNA can be caused damage, blocking them in cancer cells. Therefore, under physiological conditions, many compounds which can efficiently bind and cleave DNA are considered as potential candidates for use as therapeutic agents in medicinal applications and for genomic research. Herein, a carboxamide ligand has been synthesised by the reaction of adenine with picolinic acid (HL_1) in the presence of tetrabutylammonium bromide (TBAB) and characterized by different spectroscopic techniques. The optimized structure of HL_1 has been investigated using the DFT/B3LYP method with the 6–311++G(d,p) basis set. For the investigation of the anticancer activity the interaction of this ligand with calf thymus DNA was studied by isothermal titration method in tris buffer which was contained sodium chloride (10 mM) and pH= 7.4 at 27 and 37 °C and thermodynamic parameters were obtained. Also, the modes of binding of the ligand to ct-DNA was investigated by fluorescence spectroscopy and circular dichroism. Data indicate that this ligand interacted probability of groove binding with DNA via noncovalent mechanism.

Keywords: DNA, DFT, Molecular Docking and Carboxamide

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Studying the Novel Effects of Volatile Compounds Cinnamaldehyde and Phenyl Ethyl Alcohol in Preventing Fibrillation of Brain Related Proteins in Neurodegenerative Diseases

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ABSTRACT

Research on neurodegenerative diseases has shown that a common pathogenic factor in many of the diseases is characterised by a specific protein or peptide that aggregates. Diseases such as Alzheimer's disease (AD), Parkinson's disease (PD), prion, and Huntington's occur as a result of protein aggregation/ fibrillation. In this study, a wide range of techniques were used in order to assess the effects of volatile compounds in preventing fibrillation of brain related proteins. The techniques included over-production and purification of tau and alpha synuclein proteins, Lysozyme activity assay, SDS- and Native-PAGE, Thioflavin T fluorescence spectroscopy, Circular Dichroism spectroscopy, Dynamic light scattering, Atomic Force microscopy, Differential Scanning Fluorimetry, crystallisation and X-ray crystallography. Using the correct protein for aggregation studies related to a specific disease is important since the model protein, Hen egg white lysozyme (HEWL), used in our initial study proved to be inappropriate, especially when using volatile compounds, which were seen to act as signalling molecules affecting protein structure and function; N,N,N,N'-Tetramethylethylenediamine (TEMED), a foul smelling compound similar to putrescence and cadaverine (known as molecules related to the smell of death), was surprisingly seen to be able to activate HEWL and stabilise the enzyme both in terms of function and structure. Traditional Iranian Medicine was used to identify the appropriate volatile compounds in our study, which included cinnamaldehyde (Cin) and phenyl ethyl alcohol (PEA), giving the pleasant smells of cinnamon and rose flower, respectively. Both compounds revealed to act as precipitants affecting protein hydration levels and were involved in the reduction/prevention of fibrillation of brain related proteins including tau and alpha synuclein. The results revealed that HEWL is inappropriately used as a model protein for fibrillation studies and highlighted the importance of studying brain related proteins including tau and alpha-synuclein in AD and PD, respectively. Volatile compounds such as Cin and PEA were suggested as potential substances in the treatment of neurodegenerative diseases via the olfactory system.

Keywords: Volatile compounds, Brain related proteins, Cinnamaldehyde, Phenyl ethyl alcohol, Fibrillation

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Study on Kinetic Parameters of L-Asparaginase in the Presence of *Origanum vulgare* Alkaloids Extract

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ABSTRACT

L-asparaginase enzyme, which is widely available in nature, is used in combination with other drugs in the treatment of acute lymphocytic leukemia, lymphosarcoma, melanosarcoma and various types of cancer. This enzyme also plays an important role in the food industry and as a food processing agent in reducing the level of acrylamide formation (a carcinogenic compound) during the production of starchy food products. Medicinal plants are among the natural resources that are used in traditional and modern medicine to treat human diseases. In this study, the kinetic parameters of L-asparaginase enzyme were investigated in the presence of oregano plant alkaloid extract. For this purpose ten grams of cow liver were homogenized in 100 ml of Tris-HCl buffer with pH = 8.6 using a homogenizer, and then partial separation of the enzyme was performed with two steps of precipitation with ammonium sulfate and 60% acetone. The values of Km and Vmax were obtained as 0.45 mM and 0.027 mM/min, respectively. Alkaloid extract from oregano was extracted using ethyl acetate, petroleum ether and chloroform solvents and concentrated using a rotary device. After incubation of the enzyme with three concentrations of the alkaloid extract for 10 minutes, the kinetic parameters of the enzyme were measured and the michaelis-menton constant was determined. The Km value in the presence of oregano plant extract was equal to 0.36, 0.35 and 0.35 mM and Vmax was also equal to 0.029, 0.035 and 0.047 mM/min. Therefore, oregano alkaloid extract showed activation effects on the L-asparaginase enzyme. The results of GC-Mass showed that quinoline alkaloids are the most alkaloid compounds in the extract. According to the results obtained from this research, the use of *Origanum vulgare* alkaloid extract is suggested as an activating agent of bovine liver asparaginase enzyme for further *in vivo* and *in vitro* studies.

***Keywords*:** L-Asparaginase, Alkaloids, Michaelis constant, Activator, Nesslerizaion

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An Experimental Survey on Improved Bioavailability of β-Boswellic Acid as an Anti-Alzheimer Agent Using Gold Nanoparticles

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ABSTRACT

Alzheimer's disease (AD) is the most common form of dementia in the elderly worldwide. Tau protein aggregation is the main hallmark of AD pathology. Previous studies have indicated that terpenoids extracted from plants might have therapeutic applications in neurodegenerative disease. β-boswellic acid (BA), as a triterpenoid compound, has been shown to have neurogenesis activities; however, its application is limited by its low bioavailability. Therefore, BA conjugated with nanoparticles (NPs) has been proposed as an approach to increase its solubility and bioavailability. This study aimed to investigate the inhibitory effect of BA conjugated with gold nanoparticles (GNPs) on Tau aggregation in vitro. GNPs were successfully synthesized by the Turkevich method and then conjugated with BA through carbodiimide chemistry. In this regard, to be used as an anti-aggregation Tau protein, purified by Anion exchange chromatography. HRTEM and FESEM micrographs showed that GNPs had a rather spherical shape with uniform size, of about 13 nm in diameter. The crystalline nature of the GNP was evaluated by HR-TEM images in which selected angle energy diffraction (SAED) patterns were detected. According to UV-visible and FTIR data, BA was successfully conjugated to GNPs through the covalent method. The stability of the bare GNPs and those BA conjugated to GNPs was measured by the phase plot of the ELS ζ potential analyzer, which illustrates good stability in aqua media. The effect of GNPs-BA sample on Tau aggregation has been investigated by ThT Fluorescence experiment showed preventing inhibitory. These findings also were confirmed by CD and SDS-PAGE data that GNPs- BA can effectively bind to Tau. Further, treatment of Tau proteins with GNPs-BA resulted in amorphous Tau aggregates with shorter assembled fibers in AFM studies.

Keywords: Gold nanoparticle, Tau protein, Boswelic acid, Bioconjugation

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Interaction of Irinotecan as an Anticancer Drug with Human Serum Albumin: A Molecular Docking Approach

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ABSTRACT

As a potent inhibitor of topoisomerase, I, irinotecan is a semi-synthetic analog of camptothecin. Camptothecin is a plant alkaloid isolated from *Camptotheca acuminata* (a plant native to China), in the early 1960s. Human serum albumin (HSA) is an important serum protein that comprises 50–60% of the total plasma protein in humans. This protein is responsible for the binding and transport of many endogenous and exogenous substances such as hormones, fatty acids, metabolites, drugs, bilirubin, and other biologically active compounds present in the blood. HSA is composed of three homologous domains (I, II, and III); each domain consists of two subdomains A and B. This protein possesses two principal drug binding sites commonly designed as Sudlow site I and Sudlow site II, which correspond to the subdomains IIA and IIIA, respectively. Docking studies were conducted to identify the binding site of the anticancer drug irinotecan on HSA protein. The aim of this research was to detect the binding site of irinotecan on this carrier protein. From the Protein Data Bank (PDB), we downloaded the crystal structure of native HSA (PDB 1BM0). Hyperchem 8.0.6 was used to model the 3D chemical structure of irinotecan. In order to conduct the docking studies, Autodock Vina software was used. Vina software was employed to improve the understanding of the interaction between irinotecan and HSA. Based on the lowest free energy result, the best docking energy result was chosen. Docking indicated that the binding site of irinotecan was located within Sudlow's site I, formed by six α-helices. Apparently, several ionic and polar residues, such as Asp-107, Lys-266, His-247, Gln-204, are located in the proximity of the ligand. Docking studies were conducted to identify the binding site of the anticancer drug irinotecan on HSA protein. Most of the amino acids close to the drug are polar acids. Our result further suggested that the drug binding site on HSA is site I.

Keywords: Camptothecin, Vina software, Human Serum Albumin (HSA)

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Improving predicted affinity of 11β-HSD I using ensemble docking and learning methods

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ABSTRACT

How target flexibility should be considered in the docking procedure is a major challenge in predicting protein-ligand affinity. Nowadays, scientists pay more attention to ensemble docking as a promising solution to this issue. Albeit, missing information is on how an optimal set of conformations can be chosen in order to reduce computational costs and the number of false positives in pose prediction. In the previous studies, in order to investigate the receptors specifically, we reached favorable results. In this study, we examined the case study whose collection of x-ray structures is smaller in the RCSB database. The extracted structures were screened, using which, 23 11β-HSD I structures are selected in the ensemble dataset to generate an efficient ensemble of 11β-HSD I X-ray structures. A diverse set of ligands extracted from ChEMBL, and docked to the receptor ensemble, which leads to obtain feature set of 100 features including feature energetics of docking results, beside other eight simple molecular features of ligands, are considered in the final dataset for the machine learning (ensemble-based) affinity prediction method. Classical scoring functions such as force-field, knowledge-based and empirical function, which are prone to limitations with increase in training data size, are no longer required by applying machine learning. In this study, Random Forest (RF) ensemble learning algorithm is used for final affinity prediction. Finally, the impurity importance value of RF method is used in order to choose 11β-HSD I structures, which play more important role in ensemble docking. Experiments show that docking to only those receptors selected by RF, reduces the error. Eventually, using the mentioned methods, MSE_{Test}= 0.88, MSE_{OOB}= 0.95 for RF is obtained (hyperparameters set to the default values and models iterated 50 times). By letting machine learning select important features, higher accuracy is achieved, which is significantly better than methods not based on machine learning.

***Keywords*:** Ensmble learninig, Ensemble docking, 11β-HSD I, Random forest, Affinity.

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Neuroprotective Effect of Propolis Polyphenols-Based Nanosheets Against Rotenone-Induced Neurotoxicity in a Cellular Model of Parkinson's Disease

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ABSTRACT

Parkinson's disease (PD) is characterized by movement and cognitive disorders due to the progressive reduction of dopaminergic neurons in the brain. Several pathophysiological mechanisms such as oxidative stress, neuroinflammation, mitochondrial dysfunction and excitotoxicity have been proposed for Parkinson's disease. Polyphenols, with their ability to reduce oxidative stress and inflammation, are considered a treatment for PD. One of the compounds with high polyphenolic content in nature is propolis. Low solubility in water, low bioavailability and structural instability of the polyphenolic fraction of propolis (PFP), have limited its clinical application. Therefore, research has been conducted to improve PFP's water solubility and bioavailability. Water-soluble nanosheets of PFP (NanoPFP) have been prepared in the Faculty of Chemistry, Institute for Advanced Studies in Basic Sciences. We studied and compared the neuroprotective effect of PFP and NanoPFP in a rotenone-induced PD cellular model using SH-SY5Y cell line. Using MTT and lactate dehydrogenase release assay, as well as measuring mitochondrial membrane potential, ROS generation, and activity of antioxidant enzymes, our findings in the cell culture model confirmed that both PFP and NanoPFP show neuroprotection against rotenone-induced neurotoxicity with the NanoPFP being more efficient. The authors suggest NanoPFP as a promising candidate to protect neurons against PD progression.

Keywords: Propolis, Nanosheet, Neuroprotection, Rotenone, SH-SY5Y cells

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Molecular Dynamics Simulations of Receptor Binding Domains in Wuhan and Omicron (B.1.1.529) Variant of SARS-CoV-2

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ABSTRACT

The recent identified variant of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), Omicron (B.1.1.529), has become a global concern. The spike protein contains a receptor-binding domain (RBD) that is a key component for binding of the virus to host cells, thus causing virus attachment to host cells. Based on Structural analysis, sixteen substitution mutations have been occurred in the BA.2 sub-lineage of the Omicron variant. In this study, the sequences of Wuhan and Omicron (BA.2) variant of concern isolated from the SARS-CoV-2 were retrieved from NCBI database. I-TASSER server was used to generate the 3D structure of RBDs. 50 ns molecular dynamics (MD) simulations carried out using the GROMACS 2020.6. The sequence alignment was performed using the EMBOSS Needle server. Sixteen mutations were found in the RBD of Omicron (BA.2) variant including: G339D, S371F, S373P, S375F, T376A, D405N, R408S, K417N, N440K, S477N, T478K, E484A, Q493R, Q498R, N501Y, Y505H. The average number of hydrogen bonds for Wuhan and Omicron (BA.2) RBDs are ~124.73 and ~126.89 respectively. Also, the average value of SASA for Wuhan and Omicron (BA.2) RBDs are 138.18 and 141.86 respectively. Based on the results, Wuhan RBD is more stable than the Omicron (BA.2) RBD.

***Keywords*:** SARS-CoV-2, Omicron (B.1.1.529), receptor-binding domain (RBD)

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A Derivative of Penetratin Against α- Synuclein Oligomers Toxicity

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ABSTRACT

The aggregation of α-synuclein (α-Syn) into oligomers and amyloid fibrils is characteristic of Parkinson's Disease (PD). Although it remains unclear how this protein elicits its neurotoxic effects, recent findings indicate that the assembly of toxic oligomeric species of α-Syn (αSOs) may be one of the key processes for the pathology and spread of the disease. There is an intense focus on the discovery of novel inhibitors such as peptides to inhibit oligomer formation and toxicity. Here, using the peptide array technique, a competition experiment was performed in which a constant concentration of fluorescently labeled αSOs was challenged with different concentrations of unlabeled monomeric α-syn to select peptides with high affinity to αSOs. Also, the calcein release and MTT cytotoxicity assays were performed to investigate the effect of selected peptide on membrane permeability and cytotoxicity induced by αSOs. Finally, the uptake of the selected peptide through the blood-brain barrier (BBB) model was also investigated. Based on peptide array technique, a peptide that showed high binding affinity to the αSOs was selected. The results of the membrane permeability of large unilamellar vesicles (LUV) formed by 1, 2-dioleoyl-sn-3-phosphatidylglycerol (DOPG) in the presence of peptide, αSOs and peptide/αSOs showed that this peptide reduced αSOs-induced LUV membrane permeability. Also, the MTT cytotoxicity test on SH-SY5Y cells showed the positive effect (20%) of this peptide in reducing the αSOs toxicity. Finally, cellular uptake of selected peptide across the BBB model increased over time compared to the untreated control. We conclude that this Penetratin (a cell penetrating peptide) derived peptide can be a candidate to peptide targeting of the toxic αSOs in PD.

Keywords: α-Synuclein, Parkinson's Disease, Oligomer, Peptide

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Repurposing of FDA-approved Drugs Against Monocarboxylate Transporter 1 (MCT1) in an Open-outward Conformation by Virtual Screening and Molecular Dynamics Simulation Studies

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ABSTRACT

Tumor cells often rely on glycolysis to produce ATP rather than oxidative phosphorylation. A direct consequence of the increase in glycolytic flux is the increase in intracellular lactate levels, leading to feedback inhibition of glycolysis and induction of intracellular acidification. To prevent this, and keep the survival of glycolytic cells, lactate is exported from the cells by MCT4. Then, oxidative cells uptake this additional lactate by MCT1 and use it to produce energy. MCTs (monocarboxylate transporters) encoded by SLC16 gene family have 12 transmembrane helices and are expressed in the plasma membrane; among them, MCT1,4 are attractive therapeutic targets due to their over-expression in various types of cancers. A structure-based virtual screening by consensus molecular docking strategy followed by molecular dynamics simulations was performed on an FDA-approved library to discover MCT1 inhibitors. Protein coordinate file was downloaded from RCSB in an open-outward conformation by PDB id=6LYY. After library preparation, molecular docking calculations were performed by Autodock Vina, DOCK, and MVD programs in parallel. Finally, seven ligands that showed high docking scores and promising interactions were selected for MD simulation studies against the MCT1. For each protein-ligand complex in the membrane bilayer, RMSD of the protein backbone, ligand RMSD, RMSF, and hydrogen bonding analysis were calculated. The results showed that an angiotensin II receptor inhibitor forms one and five hydrogen bonds with Asp309 and Arg313 in MCT1, respectively, during the 100 ns MD simulation. These H-bonds are vital to prevent protein conformational changes and lactate transport. The RMSD value of this ligand remained stable at 2.1 Å during the MD simulation, and the backbone RMSD average was 1.8 Å. The RMSF values of critical residues in binding pocket (L66, T70, M151, P155, L281, D309, R313, S371) that play an important role in the inhibition mechanism were reduced. These findings indicated that the discovered ligand could have an inhibitory effect on human MCT1, paving the way for a new MCT1 inhibitor. However, more *in vitro* and *in vivo* studies have to be performed to confirm the effectiveness of this ligand.

***Keywords*:** Monocarboxylate transporter1, Virtual screening, molecular dynamics simulation, Chemical inhibitors, Cancer

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Virtual Screening, Docking, and Molecular Dynamics Simulation Studies for the Discovery of a Novel Inhibitor for MCT1 Transporter in an Open Inward Conformation

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ABSTRACT

Monocarboxylate transporters (MCTs) are members of the SLC16 gene family, containing 14 members. MCT1to MCT4 is responsible for the proton-linked transportation of monocarboxylates such as lactate and pyruvate across the cell membrane. MCT1and MCT4 transporters play a crucial role in physiological and pathological conditions. In cancer cells, ATP production predominantly depends on glycolysis. Cellular adaptation to hypoxia and proliferation is achieved via glycolytic switches in solid tumors. In this line, two types of glycolytic and oxidative cells are developed in the tumor microenvironment. Glycolytic cells absorb a lot of glucose, leading to producing a great deal of lactate and an acidic microenvironment. On the other hand, oxidative cells absorb extra lactate by MCT1 in the tumor environment; hence, MCT1 has become the hopefulness targeting in cancer treatment. Herein, we screened the FDA_approved drugs from the DrugBank and ZINC databases against the resolved structure of the MCT1 transporter in an open inward conformation, downloaded from RCSB (PDB id:7cko). Firstly, a library of compounds was prepared using the FAF-Drugs4 web server. Next, molecular docking calculations were done by three docking software: AutoDock VINA, MVD, and DOCK6. At last, molecular dynamics simulations were performed on the top-seven compounds by the GROMACS 2020 package. Pi interaction between ligand and key residues (Ser154, Tyr34, Lys38, and Tyr70), RMSD, RMSF values, and hydrogen bond analysis were calculated for protein-ligand complexes during 100 ns molecular dynamics simulation. The docking calculations and MD simulations showed that an anticancer drug has characteristics as a potential inhibitor for the MCT1 transportation mechanism. Based on hydrogen bonds analysis, the discovered ligand can form stable hydrogen bonds with lys38 and Ser154, two critical residues in the lactate-binding site of the protein. Moreover, ligand and tyr34 and tyr70 are involved in π_interaction. The obtaining findings in this study indicated that the screened ligand, which is an anticancer drug, possesses a high inhibitory potential for the MCT1 transporter in open inward conformation. Nevertheless, more *in vitro* and *in vivo* pieces of evidence are warranted to dissect the therapeutic effect of the proposed inhibitor.

***Keywords*:** Monocarboxylate transporter1, molecular dynamics simulation, Virtual screening, Docking

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Interaction of group-XIV elements of the periodic table with biomacromolecules and their effects on breast cancer cells

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ABSTRACT

The elements of group 14 (XIV) nanomaterials demonstrate a broad range of physicochemical behaviors. This group consists of carbon (C), silicon (Si), germanium (Ge), tin (Sn), and lead (Pb). This group has gathered noteworthy attention not only for their large surface area and low cost of synthesis but for their special application in nanomedicine. According to the American Cancer Society's estimates for 2022, nearly 287,850 new cases of invasive breast cancer will be identified in women in the United States and unfortunately, nearly 43,250 women will die from this kind of cancer. This paper reviewed and concentrated on the recent (<5 years) investigations about the interaction between the elements of group 14 nanomaterials with biomacromolecules. Furthermore, the effects of this group of nanomaterials on different subtypes of breast cancer cell lines were discussed. The intensity of the induced structural variation varies in this group of nanomaterials depending on the type of nanomaterials. Additionally, some nanomaterials of this group exhibit a high level of toxicity, whereas others exhibit a low level of toxicity. This review will provide useful information not only in understanding the mechanism of group 14 nanomaterials' interaction with biomacromolecules but also in developing more effective nanotherapeutics for cancer patients.

Keywords: Carbon family, Biomacromolecular interaction, Breast cancer, Nanopharmaceuticals

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Investigation of the silver nanoparticles and DNA interaction with different coatings and selecting the best coating by the AHP method

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ABSTRACT

The consumption of nanomaterials is very common in the fields of medicine and pharmacy due to their flexibility, small dimensions, and large ratio of surface to volume. One of the goals of nanotechnology-related industries is to evaluate the effect of the type of coatings on the properties of the nanoparticles. The purpose of this study was to investigate the effects of silver nanoparticle (AgNPs) coating on their ability to interact with DNA by fluorescence emission spectroscopy, zeta potential analysis, and circular dichroism (CD) spectroscopy. Then, select the appropriate nanoparticle coverage by using the analytic hierarchy process (AHP) method. The results showed that AgNPs coated with ethylene glycol interact with DNA with a higher binding constant value. The negative values of $\Delta G°$ point out that the interaction of AgNPs to DNA was spontaneous. CD spectroscopy studies also indicated the alteration in DNA structure as a result of the interaction of AgNPs and the transition of DNA from B to C and A, for AgNPs coated with sodium citrate and ethylene glycol, respectively. According to the AHP analysis, it was found that the most favorable coating for AgNPs is ethylene glycol and subsequently AgNPs without coating. According to this study, the type of coating is very effective in the interaction of nanoparticles with the macromolecules, and AgNPs coated with ethylene glycol interact with a higher binding constant. This finding is important in the pharmaceutical design and nano standardization.

Keywords: AHP method, DNA, Silver nanoparticles, Spectroscopy

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A Novel Core-shell PAMAM Dendrimer for Targeted Delivery of Doxorubicin to MCF-7 Cancer Cells

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ABSTRACT

Doxorubicin (DOX), the well-known anthracycline, has proven antineoplastic effects on chemotherapies for various types of cancer. One of the most limitations of the prescription is its toxicity originated from affecting unspecified healthy cells, especially the heart myocardium. To overcome this disadvantage, a new nano-scale core-shell polymeric system was introduced as a targeted drug delivery carrier. The synthesis of the nanocarrier was started with quantum dots, as the core, for fluorescence tracking and continued by fourth-generation poly amido amine (PAMAM) dendrons, as the shell, according to the previous literature. It was modified with folic acid (FA), as a targeting agent. Quantum dot and PAMAM dendrimer were synthesized and characterized using Fourier transform infrared spectroscopy (FTIR), high-resolution transmission electron microscopy (HRTEM), photoluminescence spectroscopy (PL), dynamic light scattering (DLS), and UV-Vis spectrophotometry. DOX's loading and release profile from the Nano carrier was studied in tumor pH conditions. The toxicity of free and DOX-loaded Nano carriers was investigated on MCF-7 cells. The obtained results were acceptable.

Keywords: Core-shell system, PAMAM dendrimer, Nanocarrier, Doxorubicin, Drug delivery

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Effect of Liraglutide Peptide Containing Iron on Corona Spike Protein: An In-silico Study

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ABSTRACT

Lactoferrin (LF) is a nutrient naturally found in mammalian milk. It is a glycoprotein of about 78 kDa and possesses two Fe^{3+} ions with high affinity. The naturally occurring iron chelator Lf exerts immunomodulatory as well as anti-inflammatory effects. Furthermore, there is evidence that LF can bind to some of the receptors used by coronaviruses (e.g., the angiotensin-converting enzyme 2 (ACE2) and consequently block their entry. On the other hand, Liraglutide belongs to a group of medications known as glucagon-like peptide-1 (GLP-1) receptor agonists and is used to treat type 2 diabetes. Investigations showed that GLP-1 receptor (GLP-1R) activation by Liraglutide leads to increasing ACE2 expression. Considering all the abovementioned facts, this study aimed to investigate the possible benefits of adding iron LF to the Liraglutide peptide to increase host immunity in coronavirus infections or not. For this purpose, Liraglutide peptide was used as a GLP-1 analogue. Then, Liraglutide peptide was modeled and tested by Modeler, Pymol, and Spdbv software, while LF (in two different isoforms, LF-α with and LF-β without iron ions) was positioned in the Liraglutide loop individually. In addition, molecular docking was performed using the Haddock server and the rate of peptide binding was examined with and without iron presence. The results indicated that the presence of iron ions in the Liraglutide peptide had no beneficial effect on the prevention of coronavirus disease infection although we expected to have more antiviral activity by Metal-based drugs. The obtained results also specified that the binding energy of the two mentioned molecules was more robust when there were no iron ions. we hope that the designed peptide (Lactoferrin plus liraglutide) may contribute usefully to the prevention and treatment of coronavirus infections.

Keywords: Liraglutide, Lactoferrin, Spike protein, Metal-based drugs.

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Chaperone-Based Soluble Expression of Recombinant L-asparaginase from Yeast Strain *Fereydounia khargensis* in *E. coli* Expression System

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ABSTRACT

L-asparaginase is used for the treatment of acute lymphoblastic leukemia (ALL). This enzyme has been isolated from bacterial, yeast, and fungal sources. L-asparaginases originating from eukaryotic sources such as yeast are more similar to human type of the enzyme and this leads to less sensitivity in patients who take the drug. However, expression of most of the eukaryotic genes in prokaryotic systems results in low expression level or inclusion bodies. The aim of the present research is to isolate, clone and recombinant expression of the soluble form of L-asparaginase from yeast type strain *Fereydounia khargensis* in *E. coli* system with the assistance of molecular chaperones. Yeast strain was obtained from microorganism collection of the Iranian Biological Resource Center (IBRC-M 30116). Whole genome sequence of the strain was analyzed and cloning primers were designed. L-asparaginase gene was cloned into pET-28 a (+) vector. With subsequent transformation into the *E. coli* BL21(DE3). The plasmid harboring the gene was co-transformed with the commercial chaperone plasmid pG-KJE8 (Takara, Japan) into the expression host. This research proved that L-asparaginase gene from *F. khargensis*, as a potential source of the enzyme, could be expressed in soluble form by co-expression with molecular chaperones DnaK, DnaJ, GrpE and GroEL, GroES. The expressed protein was estimated to be 73kDa when attached to His-tag at both ends. SDS-PAGE analysis was done following purification of the soluble fraction and confirmed the size of the expressed protein. Although the soluble/insoluble ratio of the enzyme was not drastically improved when using mentioned chaperone molecules, it can be used for soluble expression of minimum amount of such eukaryotic enzymes in *E. coli* system which is essential for the enzyme functional assay in the laboratory. Despite the suboptimal chaperone-assisted soluble expression of the enzyme, If the specification of the enzyme was in line with the research aim, it could be subsequently codon optimized and expressed in the optimum condition. So, we suggest the application of bacterial chaperones for soluble expression of fungal and yeast enzymes.

***Keywords*:** L-asparaginase, *Fereydounia khargensis*, Molecular chaperones

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The Potential Role of Paepalantine as a Therapeutic Agent against Endoribonuclease NSP15 of SARS-CoV-2: a Molecular Docking Study

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ABSTRACT

Novel Coronavirus or SARS-CoV-2 outbreak has developed a pandemic condition all over the world. Despite the rapid development of effective vaccines, new anti-viral treatments are urgently needed due to emerging SARS-CoV-2 variants and the prevalence of break-through infections amongst those already vaccinated. NSP15 (Nonstructural protein 15) is a uridine-specific endoribonuclease conserved across all coronaviruses. The nuclease activity of NSP15 helps the virus evade triggering an innate immune response. Thus, NSP15 can consider as an ideal target to treatment COVID-19 disease and the effect of natural paepalantine is investigated against NSP15 of the SARS-CoV-2. The molecular docking process was performed using Molecular Operation Environment (MOE) software to predict the mode of interaction between the best possible biological conformations of paepalantine compound in the active site of NSP15 protein. The 2D structure of paepalantine was prepared by Chem Draw ultra 8.0 software and converted into PDB format by Hyper Chem7 using AM1 semiempirical method. The paepalantine was docked into the active site of NSP15 (PDB ID: 6WXC) by MOE software. The best pose of compound with the higher score was selected for ligand-target interaction analysis by the LigX module in MOE software. The docking result showed a high potency of 6WXC as NSP15 inhibitor with binding energy of -13.60 kcal/mol. Docking studies showed that paepalantine binds strongly with some of the amino acid residues in the active site of NSP15 and its active compound could form hydrogen bonds and arene-cation stacking interactions with Ser294, Leu346 and Lys345, respectively. These results showed that paepalantine compound could be considered as promising compound for the development of COVID-19 potential inhibitors after further studies.

***Keywords*:** SARS-CoV-2, paepalantine, molecular docking

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Molecular Docking of Anthocyanin-Based Compounds with EGFR in non-Small Cell Lung Cancer

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ABSTRACT

Non−small cell lung cancer (NSCLC) is the leading cause of cancer−associated mortality in both men and women worldwide. The over expression of epidermal growth factor receptor (EGFR) has been recognized as the driver mechanism in the occurrence and progression of NSCLC. Therefore, inhibition of EGFR is considered a potential therapeutic strategy. This study focused to investigate anti-EGFR potential of anthocyanin-based compounds using *in silico* approach. The molecular docking process was performed using Molecular Operation Environment (MOE) software to predict the mode of interaction between the best possible biological conformations of anthocyanin-based compounds in the active site of EGFR enzyme. The 2D structure of anthocyanin-based compounds including cyanidin, malvidin and peonidin were prepared by Chem Draw ultra 8.0 software and converted into PDB format by Hyper Chem7 using AM1 semiempirical method. The anthocyanin-based compounds were docked into the active site of EGFR (PDB ID: 1XKK) by MOE software. The best pose of compounds with the higher score was selected for ligand-target interaction analysis by the LigX module in MOE software. The docking results showed that malvidin (-15.21 kcal mol^{-1}) to be the most potent inhibitor of EGFR as compared to erlotinib (-14.48 kcal mol^{-1}). Other anthocyanins namely, peonidin (-14.54 kcal mol^{-1}) and cyaniding (-14.14 kcal mol^{-1}) also showed potent inhibition against EGFR, the stability of these molecules with EGFR was almost more than erlotinib. According to docking results, anthocyanins bind strongly with some of the amino acid residues in the active site of EGFR such as Asp855, Lys745, Thr790, Leu844, Gly796 and Asn841. These results can provide a lead in exploring the anthocyanins in treatment of lung cancer after further studies.

***Keywords*:** EGFR, anthocyanins, molecular docking

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Study of Binding of Triptorelin to Albumin using Molecular Docking Method

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ABSTRACT

Triptorelin has a peptide structure consisting of 10 amino acids, molecular weight of 1311/473 $g.mol^{-1}$ and chemical formula of $C_{64}H_{82}N_{18}O_{13}$ with a biological half-life of 5 to 7 hours. For increasing the half-life was using some cariers such as human serum albumin (HSA), which is non-toxic and easily present in the body. Albumin is a water-soluble protein produced by the liver and circulated in plasma and is the most abundant plasma protein. It has a molecular weight of 66500 daltons and consists of 585 amino acids. the half-life of albumin in the body is 19-20 days. In this study, we investigated the drug *Triptorelin* and its effect on HSA using molecular docking method. In this study, we used Pubchem, Drugbank, and Uniprot sites to review *Triptorelin*. AutoDockTools-1.5.6, ViewerLite, Chimera 1.15 and PyRx software were also used for docking studies. First, we saved the *Triptorelin* drug from the Uniprot as a sdf file. The target protein was edited by using Chimera 1.15 software. One chain of HSA was selected by this software and also water molecules were removed from the protein and hydrogen molecules were added to its structure. Then ViewerLite software was used to ensure that the study was done correctly. The molecular docking using PyRx software was started, where the grid box for selecting the binding site was as follows. Exhaustiveness = 8, center-x = 4.8000, center-y = -22.8342, center-z = 23.7857, size-x = 25.0, size-y = 25.0, size-z = 25.0. Among the 9 molecular docking results obtained for *Triptorelin* with HSA, the best result is related to Conformation 1 with binding affinity (-9.7 $Kcal.mol^{-1}$) and RMSD Lower bound (0) and RMSD Upper bound (0). According to docking studies, we found that Conformation 1 compound with negative binding affinity and RMSD(0) has a good effect on HSA protein for targeted drug delivery and prostate cancer treatment.

***Keywords*:** HSA, Triptorelin, Prostate cancer, Molecular docking

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Green Synthesis of Gold Nanoparticles Using *Pimpinella affinis* Leaf and Stem Extracts as Reducing Agents

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ABSTRACT

Gold nanoparticles have a wide range of biological applications due to their unique properties. Nowadays, the use of biological molecules and their components for the synthesis of nanoparticles has been considered due to their environmental friendliness, which is called green synthesis. In this study, leaf and stem extracts of *Pimpinella affinis* used as reducing agents for extracellular synthesis of gold nanoparticles. Gold nanoparticles synthesized a few minutes after treatment with $HAuCl_4$ solution with different concentrations of plant extracts at 70 °C and a color change from pale yellow to red observed. UV visible spectroscopy used to measure the progress of the reaction, and the size of nanoparticles synthesized investigated by DLS method and zeta potential. Peaks formed in the range of 520 to 530 nm and the formation of gold nanoparticles with sizes below 100 nm with a zeta potential of about minus 40, indicated the optimal synthesis of gold nanoparticles by the extract of *Pimpinella affinis*. According to the above findings, this plant, which contains desirable reducing agents for the synthesis of gold nanoparticles, can be studied as a good candidate for further research.

Keywords: Gold Nanoparticle, *Pimpinella affinis*, Biosynthesis,

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Expression, and purification of galactose dehydrogenase (Gal DH) in

E. coli BL21(DE3)

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ABSTRACT

Galactose dehydrogenase (Gal DH) is a member of the dehydrogenases family that catalyzes the conversion of D-galactose to D-galactono-1,4-lactone and NADH in the presence of NAD+. This enzyme plays a vital role in screening neonatal blood serum in galactosemia by determining and measuring *β*-D-galactose and α-D-galactose. The gene construct of galactose dehydrogenase was transformed into *E. coli* BL21(DE3) for expression. The expressed enzyme was purified by NTA-Ni affinity chromatography. In this report, we describe the expression and purification of Gal DH. The expression (in LB medium at a concentration of 0.5 mM IPTG, OD_{600nm}= 0.5 at 37 °C and induction time of 5 hours) of the enzyme was confirmed by SDS-PAGE. After expression, pelleted *E. coli* cells were suspended in lysis buffer (8M urea, 50 mM Tris, and NaCl 300 mM), broken by sonication, and clarified by centrifugation at 4,000 rpm, 4 °C for 20 min, and used for protein purification by NTA-Ni (2+) affinity chromatography. Before loading the sample, the column was equilibrated with buffer (8M urea, 50 mM Tris, 300 mM NaCl, and 5 mM imidazole). After the protein sample was applied to the column, it was washed by 10-20 mM imidazole, then eluted by 250 mM imidazole. Fractions of the purified Gal DH were checked by SDS-PAGE. After expression in optimized condition, the recombinant Gal DH was purified from the crude cell extract by NTA-Ni (2+) affinity chromatography. The purification procedure yielded an enzyme preparation that was apparently homogenous as judged by SDS–PAGE, which shows a single band at 34 kDa. Due to a wide range of applications of Gal DH, its gene is expressed in *E. coli*, and purified by affinity chromatography with a yield of 90%. Expression yield after refolding and kinetic properties will be reported.

Keywords: Expression, Purification, Galactose Dehydrogenase (Gal DH), *E. coli*

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Development of a Hairpin Assembly Machinery as a Genosensor to Detect a Pulmonary Infection Biomarker

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ABSTRACT

Since early detection of biomarkers could play a critical role in hindering infectious diseases, finding the best approach to sense these biomarkers have been of great impact. Nano-biosensing technology has become an attractive subject in the research area in the past decades. This technology could pave the way to achieve cheap, feasible, specific, and sensitive detection of biomarkers in the samples. Hairpin assembly is an autonomous reaction cascade hiring two hairpins to continue its machinery which is triggered by a DNA fragment (the target sequence). Here, we created a hairpin assembly approach to sense a pulmonary infection biomarker without using any sophisticated equipment. A pathogenic chromosomal gene in a lung infection agent, *Klebsiella pneumoniae*, was selected as the target gene. BLAST software from NCBI database was used to assure the specificity of the method. The designed cascade was implemented at an isothermal room temperature. Agarose gel electrophoresis was applied to prove the implementation of the reaction cascade in positive samples. The results showed that the selected gene was exclusively found in *K. pneumoniae* which verified the specificity of the method. Gel electrophoresis results demonstrated that the structures (H1-H2-target) which were only formed when the target DNA was present, has been constructed. However, in the absence of a target sequence, H1 could not hybridize with the target and the cascade did not begin. Hence, observing a DNA fragment that has a higher molecular weight than each reaction element indicated that the machinery has been operated successfully. In this study, we developed an autonomous signal-amplifying genosensor which was found to be capable of detecting a pathogenic gene that is specifically present in *K. pneumoniae* chromosome. It is concluded from the results that this technique could be utilized to track critical biomarkers and prevent probable losses.

Keywords: Genosensor, signal amplification, *Klebsiella pneumoniae*, biomarker diagnosis.

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A Novel Direct Electrochemistry of Glucose Oxidase on a Multi-walled Carbon Nanotubes, Hydroxy-fullerene and β-cyclodextrin Composites Modified Glassy Carbon Electrode

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ABSTRACT

A direct electrochemical process of glucose oxidase on a nanocomposite containing multi-walled carbon nanotubes (MWCNTs), Hydroxylated fullerenes (HFs), β-cyclodextrin (β-CD) (as a dispersion material of carbon nanotubes) and Nafion (NF) modified glassy carbon electrode was proposed in this study. The CV of NF/MWCNTs-β-CD-HFs-GOD composite electrode in N_2 saturated PBS shows a pair of well-defined quasi-reversible redox peaks with the formal potential (E˚′) of −413 mV versus Ag/AgCl at a scan rate of 0.05 V/s. The heterogeneous electron transfer constant was calculated to be 6.28 s^{-1} and the optimal work pH value of the modified electrode in 50 mM phosphate buffer was 7. Then, the recognition and detection of glucose by the modified electrode were carried out by adding different concentrations of glucose to the detection system. The modified electrode response toward glucose was linear in the concentrations ranging from 0.25 to 2 mM, with a detection limit of 2.3 mM. The apparent Michaelis–Menten constant (K_m^{app}) was calculated to be 0.94 mM, which indicating that the modified system had a good affinity with the substrate. The prepared electrode was designed for the direct electrochemical study of glucose oxidase, and for the monitoring of blood glucose concentration in vitro.

***Keywords*:** Glucose oxidase, Direct electrochemistry, Glucose, Nanocomposite

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Electrochemical Biosensor Based on CS/Hb/GR-CS-MWCNTs Nano-hybrids for the Detection of Hydrogen Peroxide

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ABSTRACT

The detection of hydrogen peroxide plays an important role in industry, environmental protection and clinical control. In the present study, a hybrid of graphene (GR), multi-walled carbon nanotubes (MWCNTs) and Chitosan (CS) was prepared and modified on the surface of a glassy carbon electrode (GCE). Then, hemoglobin (Hb) was immobilized on GR-CS-MWCNTs/GCE surface with CS as the film forming material. And the modified electrode was prepared and denoted as CS/Hb/GR-CS-MWCNTs/GCE. The GR-CS-MWCNTs hybrid was characterized by UV-Vis spectrum, Fourier transform infrared spectroscopy, transmission electron microscopy and electrochemical impedance spectroscopy, respectively. Electrochemical behavior of Hb on the modified electrode was investigated by cyclic voltammetry, and a pair of well-defined redox peaks were obtained, which indicated that direct electron transfer of Hb was realized on the hybrid modified electrode. The apparent charge transfer rate constant and transfer coefficient for electron transfer between the electrode surface and Hb were determined to be 10.2 s^{-1} and 0.2, respectively. The linear detection range of H_2O_2 of the modified electrode was from 1.0×10^{-13} to 1.9×10^{-4} mol L^{-1}, with a detection limit of 1.2×10^{-5} mol L^{-1}. Therefore, as a third-generation electrochemical biosensor, these nanomaterials modified electrode has potential and wide application prospects.

***Keywords*:** Hemoglobin, graphene, multi-walled carbon nanotubes, hydrogen peroxide, biosensor

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Inhibitory Effect of Astragalin on Glucose Mediated Protein Glycosylation in Vitro

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ABSTRACT

In recent years, diabetes has attracted widespread attention because its prevalence is rising at an alarming rate. Advanced glycation end products (AGEs) are the main intermediate products in the process of glycation, which can lead to long-term complications of diabetes. Astragalin is a flavonoid with anti-inflammatory, antioxidant and anti-diabetes biological activities. In this paper, the anti-glycation effect of Astragalin at different concentrations on bovine hemoglobin (BHb) in vitro was studied by glycation specific AGEs fluorescence methods. First, bovine hemoglobin was incubated in pH 7.4 phosphate buffer containing 300 mM glucose and different concentrations of Astragalin at 37 °C in the dark for 14 days. Then, emission spectra of AGEs were collectied on a fluorescence spectrometer at excitation wavelength of 380 nm and emission wavelength of 400-700 nm. With the increase of Astragalus concentration in incubation solution, the fluorescence intensity of glycosylated bovine hemoglobin decreased. Therefore, Astragalus may be a new anti glycosylation agent, which may prevent diabetes by inhibiting the formation of AGEs.

***Keywords*:** Astragalin, Non-enzymatic glycosylated, AGEs, Bovine hemoglobin

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Inhibitory Effects of Rutin and Quercetin on H_2O_2-mediated Non-enzymatic Glycosylation of SOD

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ABSTRACT

One of the most important mechanisms of diabetic complications is the non-enzymatic glycosylation of proteins. In this work, the inhibitory effects of rutin and quercetin on H_2O_2-mediated non-enzymatic glycosylation of superoxide dismutase (SOD) were studied in vitro. SOD is an important antioxidant enzyme in the human body. The co-culture method was used in 50 mM pH 7.4 phosphate buffer solution at 37°C sterile conditions. After incubation for three days, the SOD activity was measured by a UV-vis spectrophotometer. The results showed that in the presence of 50 mM glucose the SOD activity decreased by about 47%, which is the same as previous reports that non-enzymatic glycosylation reduced enzyme activity of SOD. When incubation of SOD with 50 mM glucose and 50 µM H_2O_2, the activity of SOD decreased by about 57%, indicating a faster decline under H_2O_2 mediated SOD inactivity. While H_2O_2 mediated glycated SOD incubation was carried out in the presence of 20 µM rutin or 20 µM quercetin, the activity of SOD decreased by about 39% and 33%, respectively. The results showed that rutin and quercetin have certain inhibitory effects on H_2O_2-mediated non-enzymatic glycosylation of SOD. This study explained the possible role of rutin and quercetin in the prevention and treatment of diabetes and its complications from the perspective of SOD activity.

***Keywords*:** Non-enzymatic glycosylation, Superoxide dismutase, Rutin, Quercetin, Reactive oxygen species

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Comparison of the Interaction of CT-DNA with Anticancer Glycine Derivative of Pt-Complex and Cisplatin: DFT, and Molecular Docking

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ABSTRACT

More than two decades have now passed since the platinum-based drug cis-diamine dichloroplatinum [II] has been used in cancer treatment. As cellular resistance to cancer therapy increases, this is an important issue to address. By binding to DNA, small molecules disrupt important cellular processes, inhibit the growth, division of cancer cells, and thus cause cell death.The crystal structure of DNA (PDB ID: 453D) was downloaded from the RCSB protein data bank . The optimized structures of the cisplatin analog, synthesized by Sheikhzadeh et al, were performed using density functional theory (DFT) B3LYP, solved via the Gaussian09 program. AutoDock Tools (ADT) was used to prepare all input files. ADT considers macromolecules as rigid bodies to save computational time to allow for flexibility in small molecules.The grid maps of docking studies were computed using the AutoGrid4 included in the AutoDock 4 distribution. The space minimization was determined with a grid precision of 0.375 Å and a grid space of 126 Å × 126 Å × 126 Å for all complexes. The rigid docking protocol and 200 runs of the Lamarckian genetic algorithm for exploring the conformations spaces of the cisplatin complexes were applied. In this study, the interaction of cisplatin and cisplatin derivative with calf thymus DNA was compared with Autodock and density function theory simulation method. Molecular docking simulation and DFT analysis were performed to investigate the binding sites and chemical behavior of cisplatin analogs, cisplatin. Finally, the best results in terms of binding energy and poses were chosen and analyzed by AutoDock and chimera software. Molecular docking showed that, Cis-Pt $(NH_3)_2$(*tertpentyl-gly*)]NO_3, it has a higher negative binding energy than cisplatin to interact with DNA, and the Cis-Pt $(NH_3)_2$(*tertpentyl-gly*)]NO_3 complex may be good candidate for anticancer drugs. The results of Molecular docking demonstrated that *Cis-Pt* $(NH_3)_2$*(tertpentyl-gly)]*NO_3, had higher negative docking energy (-8.33 kcal/mol) than cisplatin (-10.23 kcal/mol) for interaction with DNA, therefore *Cis-Pt* $(NH_3)_2$*(tertpentyl-gly)]*NO_3 complexes can be good candidates for anticancer drugs.

Keywords: cisplatin, CT-DNA, *cis-Pt*$(NH_3)_2$*(tertpentyl-gly)]*NO_3, cancer

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MOF-derived Efficient Adsorbent for Removal of Herbicide: Response Surface Methodology, Kinetic and Thermodynamic

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ABSTRACT

Water recycling in the agriculture industry is crucial due to its high water consumption, and adsorption is a commonly used method for the elimination of pollutants due to its low cost, high efficiency, and easy operation. In this study, MgO/carbon nanoadsorbent was prepared using Mg-MOF-74 and was used to remove herbicide atrazine from liquid phase. Response Surface Methodology (RSM) was used to model the atrazine removal and investigate the effects of temperature, pH, and adsorbent mass on the adsorption capacity of atrazine. The quadratic models developed from RSM showed that the optimal conditions for atrazine adsorption were: a temperature of 45.0°C, pH of 7.0, and adsorbent mass of 0.35. The thermodynamic parameters revealed that the atrazine removal process was endothermic and spontaneous. Overall, this study successfully demonstrated the use of MOF-derived adsorbent for the removal of herbicides from water, and the findings suggest that this method could be an effective strategy for water recycling in the agriculture industry.

Keywords: MOF, atrazine, Central composite design, RSM

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The Biophysical Approach on HSA upon Interaction with Bortezomib due to Structural Recognition of Drug Delivery

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ABSTRACT

Binding of drugs to blood plasma proteins such as Human Serum Albumin (HSA) is important for specific reasons; it affects drugs activity and drugs dispositions, determinant the pharmacokinetics of the drugs, limits the concentration of free and unbound drugs and finally the distribution of the drugs in the body. Bortezomib (BTZ) is the first anticancer proteasome inhibitor that was approved by the FDA. Binding and transmission of bortezomib are often mediated by plasma proteins, and it is unclear which protein is responsible for bortezomib transporting to tissues. In this study, we loaded the bortezomib into HSA and analysis the drug binding site, binding affinity, releasing rate of the drug and interactions of the bortezomib-HSA complex by molecular docking and molecular dynamics simulations (MD). The obtained results show that bortezomib binds to a hydrophobic pocket between subdomain IA and IIA of HSA. In addition, the binding of bortezomib to albumin leads to increased flexibility and fluctuations in the residues of subdomain IIIB of albumin. As a result, HSA-bortezomib interaction causes the conformational changes with the relative loss of helical stability of protein. Further investigations of HSA-bortezomib interaction will be significant in understanding the mechanism of bortezomib transmission and improving its effectiveness as well as reducing side effects of the drug.

Keywords: Bortezomib, HSA, Drug delivery, Hydrophobic interaction, Cancer

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Investigating the Anti-aggregation Effect of Melatonin on Proteins

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ABSTRACT

Melatonin, originally discovered as a hormone of the pineal gland, is most noted for its role in the regulation of the circadian rhythm. In addition, several other effects have been identified for melatonin including the regulation of gene transcription of enzymes involved in oxidative stress. Also, the changes in the concentration of melatonin have been seen in some neurodegenerative diseases. To find out the role of melatonin in neuroprotection against diseases such as Alzheimer's, inhibition of aggregation of Tau, and α-synuclein proteins by melatonin have been investigated. In the current study, the anti-aggregation effect of melatonin on some selected proteins such as insulin was investigated using measurement of the scattering changes at 360 nm caused by protein aggregation induced with increasing temperature as well as using experimental and computational techniques to investigate a possible mechanism for the anti-aggregation effect of melatonin on proteins. Our results suggested that melatonin does not cause a significant change in the final amount of insulin aggregation, but it significantly increases the lag time of insulin aggregation in a concentration-depend manner. In summary, our results show that melatonin can delay insulin aggregation, and taking into account the results of other studies, it probably has a broad anti-aggregation effect on proteins.

***Keywords*:** Insulin, Melatonin, Anti-aggregation

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Increased Soluble Expression of Nitrile Hydratase from *Streptomyces iranensis*, via Co-expression of Separate Subunits with Bacterial Chaperones

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ABSTRACT

Nitriles are highly toxic cyanide-containing organic compounds that are widespread in nature. Nitrile hydratases (NHases) are used to detoxify nitriles by hydrolyzing them and converting them into the corresponding amides, which have many industrial applications and are of wide commercial interest. So far, several NHases from various bacterial strains have been isolated and recombinantly expressed. In this experimental research, NHase from *Streptomyces iranensis* was isolated and cloned as separate subunits in distinct multiple cloning sites of pETDuet-1 and pET-26b (+) plasmids and expressed in *E. coli*. However, the overproduction of the three subunits of NHase (α, β, and helper) was insoluble in *E. coli* and precipitated in the cytoplasm in the form of aggregated inclusion bodies. To improve the solubility of NHase subunits, the pG-KJE8 vector (Takara, Japan) containing a set of molecular chaperones (DnaK, DnaJ, GrpE, GroEL, GroES) was co-transformed and co-expressed according to the pG-KJE8 user manual. The results showed that molecular chaperones can significantly promote the soluble expression of recombinant NHase at 28-30°C. Since all three subunits of the enzyme are necessary for the normal activity of NHase, the soluble expression of the subunits was considered. Our findings indicated that the alpha subunit, as the main subunit of the enzyme, is soluble in a sufficient amount, but the beta and auxiliary subunits are less soluble. However, the presence of all three subunits together in a soluble form ensures the appropriate activity of the enzyme. Also, the use of various expression vectors to investigate the soluble expression of enzyme subunits showed that changing the vector or the presence of an S-tag does not significantly contribute to the production of soluble protein. The results of this research generally showed that using molecular chaperones is a more effective strategy than other optimization methods for the soluble expression of NHase subunits. Additionally, the expression of all three subunits in one open reading frame is not suggested due to the decrease in the expression of distant subunits compared to the promoter. Therefore, in this study, all three subunits were cloned in separate cloning sites.

Keywords: Nitrile hydratase, *Streptomyces iranensis*, pG-KJE8, Chaperones

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A New Thermotolerant and Inhibitor-Resistant Nitrile Hydratase from *Streptomyces iranensis*

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ABSTRACT

Nitrile hydratase (NHase) is an important industrial enzyme that catalyzes the hydrolysis of nitriles to their corresponding amides. NHase enzyme has a high potential in organic synthesis due to its importance in environmental studies such as the remediation of water and soil contaminated with nitrile compounds. Additionally, it finds numerous applications in industry, including the conversion of nitriles into useful chemical products and the commercial production of acrylamide. In this study NHase from *streptomyces iranensis* has been functionally expressed in *E. coli*, demonstrating significant activity in the production of acrylamide from acrylonitrile. We investigated the effect of known reagents, such as urea, EDTA, NaN3, DTT, and ammonium persulfate, which have been reported as inhibitors in various studies, on the activity of co-Type NHase. Furthermore, we examined the enzyme's activity at different temperatures ranging from 4°C to 80°C. Our study revealed that the recombinant enzyme is resistant to different inhibitors, including urea, EDTA, and NaN3, at a final concentration of 1 mM. More than 80% of the enzyme activity was retained compared to the control reaction. Regarding enzyme durability at different temperatures, we found that NHase could tolerate temperatures up to 50°C with less than a 50% reduction in activity. However, increasing the temperature to 80°C resulted in a 90% decrease in enzyme activity compared to the control reaction. In this study, we successfully produced the active form of NHase in the *E. coli* expression system. The enzyme demonstrated high potential for acrylamide production, along with resistance to high temperatures and various inhibitors. These results highlight the important and practical aspects of NHase, paving the way for further investigations into its activity under different conditions.

Keywords: Nitrile hydratase, *Streptomyces iranensis*, Inhibitor-resistant, Thermotolerant

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The Investigating of the Interaction of Favipiravir on RGD Tripeptide for the Purpose of Drug Delivery: A DFT Study

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ABSTRACT

Drug delivery as methods and technics implemented on the development of novel carrier systems has opened an amazing field to the purpose of scientists to use it as a powerful tool in efficient therapeutic delivery of drugs. Therefore, the main goal of this research is to investigate whether it is possible to use the RGD (*Arginyl-glycyl-aspartic acid*) protein as a proper carrier of *Favipiravir* (FAV) drug. For this purpose, we have computed the energetic aspects of chemisorption of FAV on surface of RGD using the DFT calculations. All of calculations were performed based on DFT at the level of B3LYP functional in conjunction with 6-31G (d) Basis set as performed in Gaussian 09 software package. The results obtained from Optimization and Frequency computations on all of the orientations proved that the adsorption of FAV on RGD occurs from the side of *fluorine* atom of *Favipiravir* on RGD hydrogen's. According to our results, this orientation is more stable than other configurations. In addition, some of the other configurations were also converted into the mentioned configuration. The calculated binding energy of FAV-RGD (-23.3 Kcal.mol-1) indicated that the main factor in the stability of the FAV-RGD system is the formation of strong hydrogen bond between *fluorine* and *hydrogen* atoms. The obtained results have been showed that FAV is strongly bound to the RGD. Moreover, it appears that the RGD can be potentially introduces as a new career of FAV drug.

***Keywords*:** Favipiravir, RGD, DFT, Drug Delivery

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A microfluidic paper-based device for creatinine measuring in urine sample

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ABSTRACT

Chronic kidney disease is one of the silent diseases that progress slowly and often without symptoms and can eventually lead to kidney loss. Early diagnosis of this disease can help detect and prevent further problems. Urine creatinine is an effective biomarker for early diagnosis of CKD. Still, the methods available in clinics are frustrating for people living in deprived areas due to high costs and 24-hour urine collection requirements. Currently, paper-based microfluidic systems are being developed due to their simplicity, cheap price, capillary and permeability of the fluid, and no need for additional equipment. For the detection of creatinine on paper, the colorimetric method was used with the 3,5-dinitro benzoic acid in an alkaline solution reagent. The reagent was dispersed on a Whatman paper a channel was created with crayon and then heated for 5 minutes. By using this method, the barrier to the device was created. As the sample wicks through the channel, the analyte and reagent interact selectively. The creatinine standard solution was used with several concentrations (from 0.25 to 2.7 g/L) for analysis. An optimal concentration of reagent was determined by comparing the lowest and highest concentrations of biomarkers. In the presence of creatinine, the color of this reagent changed from white to purple. By using a ruler, the amount of creatinine was calculated. This method does not require a camera or smartphone. This system is a simple and semi-quantitative method to determine urinary creatinine and can be suitable for point-of-care detection. In addition to being cheap and easy to use, this system is also available in remote areas.

***Keywords*:** Lab on Paper, Urine, 3,5-Dinitrobenzoic Acid, Creatinine

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Designing a biosensor based on choline oxidase enzyme to measure agricultural pesticides in the Caspian Sea

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ABSTRACT

Choline oxidase enzyme is one of the types of oxidoreductases, which makes up about 25% of known enzymes. The applications of this enzyme can be mentioned in the measurement of phosphorous substances and it is very suitable for the design of enzymatic biosensors. In this report, the electrochemical behavior of the enzyme on the Co3O4.rGO nanoparticle was investigated in the presence of choline chloride at a potential of -0/7 to -0/3 at a speed of 100, and the presence of the nanoparticle and the enzyme on the glassy carbon electrode was well established, and the electrochemical and electrocatalytic behavior of the enzyme On the modified nanoparticle and electrode, it shows uniform enzyme coverage, better reversibility, oxidation reaction and transfer rate.

***Keywords*:** Choline oxidase enzyme, biosensor, organophousphor, Co3O4.rGO nanoparticle, Glassy carbon electrode

Immobilization of Metagenome-Derived Laccase on Hydrogel and Investigation of the Function of the Immobilized Enzyme in Lignin Degradation

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ABSTRACT

Biodegradation of the lignocellulosic materials is associated with harsh processing conditions such as extreme pH and temperature, high salinity, metal ions, and organic solvents; therefore, laccases with efficient function in these complex conditions are in increasing demand. Enzyme immobilization onto nanomaterials is a promising approach for increasing the enzymes' stability, activity, and reusability to develop cost-effective, green, and sustainable biotechnological processes. Immobilized laccase as a green biocatalyst is cost-effective for the development of biorefining processes and also has many economic benefits through the reduction of lignocellulosic biowaste accumulation. In this research, the comparative analysis of free and immobilized metagenome-derived laccase (PersiLac2) on chitosan-alginate hydrogel is reported using ABTS (2,2'-azino-bis (3-ethylbenzothiazoline-6-sulfonic acid)) oxidation as a substrate. The higher performance of immobilized PersiLac1 compared to the free enzyme was confirmed in the degradation of rice straw as agricultural wastes by structural analyses (SEM and FTIR analysis) and the production of reducing sugar after hydrolysis. The free compared to the immobilized enzyme lost almost 50% of its relative activity over a temperature range from 50 °C to 90 °C. While the immobilized laccase on chitosan-alginate hydrogel maintained approximately 80% of its relative activity under the same temperature range. Examining the enzyme's reusability, it was found that after 15 cycles, 76.64% of the relative activity was preserved in the case of immobilized laccase. The laccase immobilization on chitosan-alginate hydrogel improved the stability and activity of the enzyme in different conditions compared to the control sample and represents promising support for laccase applications.

***Keywords*:** Laccase, Immobilization, Metagenome, Lignin degradation

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Cross-linking of wheat proteins by laccase for improving the quality of poultry feed

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ABSTRACT

Today's high population has led to the higher poultry feed consumption and highlights the demand for poultry feed production with improved quality. The main ingredient used in poultry feed is corn, which its consumption is limited due to low protein content and quality. To mitigate the problem, laccase cross-linking of wheat proteins can be utilized in poultry feed production. In protein crosslinking by laccase, the phenolic substrates are catalyzed and generate free radicals. Subsequently, as a result of non-enzymatic conversions, protein biopolymer networks are formed in the food matrices. In this study, the SDS-PAGE analysis evaluated a metagenome-derived laccase from tannery wastewater that catalyzed oxidative cross-linking of wheat proteins. Accordingly, the functional properties of proteins, including foaming, emulsification, and water solubility, were investigated. The reducing power and ABTS radical scavenging tests were used to evaluate the potential antioxidant activity of the wheat protein and its treatment. The results showed that cross-linked wheat proteins demonstrated higher foaming capacity, foaming stability, and emulsifying properties than controls. Moreover, the addition of mediators with laccase in poultry feed elevated the antioxidant activity to up to 90%, indicating a higher ability of proteins to react with ABTS free radicals as well as reducing power. The supplementation of cross-linked proteins with the poultry developed solubility and increased water holding capacity compared to the feed without additives. This method could provide a new opportunity for the food industry to improve product quality and protein content for feed applications.

Keywords: Metagenome-derived laccase, Crosslinking, Poultry feed

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Stability enhancement of vitamin C by loading on nanostructured lipid carrier for topical delivery

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ABSTRACT

The low solubility and stability of the drug limit its biological use, so it is necessary to increase the solubility and, thus, the bioavailability of the drug. This study discusses the formulation of nanostructured lipid carriers as one of the best methods to increase drug solubility and, thus, bioavailability. Nanostructured lipid carriers are produced from biocompatible physiological lipids and improve solubility, cellular uptake, and stability. The present study aimed to develop nanostructured lipid carriers (NLCs) to improve the stability of vitamin C. Vitamin C-loaded NLCs were prepared using a high-pressure homogenization method using natural oils. Particle size, entrapment efficiency, and sustained drug release were also studied. The Field Emission Scanning Electron Microscopy (FESEM) results showed that the NLCs were spherical with a smooth surface. The Dynamic Light Scattering (DLS) results confirmed the formation of spherical particle dispersions by NLCs on a nanoscale. According to the design expert results of the particle size, the increase in the surfactant solution decreases the particle size exponentially. The results indicated a significant improvement in the entrapment efficiency of the optimal vitamin C formulation. In vitro, vitamin C release studies showed that nanostructured lipid carriers could release vitamin C in a stable form. The present results show the potential of NLCs as a new carrier for skin delivery of vitamin C in topical treatments.

***Keywords*:** Nanostructured lipid carriers, Topical Delivery, Nanotechnology

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Immobilization of Glucose Oxidase onto Amino-Functionalized Carbon Nanofibers for Glucose Biosensing

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ABSTRACT

Enzymes are efficient biocatalysts with outstanding properties that have attracted much attention in developing industrial, clinical, and environmental electronic devices. Enzyme immobilization on a suitable substrate has been proposed as an effective process for improving the properties of enzymes, such as stability, activity, and reusability. Different carbon nanostructures as immobilization support have been used to immobilize enzymes. Carbon nanofibers (CNFs) are especially appropriate for enzyme immobilization owing to their high aspect ratio, conductivity, and chemical stability. Glucose oxidase (GOx) is a redox enzyme broadly used, specifically in glucose electrocatalysis. Here, amino-functionalized CNFs were prepared to increase solubility and promote their interaction with biological molecules. After the oxidation of CNFs (through treatment with hydrogen peroxide and UV light), an epichlorohydrin reagent was used to chlorinate them. Thereafter, carbon nanofibers with amino functional groups (CNFs-NH_2) were synthesized using ethylenediamine. To fabricate the enzymatic electrode, the glassy carbon electrode surface (GCE) was modified with CNFs-NH_2 (CNFs-NH_2/GCE). Then, for GOx immobilization, it was drop cast onto the surface of modified GCE and allowed to dry at room temperature (GOx/CNFs-NH_2/GCE). The chemical, structural, and morphological characteristics of CNFs-NH_2 were confirmed using Fourier transform infrared spectroscopy (FT-IR), field emission scanning electron microscopy (FE-SEM), and energy-dispersive x-ray (EDX) spectroscopy, thermogravimetric analysis (TGA), and atomic force microscopy (AFM). The electrochemical performance of GOx/CNFs-NH_2/GCE was studied by cyclic voltammetry (CV), electrochemical impedance spectroscopy (EIS), and differential pulse voltammetry (DPV) techniques. The GOx/CNFs-NH_2/GCE indicated a pair of well-defined redox peaks with a formal potential (E°′) of -0.447 V. The amount of electron transfer rate constant (k_s) for immobilized GOx was obtained to be 6.16 s^{-1}. These results demonstrate that CNFs-NH_2 as a suitable microenvironment leads to favored immobilization of GOx and the establishment of fast electron transfer between the GOx redox center and GCE surface. Also, glucose detection via GOx/CNFs-NH_2/GCE in the linear range of 0.2-2.0 µM reveals a detection limit of 85.0 nM with high sensitivity (38.22 $\mu A.\mu M^{-1}.cm^{-2}$). This biosensor provides an appropriate platform for glucose determination and CNFs-NH_2 can also be used to immobilize biological molecules, especially enzymes.

***Keywords*:** Glucose oxidase, Immobilization, Carbon nanofibers, Amino-functionalization, Biosensor

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Electrochemical Determination of Gallic Acid Using a Sensitive Sensor Based on g-C_3N_4/AuNPs Modified Carbon Paste Electrode

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ABSTRACT

Gallic acid (3,4,5 hydroxybenzoic acid) is an important phenolic acid in industry and exists in plants as free or conjugated form. Gallic acid is used in food, medicine, paper and photography industeries, besides its therapeutic and antioxidant properties. Using modified electrodes to identify trace elements and chemical markers is a common method in electrochemistry. Graphitic carbon nitride (g-C_3N_4), is a graphite-like material with a two-dimensional layered structure that can improve the kinetics of electron transfer reactions occurred on the modified electrode surface. It is a class of polymeric materials mainly composed of carbon and nitrogen covalently bonded by π-conjugation. Application of gold nanoparticles beside g-C_3N_4 (g-C_3N_4/AuNPs) in electrochemical sensors is of high importance and innovation. In this study, g-C_3N_4/AuNPs nanocomposite was synthesized by in situ wet chemical reduction method to modify the carbon paste electrode (g-C_3N_4/AuNPs/CPE). Analytical methods such as FTIR, XRD, EDX and SEM images were used to characterize g-C_3N_4/AuNPs structure and morphology. Electrochemical impedance spectroscopy (EIS), cyclic voltammetry (CV) and differential pulse voltammetry (DPV) methods were used to investigate the electrodes conductivity and electrochemical behavior of gallic acid on the surface of the g-C_3N_4/AuNPs/CPE. The EIS results showing that the charge transfer resistance (R_{CT}) of the modified g-C_3N_4/AuNPs /CPE was greatly reduced compared to the bare CPE (250 vs. 1500 Ω, respectively). The CV voltammogram of g-C_3N_4/AuNPs/CPE were recorded in phosphate buffer (PBS; 0.1 M, pH 2.0) containing 2.5 µM GA with scan rate of 0.1 Vs^{-1}. In this cyclic voltammogram the anodic and cathodic peaks for GA was observed around potentials 0.5 and 0.45 V, respectively. Also, regards to GA determination through DPV, the linear range of 0.16-4.0 µM and detection limit of 0.25 µM were obtained. Furthermore, due to the presence of GA as a potential marker with plant origin in honey, the proposed g-C_3N_4/AuNPs/CPE was successfully used to its measurement in thyme honey (0.016 mg/g). Due to the favorable performance of the fabricated g-C_3N_4/AuNPs/CPE, it can be used to measure gallic acid in food products of vegetable origin, including honey, herbal extracts, etc.

***Keywords*:** Gallic acid, Carbon paste electrode, Differential pulse voltametry, g-C_3N_4/AuNPs nanocomposite

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Design a cMWCNTFET-Based Biosensor via Cytochrome *c* Immobilization to Detect Low Trace of Hydrogen Peroxide

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ABSTRACT

Hydrogen peroxide (H_2O_2) has biological roles including proliferation and gene expression. Early detection of excess H_2O_2 is vital considering its harmful effects. Besides titration, spectrophotometry and biosensors methods to detect H_2O_2, field effect transistor (FET) based biosensor is a modern technique considering high sensitivity for molecular biosensing. Here, first multiwall carbon nanotube was carboxylated with acidic treatment (cMWCNT) as a substrate for biomolecule immobilization and FET channel semiconductor. Then, an N-type cMWCNT field effect transistor (cMWCNTFET) was designed. Thereafter, 2.0 µL of Cytochrome *c* solution (Cyt *c*, in 1 M PBS) was immobilized on the cMWCNTFET channel (Cyt *c*/cMWCNTFET). Optimal concentration of cMWCNT, Cyt *c* and pH of PBS was determined via linear sweep voltammetry with applying potentials to gate (V_{GS}) and drain (V_{DS}) in two ways (V_{GS}= 1.0 V, V_{DS}= 0 to 0.4 V and V_{DS}= 0.2 V, V_{GS}= 0 to 0.2 V; scan rate of 0.1 $mV.s^{-1}$). Afterwards, the output current was measured by amperometric technique (V_{DS}=Edc= 0.2 V, V_{GS}=1.0 V) in the presence of different H_2O_2 concentrations (10.0 fM to 10.0 nM) at the Cyt *c*/cMWCNTFET channel. Finally, to test biosensor selectivity, leucine, tyrosine, ascorbic acid, glucose (1.0 mM) and H_2O_2 (1.0 nM) was loaded respectively on the Cyt *c*/cMWCNTFET channel for measuring the output current as it is described above. Investigation of the Cyt *c* immobilization, using raman spectroscopy analysis and scanning electron microscope (SEM) imaging, was performed. Optimal concentration of cMWCNT and Cyt *c* was 1.5 and 0.25 $mg.ml^{-1}$ respectively, also the optimal pH of PBS was 5.5. The response time and detection limit was determined 1 second and 10.0 fM, respectively. Linear response range was 10.0 fM to 1.0 nM. This Cyt *c*/cMWCNTFET biosensor is very sensitive compared to other platforms. Biosensor selectivity was investigated as it showed constant current while loading interfering substances and a significant change in current while loading H_2O_2. The designed platform (Cyt *c*/cMWCNTFET) could be used for selective and sensitive H_2O_2 biosensing plus immobilization of various biomolecules (protein, nucleic acid, etc.) and as a point of care (POC) diagnostic tool.

***Keywords*:** Field effect transistor, Hydrogen peroxide, Cytochrome *c*, Carbon nanotube, Biosensing

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Authentication of Iranian Honey Samples: Physicochemical Parameters Investigation Along with the Electrochemical Measurement of Gallic Acid by g-C_3N_4/AuNPs Modified Carbon Paste Electrode

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ABSTRACT

Honey is a natural food with therapeutic and health benefits for humans. Interest in honey authentication has increased in relation to botanical and geographical origin and fraud. Phenolic compounds are formed in the plants nectar to attract pollinating insects and found in honey owing the nectar processing by bees. Polyphenol gallic acid (GA) is used as a chemical marker in food analytical researches. Here, to investigate the honey authentication, some physicochemical parameters of Iranian honey samples (thyme, astragalus, coriander, barberries, eucalyptus and ziziphus) such as pH, diastase activity, sucrose, proline and hydroxymethyl furfural (HMF) contents were measured according to Iran national standards organization (INSO 92). Also, the modified carbon paste electrode with synthesized g-C_3N_4/AuNPs nanocomposite (g-C_3N_4/AuNPs/CPE) was used to GA determination in honey samples by differential pulse voltammetry technique (DPV) based on GA oxidation peak at 0.5 V. Sucrose content in honey samples was ranged 0.97 to 7.70 g/100 g .According to the codex committee on sugars (CCS), just this parameter in ziziphus honey (7.70 g/100 g) exceeded 5.0 g/100 g, due to its higher content in ziziphus flower nectar. Acidic pH was obtained for all honey samples; however the pH 6.25 for ziziphus honey exceeded the standard range (3.40-6.10), because of fermentation occurrence. All samples were situated at the standard proline content (≥180 mg/Kg). The highest and lowest proline contents were obtained for thyme and barberry honey samples; 843.0 and 340.0 mg/Kg, respectively. The diastase activity and HMF were used to determine the freshness and overheating of honey that registered in all samples 9.10-17.08 DN (standard: ≥8 DN) and 0.67-26.30 mg/Kg (standard: ≤40 mg/Kg). The GA content in thyme, barberry, astragalus, eucalyptus, and coriander honeys were 0.016, 0.015, 0.014, 0.006 and 0.004 mg/g, respectively and there was no oxidation peak for GA in ziziphus honey. Honey authentication has complexity and very different depending on the time of harvest, packaging, botanical origin, storage time, and degree of heat treatment. Here, g-C_3N_4/AuNPs/CPE was successfully used to GA identification in honey samples and accordingly recommends to qualification and prevent honey frauds.

***Keywords*:** Gallic acid, Iranian honey, Physicochemical parameters, g-C_3N_4/AuNPs

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Effect of pomegranate polyphenols in bulk and nano-sheet form on alpha-synuclein fibrillation

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ABSTRACT

Parkinson's disease is the second most common neurodegenerative disease in the world. A pathological feature of Parkinson's disease is the accumulation of intracellular filamentous aggregates of alpha-synuclein. Alpha-synuclein protein is a 15 kD disordered protein that forms beta-sheets under specific conditions and creates oligomers, protofibrils, and fibrils step by step. Cells that produce dopamine are killed by toxic aggregates of alpha-synuclein. In this regard, many compounds have been tested for their ability to inhibit the fibril formation of alpha-synuclein. Among them, polyphenols, which are found in large amounts in plants and herbal remedies including pomegranates, are beneficial in preventing protein aggregation. Although numerous studies have demonstrated that polyphenols have anti-amyloidogenic properties, they are poorly soluble in water and are rapidly metabolized and eliminated. Furthermore, many of these compounds cannot cross the blood barrier, which further limits their biological effects. This limitation could be overcome through their nanonization. Our study examined the effects of pomegranates' polyphenols on alpha-synuclein fibrils in bulk and nanosheet form to see if they could inhibit or reduce fibril formation. To determine whether the compounds have inhibitory effects, we applied ThT, Congo red, and ANS fluorescence assays. Pomegranate polyphenols, both bulk and nanosheet forms, reduced the lag time of fibril formation as well as the ThT fluorescence intensity in kinetic studies using ThT assay with the nanosheet being more effective. Our primary results showed that there is a promising effect of pomegranate's polyphenols nanosheets in preventing alpha-synuclein fibrillation.

Keywords: Alpha-synuclein; Pomegranate's polyphenols; Parkinson's disease; nanosheets

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Inhibition of alpha-synuclein fibrillation by green tea polyphenols

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ABSTRACT

Parkinson's disease (PD) is the second most common neurodegenerative disorder and it is characterized by a distinct age-independent loss of dopaminergic neurons in the substantia nigra pars compacta (SNpc) which is decreased dopamine levels. Misfolding and aggregating of a 140 amino acid protein called alpha-synuclein (α-Syn) into intracellular filamentous aggregates is a pathological feature of PD. A30P, A53T, E46K, and H50Q mutations in the α-Syn are shown to be involved in early-onset PD. Therefore, the development of drugs that lead to inhibition of α-Syn aggregation can be a promising method for the treatment of PD. Various studies have confirmed the inhibitory effect of natural polyphenols that are abundant in food and herbal remedies. Green tea is a rich source of polyphenols. The main component of green tea polyphenols is catechins. On the other hand, despite numerous reports showing the anti-amyloidogenic effects of natural polyphenols, most of these compounds have low solubility in water and are rapidly metabolized and eliminated upon entering the bloodstream. Nanonization has been introduced as a strategy to overcome this limitation. In this study, we examined the effects of green tea polyphenols on α-Syn fibrillation in the bulk and nanoparticle forms to investigate if they can inhibit or reduce the fibrillation. For this purpose, after the synthesis of nanoparticles using $CuSO_4$ at a temperature of 100 ºC, we used ThT, Congo red, and ANS assays. Both bulk and nanoparticle forms were effective in inhibition of α-Syn fibrillation with the nanoparticles being more successful. Our primary data showed the promising effect of green tea polyphenols nanoparticles is preventing α-Syn fibrillation.

Keywords: Alpha-synuclein; Parkinson's disease; fibril; Green tea polyphenols

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A520-MOF diminished Doxorubicin disturbance for hemoglobin oxygen affinity

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ABSTRACT

A520 as a member of metal organic frameworks (MOFs) family is a new porose material[1] with diverse applications such as biosensing and drug delivery [2]. Doxorubicin (DOX) as a dangerous chemotherapy drug can generate harms for patients bodies. Our results shown DOX disturbing hemoglobin functional species to methemoglobin as a radical source [3]. In this study,the generation reactive oxygen species (ROS) [3] by Doxorubicin against hemoglobin was controlled by A520 as MOFs in physiological pH 7.4 and investigated by biophysical methods such as UV/Vis spectroscopy, circular dichroism (CD), fluorescence and FESEM. The main achievements of this work shown oxyHb outreached by DOX loaded on A520 as a compatible process.

Keywords: Hemoglobin, A520 (MOFs), Reactive oxygen species, Doxorubicin, oxyHb

The role of different ratios of copper ion on the αB-crystallin aggregation in NaCl environment: cataracts lens

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ABSTRACT

The αB-crystallin is a member of the small heat shock protein family (sHSP) with chaperone ability and structural properties, which plays a protective role in the eye lens and other tissues. Copper is an essential divalent ion in the eye's lens, while the concentration of this ion increases in the case of a cataractous lens. Also, due to ageing and destruction of the sodium-potassium pump, the concentration balance of Na/K ions will be disrupted. As a result, the concentration of sodium in the cell becomes dominant. The interaction of αB-crystallin and copper ion in the presence of 100 mM NaCl have illustrated the increased chaperone activity of the sHSP on the other proteins aggregation. The current report investigates the kinetic of αB-crystallin thermal aggregation incubated for 96 hours at 37 °C in the presence of Cu^{2+} at various ratios to αB-crystallin in 100 mM NaCl at 59°C via spectroscopic study. The results indicate that the ratio of 1:1 has no effect on the lag time but decreases the plateau height. The ratio 10:1 induced aggregation of αB-crystallin at 37 °C, but a change in the temperature plays different characterizations such as of aggregation, precipitation, size inclusion, lag time and plateau deformation. Therefore, NaCl plays a prominent role in the αB-crystallin structure to face more copper ions on aggregation, prolonging the cataract process.

Keywords: αB-crystallin, Aggregation, Copper ion, NaCl environment, Cataractous lens

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Inhibitory Effect of ChCl-Asb Natural Deep Eutectic Solvent on Amyloid Fibrillation of Insulin

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ABSTRACT

Amyloids are fibrillar protein states that are famous characteristics of neurodegenerative disorders including Alzheimer's and Parkinson's diseases. Investigations have shown that each amyloid proteins assemble into specific toxic properties and morphologies. In this report we investigate the inhibitory effect of a natural deep eutectic solvent (DES) based on ascorbic acid and choline chloride. Deep eutectic solvents are a new class of ionic liquids (ILs) analogues because they show many properties of ILs. The behavior of the DES on insulin fibrils was investigated by using ThT fluorescence, confocal and intrinsic flourescence spectroscopy as well as circular dichroism spectropolarimetry (CD). The results showed that the native structure of insulin was maitained in the presence of cholinium chloride ascorbic acid (ChCl-Asb). The ChCl-Asb was added from the first step to the monomer state in fibrillation process and also have assayed the retrieval behaviour of mature fibrils to monomer state. Circular dichroism and flourescence spectroscopies measurements showed that secondary and tertiary structure of insulin maintain until the end of reaction in the presence of ChCl-Asb respectively. It can be concluded that natural deep eutectic solvents as a green ionic liquids can be coined as an antifibril reagent for insulin and may have applications to remediate neurodegenerative diseases.

Keywords: Deep eutectic solvent, Green solvent, Amyloid, Ionic liquids, Insulin, Inhibition

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Leucine conjugated SPIONs inhibit mTTR aggregation by impacting the unfolding mechanism

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ABSTRACT

Transthyretin (TTR) is a homo-tetramer protein that transports thyroxin and retinol in plasma.

Mutant or wild-type misfolded TTR are capable of aggregation both in vitro and in vivo, when this happens in the body, partial or systemic amyloidosis (ATTR) may emerge among patients. The significance of the monomer activation for triggering the aggregation and/or fibrillation of TTR has been emphasized previously. Inhibition of both pathways in the presence of amino acid conjugated superparamagnetic iron oxide nanoparticles (SPIONs) has been successful as well. A variety of biophysical assays were executed to monitor the unfolding of a mutant TTR named monomer TTR (mTTR) which is incapable of association into a tetramer. SPIONs were synthesized by a chemical co-precipitation method followed by conjugating with amino acids via an epoxy silane ([3-(2,3-epoxypropoxy) propyl] trimethoxysilane) linker. The findings suggest that the unfolding of mTTR follows a two- state mechanism which is conducted by a cooperative behavior in the absence of the amino acid conjugated SPIONs. On the other hand, in the presence of a synthesized hydrophobic SPION conjugated with leucine, the unfolding of mTTR differentiates from a two-state system and also the cooperativity decreases significantly, while in the presence of a synthesized hydrophilic SPION conjugated with glutamine, mTTR unfolding doesn't change and only a reduction in the amplitude of conformational changes was observed.

These findings support the idea that hydrophobic surfaces of the NPs maintain the protein's native structure and halt conformational alterations needed to trigger protein aggregation, so these NPs have the potential to be introduced as artificial chaperones.

Keywords: Transthyretin, Protein aggregation, hydrophobicity, SPIONs

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Green tea polyphenols-based nanoparticles inhibit amyloid fibril assembly and cytotoxicity of human insulin

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ABSTRACT

Among several types of molecules with the capacity to modulate amyloid fibrillation process of amyloidogenic peptides/proteins, naturally occurring small molecules, and especially certain natural polyphenols, have attracted a lot of attention. However, poor water solubility and low bioavailability of these compounds have considerably restricted their biological and medicinal applications, leading to attempts to overcome these limitations. Protein samples were incubated with increasing concentrations of bulk or nanoparticles of GTPs followed by incubation under amyloidogenic conditions. The AFM images revealed spherical morphology with an average diameter of 10 to 20 nm of GTPs nanoparticles. It can conclude that GTPs, in either bulk and nano forms, can modulate human insulin fibrillation process dose-dependently, where nano form was found much more effective. Our results suggested that prolongation of the nucleation phase through interaction with and stabilizing monomeric species, and redirecting human insulin aggregation towards oligomeric species is the mechanism of action of green tea polyphenols-based nanoparticles.

***Keywords*:** Green tea polyphenols, Nanoparticle, Human insulin, Amyloid

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Activation Mechanism of Human Carbonic Anhydrase Enzyme: Theoretical Investigation

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ABSTRACT

Proteins, in general, and enzymes, in particular, play an important role in chemical and biological processes. Carbonic anhydrases (CAs) are metalloenzymes, that catalyze CO_2 hydration to bicarbonate and protons. CA enzyme has both inactive and active forms. The inactive form of the enzyme reacts with the activators, unlike the active form that reacts with the inhibitors. So far, more research has focused on inhibitation mechanism and their mechanisms are known, while less involved in the field of activation mechanism. Amins, amino acids and their derivatives act as suitable activators for many isoforms of the human carbonic anhydrase (hCA). The activation mechanism of hCA has been investigated using quantum mechanical calculations. The hybrids calculations were carried out by applying the ONIOM model. The DFT and semiempirical PM6 methods have been employed to calculate in detail the electronic structure and electronic energy of different compounds and complexes throughout the reaction pathway in QM and QM' layers, respectively. Thermodynamic functions for all of the reactions and for the complexations between activator and hCA were evaluated. The calculated results indicated that protonable moiety of activator participate in proton transfer from zinc-bound water molecule and lead to formation of the catalytically active species of CA enzyme, hydroxide coordinated to the zinc ion.

Keywords: Carbonic Anhydrase, Mechanism, Thermodynamic functions

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Electrochemical DNA Nano-biosensor Based on MXene Quantum Dot@AuNPs Nanocomposite for Detection of HTLV-1 by Methylene blue

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ABSTRACT

The *human T-lymphotropic virus type 1* (*HTLV-1*) causes Adult T-cell Leukemia/Lymphoma (ATL). At least 5–10 million individuals globally are infected with *HTLV-1*. Mother-to-child, sexual transmission, tainted blood products are the main routes of *HTLV-1* transmission. Thus, the early detection of suspect individuals should be the cornerstone of efforts to combat the spread of *HTLV-1*. PCR is the most used diagnostic methods today, it has several limitations, such as being time- and money-consuming. In this study, a rapid electrochemical test with labeling is created as a solution. The MXene Quantum Dot@AuNPs were synthesized to modify the surface of glassy carbon electrodes as an amplifier for electrochemical signal and surface enhancement, allowing for the identification of the *Tax* gene region over the course of 30 minutes. In order to hybridize with the methylene blue-labeled specific RNA complementary target, the synthesized nanocomposite MXene Quantum Dot@AuNPs and Probe DNA were fixed to the surface of the glassy carbon electrode. This oxidation agent intercalates into the DNA double helix as an electrochemical indicator, greatly enhancing the electrochemical signal. As a result, using the differential pulse voltammetry (DPV) approach. the calibration curve was examined by the reduction of MB with varied quantities of target RNA ranging from 1 femtomolar to 100 nanomolar, increasing with at least a detection limit of 1.01 fM, a positive slope, and a correlation coefficient of 0.9716. The findings indicated that this biosensor might be utilized to implement a rapid, precise, and economical *HTLV-1* test in order to early detection of virus.

Keywords: Electrochemical biosensor, Methylene blue, *HTLV-1*, MXene Quantum Dot@AuNPs, DPV measurements

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Investigation and Characterization of Bortezomib - Loaded Albumin Nanoparticles as Nanocarrier

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ABSTRACT

Multiple Myeloma (M.M) is a type of hematologic cancers and its first symptoms are pathologic fractures, hypercalcemia and renal failture. Bortezomib (Velcade) is a proteasome inhibitor drug that results in effects such as disruption of the cell cycle and induction of appoptosis. Treatment of M.M. by bortezomib has some side effects such as digestive disorders and peripheral neuropathy. To prevent of these problems, we can use Human Serum Albumin (HSA) as nanocarrier to deliver bortezomib to target tissues. Encapsulation of bortezomib-loaded HSA nanoparticles is done by NAB technology (No need to surfactant or cross-linker). After mixing aqueous phase (albumin solution) and organic phase (drug solution), high pressure homogenization forms final stable nanoemulsion. Then rotary evaporation of organic solvent, results in forming drug-loaded albumin nanoparticles. Analysis of binding of drug to albumin is done by flourescence spectroscopy. (Excitation in wavelength: 340-360 nm and Emission in wavelength: 450-460 nm). The shift observed in flourescence (decrease of emission in wavelength: 453 nm), showed binding between albumin and drug that results in decrease of flourescence intensity. HSA can be a suitable nanocarrier to bind to bortezomib and deliver it to target tissue. In primary levels of work, we found that binding of drug to albumin, has done successfully.

***Keywords*:** Albumin, nanoparticle, bortezomib, nanocarrier, drug delivery

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Investigation on Caspase 3 and Caspase 7 Enzymes Activities and RNA Level in Blood Anuclear Cells (RBC) under Osmotic Stress

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ABSTRACT

Caspase 3 and caspase 7 play important roles in apoptosis and are related to each other. While it is clear that most nucleated cells are capable of caspase dependent to apoptosis, the roles of apoptosis regulatory molecules in anucleated cells and their possible functions are almost unknown. In the present study, to measure the activities of caspase 3 and 7 enzymes, mature RBCs lacking any nuclei were subjected to osmotic stress under hypertonic and Isotonic condition. Both of them were incubated at 37°C for 24 hours. After lysis of RBCs samples using ultrasound waves, hemolysates of test and control cells were prepared and used to measure the caspase 3 and caspase 7 enzymes activities using colorimetric method. And total RNA was extracted as well. The quality and quantity of the extracted RNAs were evaluated by NanoDrop2000c spectrophotometer (Thermo Fisher).The results showed the presence of caspase 3 and 7 and enzymes activities in RBCs in spite of they lose their nuclei in the mature stage. total RNA increased in hypertonic stress as well. The RBCs do not have any nuclei and genomic DNA, probably contain pre-mRNA encoding the caspase 3 and caspase 7 enzymes expressions.

Keywords: RBC, Caspase , Osmotic Strees , RNA

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An In-silico Insight to Investigate the Self-aggregation of Natural Anticancer Drugs in Rational Drug Design

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ABSTRACT

More recently, some effective and known natural chemotherapeutic drugs against a wide range of cancers, including colorectal, breast, ovarian, lung, etc, had been introduced. Of these, paclitaxel (PX) and curcumin (CUR) are potentially active against a broad range of cancers and stabilize microtubules and inhibit late G2 or M phases of cell cycle, so they induce cell death by DNA fragmentation. PX molecules small size, enhancing their aqueous solubility and for efficient and better chemotherapy by PX they had been reported to be merged with another compound. Moreover, CUR has shown to be safe with no significant side effects compared to other anticancer drugs. Here, we had investigated the in-silico studies to show that how the mixture of CUR and PX together would enhance the anticancer effects and lower the usage doses of each one. Herein, the self-aggregation and molecular properties of interaction of two potential natural anticancer drugs PX and CUR in the water (WT) system was reported by employing the classical molecular dynamics method. All simulations were performed using GPU-enabled version of NAMD-2.12 package with the CHARMM-36 force field. We had studied three systems of CUR- WT, PX- WT and mixture of PX and CUR in the water for a 50 ns simulation time. Mixed solution containing PX and CUR have been investigated by self-diffusion of the molecules, with particular emphasis on their center of masses mean square displacement. In the mixture the CUR represented more diffusive regime than PX which indicated PX superior aggregation. The structural parameters, root mean square deviation of considered natural drugs showed no deformation. The energetic analysis indicated the self-aggregation of PX molecules alone and in the complex with CUR had been occurred efficiently. The collected data support that the considered natural drugs facilitate their aggregation in the water system. Overall, the current study may be applicable in the fundamental science of the biophysical chemistry of multiple natural drugs with no resistance in the presence of each other, as well as in the drug designing systems.

***Keywords*:** Natural anti-cancers, Competitive aggregation, Drug design, Molecular dynamics.

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Investigating the Structural Features of UiO-66 Metal-Organic Framework for Curcumin Delivery

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ABSTRACT

Metal-organic frameworks (MOFs) are among the most popular and widely used drug carriers. Although MOFs are good candidates for drug delivery, optimizing the synthesis conditions according to performance is one of the essential characteristics of expanding the use of these (nano)materials in the biomedical field. UiO-66 has been one of the most used MOFs in recent years, and many applications of UiO-66 have been reported. Modulators are one of the synthetic variables of UiO-66, which create differences in material morphology, crystallinity, porosity, and particle size. In this work, UiO-66 and UiO-NH_2, with and without modulators were synthesized. X-ray diffraction (XRD) patterns and Field Emission Scanning Electron Microscope (FESEM) images showed the successful synthesis of materials. Examining the presence of NH_2 functional group and structural differences for each sample and the performance of these variables are interesting. For each substrate separately, the drug loading amount was measured for 12 hours in a dark room with a curcumin concentration of 0.5 mg/mL and a MOF concentration of 2 mg/mL in ethanol solution. The results showed that the best loading rate with 37.6% is related to UiO-66-NH_2 synthesis without a modulator. A cytotoxicity test was performed on the MCF-7 cell line considering the same conditions. The lowest level of cytotoxicity related to UiO-66 without a modulator with the highest cell viability was selected (64.4% for 1 mg/mL). The results showed the difference in the performance of nanocarriers due to the change in morphology, porosity, and crystallinity percentage. These characteristics with the presence of the NH_2 group and without it indicate the difference in van der Waals interactions between the drug and the nanocarrier. Also, the difference in the cytotoxicity level is based on the concentration of the (nano)materials and the way the nanocarrier interacts with the cell. This study shows to what extent the presence of the NH_2 group is effective in drug absorption and cytotoxicity with structural features caused by the presence and absence of modulator in the synthesis conditions.

Keywords: MOFs, UiO-66, Curcumin, Drug delivery

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Structural and Functional Characterization of a Myopathy-Associated Mutation in Human αB-crystallin

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ABSTRACT

Crystallins are the most abundant proteins in the vertebrate eye lens which belong to the family of small heat shock proteins (hsps). Among the different crystallins, α-crystallin which includes two subunits αA and αB, has chaperone activity. This guardian protein of eye lenses has important ability for the specific interaction with denatured/unfolded proteins and in this way prevents their accumulation during various stresses. Since αB-crystallin, additional to the lenticular tissue, is expressed in other tissues, mutations in this protein are related to not only cataract disorder but also to the other pathological states including Parkinson's, Alzheimer's and cardiomyopathy. In this study, a genetic mutation, occurring in the α-crystallin domain (ACD) of human αB-crystallin which related to the myopathy development, was created by site directed mutagenesis. The mutant protein was purified by an ion exchange chromatography in high purity. Different spectroscopic methods were applied to investigate the detailed structure of the mutant protein. We indicated that the mutant protein has a different structure and folding compared to the wild-type protein counterpart. The results of our investigations also suggest that this mutation causes an important change in the chaperone activity of human αB-crystallin. Overall, the structural and functional changes in human αB-crystallin as occurred by this mutation can be attributed to its pathogenicity in the myopathy disease.

Keywords: Small heat-shock proteins (hsps), Human αB-crystallin, Chaperone, Mutation, Myopathy disease.

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Improving the Production and Stability of M-MLV Reverse Transcriptase

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ABSTRACT

Retroviruses insert themselves into the host cells with the help of the reverse transcriptase, RTase, encoded by the *pol* gene. This enzyme possesses two activities; DNA polymerase and ribonuclease. Various methods have been exploited in order to improve its production and purification efficiency as well as thermal stability, which include the removal of structural domains, creation of point mutations, deletions, substitutions, and chemical modifications. In addition to its importance in various diseases, RTases are used for research purposes such as cDNA synthesis, creating genetic libraries, and diagnostic tests based on real-time PCR. In this research, we optimized the production of Molony Murine Reverse Transcriptase in *E.coli* BL21(DE3) bacteria. About 13 mg protein was isolated from one liter of culture with greater than 95% purity using just a single step. Due to its importance in various applications, the stability of enzyme was studied in the presence of glycerol and Triton X-100 as stabilizing agents by difference UV-Visible spectroscopy. This study found that the protein had a melting temperature of 42°C, and the addition of glycerol could increase its stability by 20°C. Inclusion of glycerol and Triton X-100 lead to the stabilization of the enzyme through the prevention of aggregation by forming micelles and preventing intermolecular interactions, respectively.

Keywords: Moloney Murine Leukemia Virus, Enzyme, cDNA synthesis, Spectroscopy, Temperature

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Predictive Modelling of Interfacial Tension between Aqueous Phase Containing Zein Composite Particles and Oil Using Artificial Neural Network Methods

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ABSTRACT

Measuring the accurate value of interfacial tension (IFT) is an important subject in science and industry for emulsions. Since measuring IFT requires expensive and accurate equipment, models for estimating IFT can help to save time and costs. The aim of this work was to use artificial neural network (ANN) to predict IFT between an oil phase (canola oil) and an aqueous phase containing zein or zein/Persian gum particles. The proposed ANN model was trained and tested using a set of input (pH, total concentration, and mixing ratio during ≈8000 s) and output (IFT) data generated from a drop shape analyzer instrument. In this study, feed forward and time delay neural networks were employed in order to model IFT. The architecture of the ANN model was examined by increasing the number of neurons in the hidden layers of each network to obtain the best model for predicting IFT with the least squares of error. Different ANN architecture model have been constructed to examine the prediction accuracy of the models. The results of the ANN models were consistent with the experimental data ($R2 > 0.99$). The overall score of time delay networks is found to be higher than feed forward model with 57 neurons in the hidden layer. For this model, RMSE value of components is 0.0796. This research provides a fast and effective method to predict IFT using time delay neural network with high accuracy.

Keywords: Atrificial neural network; Interfacial tension; Modeling; Zein; Persian gum

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Spectroscopic Analysis and Molecular Modeling on the Interaction of Naphthalene-Based Schiff Base with Human Serum Albumin (HSA)

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ABSTRACT

Studies on supramolecular interactions of drugs or organic compounds with biological macromolecules have significantly contributed to the understanding of the structures and functions of bio-macromolecules and some biophysical processes. By binding to human serum albumin (HSA), most drugs circulate in plasma and reach the target tissues and their distribution is mainly controlled by HSA. Hence, drug binding to proteins has becomes an important determinant of pharmacokinetics, e.g. prolonging in vivo half-life, restricting the unbound concentration and affecting distribution and elimination of the drug. HSA is the most abundant protein in human blood plasma and has high affinity to many endogenous and exogenous compounds, serving as a solubilizer and transporter for drugs and other organic molecules to their targets. In this study, new Schiff-base {N,N′-Bis(2-hydroxy-3-methoxy-benzylidene)-naphthalene-1,5-diamine (NSL), has been synthesized by the reaction of 1,5-naphthalenediamine (p-ND) with the 2-hydroxy-3-methoxybenzaldehyde and characterized by UV–Vis, FT-IR, ^{1}H-NMR, and mass spectroscopy. Interaction between Naphthalene-based Schiff base (NSL) with HSA was studied by means of fluorescence spectroscopy and circular dichroism. The intrinsic fluorescence of HSA was quenched by NSL, which was rationalized in terms of the static quenching mechanism. The results show that NSL compound can obviously bind to HSA molecules. According to fluorescence quenching calculations, the bimolecular quenching constant (K_q), apparent quenching constant (K_{SV}) at 27 °C was obtained. The binding constants, K, is 23.5 L.mol^{-1} and the number of binding sites (n) is 1. Also, molecular docking results suggested that the binding site of NSL was site IA of HSA.

***Keywords*:** HSA, DFT, Molecular Docking, Schiff base, Circular Dichroism

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Dual Effects of Oxidation on the Structure and Chaperone Activity of Human αB-Crystallin

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ABSTRACT

The eye lens has a high density of crystallin proteins which are necessary for its high refractive power. In addition to its structural role in the lenticular tissue, α-crystallin (αA- and αB subunits) with its chaperone activity plays a vital role in suppressing the aggregation of the damaged proteins which are mostly produced by post-translational modifications (PTMs) including oxidation. Peroxynitrite (PON) and hydrogen peroxide (H_2O_2) are two cataractogenic and highly potent oxidative agents that their formation has been indicated to increase under pathological conditions such as diabetes mellitus (DM) and inflammation. It has been also indicated that peroxynitrite has a biphasic effect so it has a physiological role in the low concentrations and pathological consequences at the high levels. We investigated the structure and function of human recombinant αB-crystallin under both partial and extensive oxidation by the above mentioned oxidative agents using electrophoresis and various spectroscopic methods. The partially oxidized form of human αB-crystallin with a slight structural alteration indicated a reduction in the oligomeric size distribution and the enhancement of its chaperone activity. In the presence of a high level of these oxidizing compounds along with profound structural changes, the chaperone activity of this protein was also significantly reduced. Overall, the enhancement of chaperone activity in human αB-crystallin during incomplete oxidation may be a natural defense mechanism to overcome the damages caused by oxidative stress, especially in diabetes and other pathological diseases.

Keywords: Human αB-crystallin, Oxidative stress, Chaperone activity, Structural change, Defense mechanism.

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The Structural and Functional Changes in a Cardiomyopathy-Associated Mutant αB-Crystallin

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ABSTRACT

Crystallin proteins (α, β, and γ) with a high concentration and stability in the eye lens play an important role in the transparency of the lenticular tissue. α-crystallin chaperone (αA and αB) directly plays a prominent role in maintaining the transparency of this tissue by preventing the deposition and accumulation of improperly folded proteins. While αA-crystallin is mainly limited to the eye lens, αB-crystallin is also found in many other tissues. The correct interaction of αB-crystallin with the intermediate filaments, especially desmin protein, plays an important role in preventing myopathy. In the current study, an arginine residue was substituted with tryptophan in the α-crystallin domain (ACD) of human αB-crystallin using site-directed mutagenesis. Genetic studies have previously confirmed that this mutation is associated with myopathy. After proper expression of the mutant protein in its bacterial host, it was purified well by ion exchange chromatography. The structural analyses of the mutant protein as performed by CD, Raman, fluorescence, FTIR, and DLS techniques. This mutation causes important structural changes in the human αB-crystallin protein. Also, the results of our study showed a larger oligomer size of mutant protein which causes less chaperone activity compared to the wild-type counterpart due to the inverse relationship between the oligomer size and chaperone activity. The results of this research suggest that the pathogenic relationship of this mutation with myopathy development can be explained by the fundamental changes in structure and chaperone activity of the mutant αB-crystallin.

Keywords: αB-crystallin, Chaperon activity, Structure, Mutation, Cardiomyopathy.

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Biophysical Analyses of a Cataract Causing Arginine-Based Missense Mutation in Human αB-crystallin.

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ABSTRACT

Cataract disease, as the main cause of blindness in the world, is the result of unfolding and aggregation of at least three groups of crystallin proteins (α, β, and γ) in the eye lenses. Human αB-crystallin or small heat shock protein B5 (HSPB5) is a ubiquitous protein found not only in the eye lenses but also in the other tissues such as the heart, muscle, and brain. Consequently, the occurrence of genetic mutations in HSPB5 can cause deleterious effects in many tissues. Previous studies have shown that there are a number of mutations in which an arginine residue is substituted in the primary structure of human α-crystallin (αA and αB subunits) by other amino acid residues, and this replacement can lead to the development of cataract and myopathy, or both. In the current study, we investigated the structure and function of HSPB5 after a missense mutation at the specific arginine residue contributing to the cataract disease. We utilized different spectroscopic techniques to probe the structural alteration and to assess the chaperone activity of the mutant protein. Structural studies suggested that the mutation in the arginine residue could alter the secondary and tertiary structures of the recombinant protein. Oligomerization study with dynamic light scattering (DLS) revealed a different quaternary structure for the mutant protein. Also, the mutant protein indicated different stability and chaperone activity compared to the wild-type protein. In conclusion, our results proposed that Arginine-based pathogenic mutation, which is associated with cataract development, can significantly alter the structure, stability and chaperone function of HSPB5.

Keywords Human αB-crystallin (HSPB5), Missense mutation, Chaperone activity, Cataract, Structural alteration.

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Induction of Tau Protein Aggregation by Formaldehyde and Its Inhibition By B-D Mannuronic Acid/BDM (M2000): Introducing A Potential Drug Candidate for The Use in Treatment Regimen of Alzheimer's Disease

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ABSTRACT

The β-D-mannuronic acid/BDM (M2000) as a homopolymer of Alginate has antioxidant activity and other beneficial properties which have been examined in different age-related disease models including Alzheimer's disease. Hyperphosphorylation and subsequent aggregation of tau protein as neurofibrillary tangles (NFTs) is one of the typical pathological characteristics in those who have memory loss. It has been reported that formaldehyde induces hyperphosphorylation and polymerization of Alzheimer's disease associated protein both *in vitro* and *in vivo*. Meanwhile, excessive formaldehyde level is related to aging, leading to toxic damage involving reactive oxygen species (ROS) and inflammatory responses, which may increase the risk of spatial memory deficits. This study was performed with the aim to assess the impact of BDM on formaldehyde-induced tau protein aggregation using SDS-PAGE, fluorimeter, fluorescence microscopy (FM), and transmission electron microscopy (TEM). The formaldehyde increases the formation of β-sheet structure in tau protein, leading to the amyloid structure formation. Also, the formaldehyde-induced tau protein aggregation was partially and fully inhibited after treatment with 2 and 20 μM BDM, respectively. According to our results, BDM showed a dose-dependent inhibitory effect on the tau protein fibril formation. Probably, the antioxidant feature of this compound plays an important role in neutralizing the process of induction of tau protein aggregation by formaldehyde. Therefore, BDM can be considered as a potential therapeutic agent in the treatment regimen of Alzheimer's disease.

Keywords: Tau protein, Formaldehyde, Amyloid fibril, β-D-mannuronic acid/ BDM (M2000), Alzheimer's disease.

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Application of Incretin Therapeutic Peptides in the Management of Type 2 Diabetes; a New Production Strategy and Introduction of Two Potential Incretins.

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ABSTRACT

Currently, the rapidly growing disease of diabetes mellitus (DM) is one of the most important global challenges. Therefore, different strategies are used to treat this metabolic disorder, one of which is the application of incretin peptide medicines. Research shows that more than fifty percent of the insulin secreted from the pancreas is due to the action of the incretin peptide hormones of intestinal origin (GLP1 & GIP), and what is called the incretin effect is severely impaired in type 2 DM. Natural incretins have a very short half-life due to the enzymatic digestion or relatively fast renal excretion. Pharmaceutical analogues of incretins that are produced based on GLP-1 or Exendin-4 have a relatively high half-life, which increases their biological performance. Today, incretins have become an essential part of the treatment regimen for type 2 DM and obesity. In the present study, the gene constructs of two drugs, liraglutide and an exenatide analogue, were designed as hybrids with human αB-crystallin for expression in the bacterial host system. After purification of the hybrid proteins, the therapeutic peptides were separated from the carrier protein by a specific chemical cleavage method, then the therapeutic peptides were purified by gel filtration chromatography and the exact peptide masses were determined by mass spectroscopy. Structural studies suggested that α-helix and β-sheet are dominant in the therapeutic peptides and in the hybrid proteins, respectively. Subcutaneous injection of the therapeutic peptides and their corresponding hybrid proteins not only reduced the blood sugar level in the healthy and diabetic mice but also stimulated effective insulin secretion from the pancreas of healthy mice. Therefore, the hybrid proteins can be a better substitution, especially for liraglutide in the treatment regimen of diabetic patients, where the non-enzymatic glycation of albumin disrupts the binding of this drug to the carrier protein. The results of this research not only suggest a new strategy for the production of therapeutic incretin peptides but also introduce two novel potential incretin drugs with the ability to act in a more extended period of time, which are likely to be useful in the treatment of diabetic patients.

Keywords: Diabetes mellitus (DM), Liraglutide, Bacterial expression, Structural analyses, Bioactivity assessment.

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Gold nanorod etching as a signaling process for development of ultrasensitive biosensors

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ABSTRACT

Etching is a chemical process that changes the optical properties of metallic nanoparticles by oxidizing their constituent atoms. As a common example, gold nanorods (AuNRs), when etched into small nanoparticles, are appeared as a powerful tool in the development of numerous biosensors due to the unique optical properties resulted from the excitation of **localized surface plasmon resonance (**LSPR). The etching of AuNRs leads to a decreased AuNRs aspect ratio and the blue-shifted longitudinal LSPR band. Etching of the AuNRs makes it feasible to fabricate a sensor with satisfactory characteristics such as selectivity, sensitivity, detection limits, and response time. **LSPR is an optical phenomenon produced by a light beam impact on** the conductive nanoparticles smaller than the light wavelength. LSPR is the consequence of an incident light interaction with the superficial free electrons at the conduction band. Generally, LSPR as a label-free sensing technique exhibits a superior sensitivity **depending on** the size, shape, and structure of the conductive nanoparticles. So far two types of biosensors were developed in the Laboratory of Bioanalysis, Institute of Biochemistry & Biophysics, University of Tehran based on the etching of AuNRs: The blue shift of AuNRs longitudinal plasmonic peak, resulted during etching process, was reported as an optical signal for two independent sensing systems: i) A genosensor for detection of H. pylori at aM level. B) An immunosensor for monitoring prostate specific antigen at pM level.

Keywords: Gold nanorods, Etching, Localized surface plasmon resonance, Biosensor

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Thymoquinone prevents protein glycoxidation and aggregation formation: A biophysical aspect

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ABSTRACT

Thymoquinone (TQ) is a naturally occurring substance with antioxidant, anti-inflammatory, antiproliferative, and proapoptotic properties. In this study, TQ's physiological interactions and binding characteristics with proteins like Bovine Serum Albumin (BSA) and Hemoglobin (Hb) have been studied. The binding interactions of the TQ, with BSA/Hb, were investigated by computer simulation. The protein's secondary structure was examined using circular dichroism (CD). The non-enzymatic glycation process was analyzed with parameters like browning, fructosamine content, carbonyl content, individual advanced glycated end products (AGEs) content, and total AGE spectroscopically. The glycation-induced aggregates of amyloid β-structure were assessed with congo red and Thioflavin T. Also, the degree of glycoxidative DNA damage was assessed using agarose gel electrophoresis. The results indicate that the TQ provided a high physiological binding constant (Kb =1.364 x 104 M-1) at 25ºC with bovine serum albumin (BSA) as compared to hemoglobin (Hb). The dynamic interaction was observed to be spontaneous with negative Gibb's energy. The secondary structure of BSA was preserved while glycation-induced thermal aggregation was inhibited. The computational analysis determined that the binding between BSA/Hb and TQ occurred through van der Waals forces, hydrogen bonds, and hydrophobic interactions with significant steric stability. Our research shows that the interaction of glucose at the glycation site is disrupted by the interaction of TQ with BSA/Hb. To examine the structural perturbation mechanism of BSA/Hb at various time intervals in the absence/presence of TQ, we carried out a time-based (28 days) in-vitro glycoxidation investigation at 37 °C. In the absence of TQ, extended glycoxidation results in the development of amyloid, but in its presence, the process is inhibited. Our study investigated and characterized the protein states that have undergone glycoxidation alteration. Our results suggested that TQ may influence how glucose interacts with BSA/Hb, preventing glycoxidation and the formation of aggregations, establishing TQ as a potential therapeutic agent.

Keywords: Aggregation, Hemoglobin, Glucose, Glycoxidation, Thymoquinone

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Reconstruction and Application of Genome-scale and Context-specific Metabolic Models

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ABSTRACT

Metabolism as a collection of interconnected chemical reactions within a cell is one of the most important aspects of our molecular analysis of biological systems. Also our detailed knowledge about metabolism is more comprehensive and more accurate in comparison with other biological networks. Accordingly, application of systems biology in analysis of metabolic networks provides results that are more meaningful and more predictive. This goal is achieved in a pipeline that starts with reconstruction of a genome-scale model (GSM). A GSM, as a knowledge base, accumulates all related genomic, biochemical and physico-chemical information. Step by step protocols for bottom-up reconstruction of GSMs from raw data have been suggested[1]. Omics data gathered from a specific condition, tissue or cell type can be used to convert a GSM to a context-specific model (CSM) that is expected to be a realistic representation of metabolism in that context. These models then can be used to predict biological capabilities and phenotypes via a set of mathematical methods reffered as constraint-based modelling. As an alternative to bottom-up reconstruction approach, the orthology-based strategy uses a previously reconstructed model of a reference organism to infer a GSM of a target organism. As an example of this approach, the iMM1865, one of the recently reconstructed GSMs for *Mus musculus*, will be presented here. This GSM is based on the last version of the human metabolic network and is validated against a lot of functionality tests and experimentally derived gene essentiality data. Tissue-specific embryo heart models were also reconstructed from this GSM to fascilitate the validation procedure[3]. As an example of application of CSMs in analysis of biological capabilities and phenotypes, a brief reviwe of a recenet work is also provided that uses CSMs to assess the triple negative breast cancer primary and metastatic tumors[4]. Our knowledge about the extent of metabolic reprogramming in the course of metastasis and adaptation of cancer cells to their new microenvironments could be important in development of new therapeutic strategies.

Keywords: Systems Biology, Metabolic Network Reconstruction, Genome-scale Models

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Targeted anticancer drug delivery system based on hyaluronidase enzyme immobilized on polyamidoamine dendrimer: An efficient nonovehicle for diffusion into tumors

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ABSTRACT

The condensed extracellular matrix (ECM) surrounding cancer cells results in the formation of a biophysical barrier versus chemotherapeutic drug penetration into deeper regions of many solid malignancies. To cope with this drawback, the present perspective inquired the therapeutic potential of a hyaluronidase (Hyal)-modified hyper-branched poly (amide amine) (PAMAM) loaded with anticancer drug methotrexate (MTX) to improve breast cancer chemo-resistance through reducing the hyaluronic acid accumulation as a major component of tumor ECM. The MTX-loaded into carboxylate PAMAM/Hyal/PEG (PAMAM-MTX/SA/Hyal/PEG) via different techniques. The decoration of as-prepared pH-responsive nano-platform with a relatively low-density layer of polyethylene glycol (PEG) improved its stability and performance. These processes were characterized by Fourier transform infrared (FTIR), transmission electron microscopy (TEM), surface potential, dynamic light scattering (DLS), and enzymatic activity assessment. The blood compatibility as well as cytotoxicity of various nano-formulations was evaluated using an MTS-based assay on MCF-7 and MCF-10A cell lines. Despite of short half-life of pristine hyaluronidase, the enzymatic studies revealed that the Hyal-based platforms displayed enhanced enzyme stability, especially against protease degradation, and prolonged half-life after incubating in human plasma. The MTX-loaded into carboxylate PAMAM/Hyal/PEG (PAMAM-MTX/SA/Hyal/PEG) exhibited a high MTX loading capacity as well as outstanding ability for controlled release of MTX. The results of hemolysis assay confirmed the good blood safety of prepared nanoplatforms. The cytotoxicity of various nano-formulations using an MTS-based assay on MCF-7 and MCF-10A cell lines revealed that PAMAM-MTX/SA/Hyal/PEG was more efficient against the tumor cells than the free MTX over 72h treatment. Besides, the effect of PAMAM-MTX/SA/Hyal/PEG against MCF-7 cells showed noteworthy induction of apoptosis. Furthermore, PAMAM-MTX/SA/Hyal/PEG nanosystem facilitate further significant uptake by MCF-7 cells and penetration in MCF-7 3D tumor spheroids than free MTX, thus indicating much better anticancer efficiency *in vitro* and adjuvant effect of Hyal-based nanosystem. This outlook suggests novel type of multifunctional nano-platform to improve cancer therapy, by effective modulation of tumor microenvironment.

***Keywords*:** Hyaaluronidase, Methotrexate, Extracellular matrix, Hyaluronic acid, Drug resistance

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MicroRNA at RISC: a functional excitement An outlook on chemical biology of microRNA

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ABSTRACT

MicroRNA (miRNA), as a distinct class of biological regulators and a "guide" member of non-coding RNA-protein complexes (RNPs), regulates more than 60% of protein-coding genes expression through base-pairing with targeted messenger RNA (mRNA) in the RNA-Induced Silencing Complex (RISC). The primary determinant of miRNA recognition site and the efficiency of translation repression is the level of sequence complementarity in the corresponding binding site of the target mRNA.

In our recent work in collaboration with Dr. Petzold lab, published in *Nature*[1], we showed the crucial role of miRNA34a-mSirt1(silent information regulator1) structural dynamics in molecular recognition by the Argonaute RISC protein. $R_{1\rho}$ relaxation-dispersion nuclear magnetic resonance revealed a dynamic switch based on the rearrangement of a single base pair between miR-34a and its recognition site in the 3'UTR of Sirt1 that elongates a weak seven-base-pair seed in ground state(GS) to a complete eight-base-pair seed in transient excited state(ES). Using replica-exchange molecular dynamics simulations(REMD) [2], we derived the 3D conformational ensemble of GS and ES, which are differed in global inter-helical bend angle and adopt different binding mode in human Argonaute2 protein(hAgo2), showed by slow-growth simulation of miRNA-mRNA-Argonaute ternary complex. The proposed conformation of excited state captured using mutate-and-chemical-shift-fingerprint (MCSF) in favor of ES bending angle topology. The level of downregulation of variant mRNA targets in trapped excited showed a two-fold increase in RISC activity compared to ground state. The binding mode of this transient state in hAgo2 is reminiscent of an active state in prokaryotic Ago [3,4] confirms the robustness of the proposed model. Moreover, biophysical and in-cell functional results supported the proposed coordination of miRNA-mRNA in Ago, showing a significant increase in downregulation of five selected mRNA targets of miR-34a upon GS to ES transition. Therefore, suggesting this mechanism could be a widespread feature of many miRNA-target complexes with similar recognition sites. Using multidisciplinary chemical approach, we provided a model describing biological mechanism of miRNA silencing in RISC. Incessant interests in adapting RNA-guided nuclease machineries for biological applications, therapeutic, and diagnostic, advocate for more interdisciplinary investigations to exploit RNA conformational dynamics for designing better guide RNAs in favor of corresponding application.

Keywords: microRNA, Molecular dynamics simulations, RNA structural dynamics, RNA structure-function relationship

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How can molecular dynamics simulation methods boost drug design and drug discovery projects?

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ABSTRACT

Molecular dynamics (MD) simulation, a solution Newton motion equation for producing atomic trajectories, is one of the best methods for describing biomolecular motion. In this review, I intend to introduce the current advances in the MD field with a focus on recently published documents corresponding to our research group. Depending on the project aim and systems to be simulated, various methods were set up. The free energy of the β-catenin/LRH-1 complex as well as the contribution of the related residues to the binding energy was estimated using MM/PBSA computations. To find the potential pockets on FOXM1-DBD, MDpocket was used to detect and comprehensively analyze the pockets on the protein. To investigate the molecular basis for the membrane selectivity of Pleurocidin, the interaction of the peptide with the different membrane models was investigated by canonical MD (CMD) simulations methods. A steered molecular dynamics (SMD) approach was used to investigate the mechanism of arginine transportation through cationic amino acid transporter 1 (CAT-1). The SMD simulations illustrated that the hydrogen bonds between arginine and the CAT-1 residues are crucial for the transportation process and a network of hydrogen bonds forms and breaks during arginine transportation. Based on the MDpocket data, the helix3 and the N-terminal loop of FOXM1-DBD accommodated the pockets for the binding of this transcription factor to the related ligands. By MM/PBSA approach, an affinity binding model with sequence DXMXXPQQTE was constructed to design the related affinity peptide [3]. The CMD calculations showed that that the N-terminal region of Pleurocidin has a crucial role in the interactions of the peptide with the membrane models. Pleurocidin, due to the presence of the anionic lipids and the PC head groups, had more proper interactions with the DOPC/DOPG (3:1) membrane than with the other bilayers. The role of molecular dynamics simulation in molecular biology has undergone tremendous changes. In fact, the current role of MD simulations is far beyond confirming the experiments and it has shifted from a niche method mainly applicable to model systems into a cornerstone in molecular biology.

Keywords: Molecular dynamics, Pleurocidin, MM/PBSA, Arginine transportation

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Transition from quantity to quality in Iranian scientific publications

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ABSTRACT

With the expansion of graduate education courses in Iranian universities and the need to publish research results related to students' theses and dissertations, the number of articles in the country increased dramatically. According to the number of indexes recorded on the Web of Science of the Clarivate Analytics Institute of Scientific Information, in a total of three fields of science, social sciences and humanities and art, our scientists published 1812 and 52230 scientific documents in 2001 and 2021, respectively, which led to the improvement of Iran's ranking from 45 to 16. During these last two decades, quantitative approach in the first decade and qualitative approach in the second decade have been encouraged in scientific publications. The increase in the number of articles published by Iranian scientists in the world's top journals along with increasing the Iran's ranking in terms of citations compared to the number of scientific documents in many fields, as well as the overall, show the improvement of the quality of scientific publications. Here, Here, the competition of different fields in terms of the number of scientific documents and citations, along with their global ranking, based on data from the scientific database Scopus, is investigated.

***Keywords*:** Quantitative of scientific documents, Qualitative of scientific documents, Web of Science, *Clarivate Analytics*, Scopus

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NMR Probes of Dynamics in Protein Aggregation and Phase Separation

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Keywords: NMR, Amyloid-beta, Phase separation, Singlet-state, Quadrupolar NMR

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ABSTRACT

Biomolecular dynamics play a major role in physiological and disease-related processes such as protein aggregation and liquid-liquid phase separation. NMR spectroscopy is a powerful technique capable of reporting biomolecular dynamics at atomistic resolution and on a broad range of timescales from pico- to milli-seconds. In this talk, I will present recent research conducted in my group in connection with Alzheimer's disease-related amyloid-beta (Abeta) aggregation and biomolecular phase separation in a number of model systems. In relation with Abeta, I will introduce novel probes of peptide dynamics, including relaxation of glycine-based singlet-states and rotational dynamics of arginine side chains, and demonstrate how their application in combination with other experimental and computational probes enables accessing the hitherto inaccessible motional modes of Abeta. In relation with the phase separation, I will demonstrate how fluorine and quadrupolar NMR-based methods allow monitroing component exchange between different phases and water and ions dynamics in condensed phases.

Peptides Against Growth Factor Pathogenesis: Structural-Based Design and Theranostic Evaluations S.

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ABSTRACT

Growth factors play pivotal roles in the initiation and development of cancers. Metastatic tumors are responsible for ninety percent of cancer mortalities. Despite significant advances in the understanding of molecular and cellular mechanisms of tumor metastases, there are limitations in preventive treatment of metastatic tumors. Much evidences arising from laboratory and clinical studies suggest that growth factors and their receptors are implicated in cancer metastases development. Angiogenesis, the formation of new blood vessels from the pre-existing vasculature, is stimulated by different growth factors, and is a prerequisite for metastasis of tumor cells. The major angiogenic growth factor is vascular endothelial growth factor (VEGF). The biological function of VEGFs, including VEGFA-F and placenta growth factor (PlGF) is mediated by three structurally related receptor tyrosine kinases (RTKs), denoted VEGFR1 (FLT-1), VEGFR-2 (FLK-1 or KDR), and VEGFR-3 (FLT-4). Several small-molecule tyrosine kinase inhibitors (TKIs) and VEGF/VEGF receptors (VEGFRs) blocking antibodies and protein drugs are employed clinically to block pathological angiogenesis. In recent years, peptides emerged as attractive option for drug discovery and development. Their target specificity and potency, ease of synthesis, low toxicity, bioavailability, and the possibility of chemical modification render therapeutic peptides as new generation of therapeutics. Based on the complex structure between VEGFA, B and PlGF with VEGFR1 and VEGFA with VEGFR2, we have designed a series of VEGF antagonist peptides, whose interaction with VEGFR1 and VEGFR2 suppressed the downstream signaling of the growth factors in both endothelial and tumoral cells, and inhibited angiogenesis, tumor growth and metastasis. In addition, we have shown that the tumor targeting peptides may shed new lights on the status of tumor metastasis and cancer diagnosis.

Keywords: Peptide design, growth factors, cancer therapy, diagnosis

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Metformin Self-aggregation in Aqueous Solution, Molecular Dynamics Insight

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ABSTRACT

One of the natural remedies used to treat diabetes type 2 is metformin, which is effective in lowering the blood sugar levels by improving the way the body handles insulin. Researchers are also studying the use of metformin in a wide range of diseases, including cancer. It has been observed that using Metformin would cause side effects such as heartburn, nausea, weakness, or a metallic taste in the mouth may occur, which is undesired for patients. In order to improve the performance and increase the efficiency of drug in lower doses and also to reduce the possible side effects of Metformin, we have investigated its interaction and aggregation possibility in TIP3P solvent model during molecular dynamics (MD) simulation. All the MD simulations were done using NAMD package with CHARMM-36 force field. The aggregation process was investigated during 100 ns simulation time with time step was set to 1 fs. The structural parameter such as the root mean square deviation of aggregated Metformin molecules shows no significant deformation on their conformation during aggregation process. The number of hydrogen bonds of aggregated molecules in water was measured. The energetics analysis including the non-boning and van der Waals interaction energies of aggregated drugs had been calculated. The negative value of electrostatics contribution during the 100 ns simulation trajectories shows favorable interaction and aggregation of molecules in aqueous media. After 100 ns of simulation trajectories in aqueous media, a good capability of Metformin drug for its molecular aggregation was obtained. The root mean square deviation analysis indicates no structural reformation of self-aggregated molecules during simulation trajectories.

Keywords: Aggregation, Metformin, Molecular dynamics simulation

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Characterization of Sodium Dodecyl Sulfate Adsorption onto the Boron Nitride Nanotube: A Molecular Dynamics Investigation

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ABSTRACT

Nanoscience amplification causes rapid and efficient development in drug delivery. In recent years, we have observed the improvement of a category of materials called nanotubes to be used in medical and sensing applications. Nanotubes' growth in clinical applications, sufficiently reduces side effects and enhanced therapeutic effects. One of the best applicable nanomaterials for biomedical applications is boron nitride nanotube. Sodium dodecyl sulfate (SDS) is an anionic surfactant used in many cleaning and hygiene products. This compound is the sodium salt of the carbon an organosulfate. Its hydrocarbon tail combined with a polar "headgroup" give the compound amphiphilic properties and so make it useful as a detergent. SDS is also component of mixtures produced from inexpensive coconut and palm oils. SDS is a common component of many domestic cleaning, personal hygiene and cosmetic, pharmaceutical, and food products, as well as of industrial and commercial cleaning and product formulations. Molecular dynamics method was used to study the adsorption of SDS molecules onto boron nitride nanotube. Periodic boundary condition was applied to studied system and the time step was set to 1 fs and a final 100 ns simulation was done in NPT ensemble using NAMD package in 310 K. The RMSD analysis of SDS molecules shows no structural reformation during adsorption process. The number of hydrogen bonds and energy contributions presents a good adsorption along simulation time. The center of mass differences of SDS and boron nitride nanotube indicates the favorable adsorption via reducing their distances.The structural and energetic analysis indicates that SDS adsorption onto boron nitride nanotube was well occurred in water system and the boron nitride nanotube can be considered as a favorable candidate for surfactant molecules as other drugs and organic molecules.

Keywords: Sodium dodecyl sulfate, Nanoparticels, Molecular dynamics simulations

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Micellization and Self-aggregation Behavior of an Anionic Surfactant in an Aqueous Solution: Classical Molecular Dynamics Approach

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ABSTRACT

Surfactants, surface active agents, are recently employed in numerous processes in both fundamental and applied scientific research area. A recognized property of Sodium dodecyl sulfate (SDS) surfactant is the establishment of various types of colloidal-sized clusters in solutions, called micelles, having particular significance in pharmacy due to their novel property to enhance the solubility of feebly soluble substances in water. Surfactants molecular aggregation takes place over a sharp range of concentration known as critical micelle concentration (cmc). In this study the aggregation of SDS molecules in aqueous solution was investigated to understand their micellization and interfacial behavior in water. Herein, the molecular dynamics method was used to study the aggregation behavior of 4 SDS molecules in the water box. Four SDS molecules were put in the water system, and the periodic boundary condition was applied to the system. The time step was set to 1 fs, and a 100 ns final simulation run in the NPT ensemble was done in 310 K using the NAMD package. The RMSD analysis of the four SDS molecules represented no structural reformation during 100 ns trajectories. The RDF of SDS molecules with water molecules and other SDS molecules indicated a good aggregation of ligands with each other. The RDF diagrams showed that ligands 4 and 1 of SDS were well aggregated with sharp peak represented in 8 Å and ligands 3 and 1 located in the next rank. Moreover, the energy contributions show SDS molecules stability during 100 ns simulation time. The obtained results indicate favorable molecular aggregation of SDS molecules in an aqueous solution. The structural and energetic analysis reveals the interaction of the head and tail groups of SDS molecules and plays a dominant role in their stability in the water system.

***Keywords*:** Sodium dodecyl sulfate, Aggregation, Surface activity, Molecular dynamics simulations

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Bioeconomy and the Crucial Role of Basic Science in Shifting from the Fossil-Based Economy

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ABSTRACT

In the late 19th century and the early stages of mass production, up until the Second Industrial Revolution, the global economy heavily relied on the exploitation of natural resources and mines. However, as the world transitioned into the 20th century, the reliance shifted towards fossil fuels, a trend that persisted well into the 20th century. This fossil-fuel-based economy led to unsustainable development and a growing environmental crisis, including the pressing issue of global warming. In recent years, there has been a growing consensus among global development thinkers and experts regarding the imperative need to shift from a fossil-based economy to a bio-based economy. This transition is seen as a solution to address the significant challenges facing our society in the realms of social, economic, and environmental sustainability, thereby fostering the conditions for sustainable development. Notably, it has become a global consensus that by 2050, as the world economy is expected to double in size, there will be a shift towards non-fossil energy sources for vehicles, including clean fuels like hydrogen. The global focus will also increasingly shift towards the production and utilization of electric vehicles. Furthermore, it is anticipated that by 2050, approximately ninety percent of the world's total electricity will be generated from renewable and recyclable energy sources. Bioeconomy, guided by ecological considerations and the principles of sustainable development, strives to maximize the value derived from biological resources. This includes the production of value-added products such as food, animal feed, bio-based products, and energy. The approach encompasses services and the design of processes that align with knowledge, innovation, and technology, all with the aim of achieving a profitable and sustainable economy. Bioeconomy demonstrates robust innovative potential, driven by its broad application of basic sciences, particularly various fields of chemistry and nanotechnology. A crucial aspect of bioeconomy is the transition to a hydrogen-based economy, often referred to as the hydrogen economy. In response to technological and economic trends, many countries, including European Union member states, North America, and Southeast Asia, have incorporated bioeconomy-based policies into their macro-level policies and development plans. Other nations, recognizing the pivotal role of bioeconomy in sustainable development, are in the process of formulating documents and national development programs grounded in bioeconomy principles. All of this underscores the need for high-level binding documents that align economic policies with the principles of sustainable development, fostering preparedness to address the

challenges and requirements of food supply, environmental protection, clean air provision, and the transition to renewable energy sources. However, it's important to note that the necessary technologies to fully realize bioeconomy policies and create conditions for sustainable development are not yet fully available. As a result, the practical implementation of bioeconomy policies necessitates efficiency improvements and substantial structural revisions, often requiring significant research and investment, particularly in basic sciences with a strong emphasis on chemistry. The author anticipates that the United Nations' designation of 2022 as the Year of Basic Sciences and Sustainable Development will foster a greater appreciation for the role of basic sciences and facilitate the elimination of organizational and structural divisions between basic sciences and technology. This integration can manifest across various practical fields, including medicine and industry, and support the implementation of sustainable development policies based on bioeconomy knowledge, both within Iran and the surrounding regions.

Keywords: Bioeconomy, Energy, Fossil-Based Economy, Basic Science

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