Abstract No.77

Binding Affinities Prediction for a Series of New Nucleosides as Possible Inhibitors of Adenosine Demaninae Using Molecular Docking Approach Methods

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Adenosine deaminase (EC 3.5.4.4), a key enzyme in purine metabolism, catalyzes the irreversible hydrolytic deamination of active adenosine or 2′-deoxy-adenosine, which yields the inactive metabolite inosine or 2′-deoxyinosine and ammonia. It has been suggested that modulating adenosine deaminase activity may be a target for chemotherapy. Therefore, adenosine deaminase inhibitors may be used both as drugs and co-drugs in combination with certain anticancer or antiviral agents which are adenosine analogues. So that understanding the interaction of adenosine deaminase with its inhibitors is then critical for the development of the next generation of pharmaceutical agents. In the present work we used the molecular docking approach to estimate the adenosine deaminase–inhibitor binding affinity. A novel and robust automated docking method that predicts the bound conformations of flexible ligands to adenosine deaminase has been tested, that estimates the free energy change upon binding. Automated docking was carried out by means of the AUTODOCK 4.0 program. The method has been tested on 14 ligand-adenosine deaminase complexes. Our results clearly showed that, van der Waals effects can play a significant role in determining estimated free energy of binding. The results also indicate that the active siteis a hydrophobic pocket. It has been demonstrated that inhibitor2 (2-((6-amino-9H-purin-9-yl)methoxy)cyclohexyl benzoate) has lowest free energy of binding, so that van der waals energy have a greater share in these interactions. Therefore, inhibitor2 potentially has the highest inhibitory effect on adenosine deaminase.

Keywords: Adenosine Deaminase Inhibitors, Estimated Free Energy of Binding, Docking Method.

Abstract No.78

Study of the Structure-Activity Relationship of Pyraziamidase Using Molecular Docking and Molecular Dynamics Simulations

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Pyrazinamide (PZA) - an important drug in the anti-tuberculosis therapy, activated by an enzyme Pyrazinamidase (PZase). Mutation in pncA gene coding for PZase is a major mechanism of PZA resistance in Mycobacterium tuberculosis, however how mutations affect the structure of the pyrazinamidase, and how structural changes affect the enzymatic function is unknown. Application of molecular docking and molecular dynamics simulation techniques have become a conventional computational methodology to calculate significant processes at the molecular level .This computational methodology is particularly useful for analyzing the dynamics of protein-ligand systems. In this study, computer simulations were employed to elucidate the molecular events which lead to pyrazinamide resistance in M. tuberculosis mutants. This study has reported the results from molecular docking and MD simulation of wild type and five clinical resistance mutant types of pirazinamidase (PZAse) in complex with its ligand, pyrazinamide .Physical-chemical and structural parameters of each pyrazinamidase were calculated. computer models of mutated pyrazinamidases, indicate a low structural stability during the MD run for some mutants and the structural parameters explained a high variability of the enzymatic function and resistance level. This study showed the relationship a single amino acid substitution with PZAse activity and strain PZA resistance.

Keywords: Pyrazinamidase, Enzymatic Kinetics, Docking, Molecular Dynamic Simulation.

Abstract No.79

The Study of Teratogenic Effects of Dicholorometan Extract of Nerium Oleander Plant on Chick Embryo

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Nerium oleander is a kind of medicinal plants and has different biological activity such as antibacterial,antioxidant and cytotoxic effects. In the present work we used this plant leaves extract for evaluation of teratogenic effects on chicken embryo,For investigation,at first, dichlorometan extract of the leaves preaperd. Dicholoromethan extract solutions in DMSO were injected in air sac of chicken eggs at concentrations of ,5,10,20,40,60 and 80 µg/eggs 72h after incubation recording of survival fraction of the chickens at 19th day was showed that 73.4, 66.7, 53.3, 46.7, 35.7and 26.6 percents of embryos were alive, respectively statistic analysis of the results showed that the extract induces mortality with LD50 of 24.80 µg/egg. The study of incidence of morphological and skeletal abnormality in the treatment groups showed that club foot, beak deformity and gastroschisis was occurred in morphology while caudal vertebrates deletion, unossification or uncalcification of caudal vertebrates and shortness of tibia were appeared in skeleton of the chickenes. These data imply that the lethal effect of extract against chicken embryo was occurred in a dose-dependent manner. The study of the embryotoxcity of dicholoromethan extract showed that, The leave extract of this plant can be used as a chemotherapy agent.

Keywords: Nerium Oleander, Toxicity, Abnormality, Chick Embryo.

Abstract No.80

Identification of Molecular Weight of Oocyte Vitellogenin Protein of Iranian Caviar in time of Inducing in Liver by Treatment of 17 Beta Estradiol Hormone, Secreted in to Bloodstream and Stored in Oocyte in Iranian Sturgeon as a Yolk Protein

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Iranian Caviar fish"Acipenser persicus" exist in the Caspian Sea basin (north of Iran). Unfortunately, nowadays, this fish has become an endangered species and listed as threatened, vulnerable, and endangered throughout their ranges. Population numbers of this fish has suffered a decline as a result of natural and anthropogenic factors such as the construction of dams, water pollution, over-fishing and commercial operations for Caviar production. This fish consume for Caviar production and good flesh quality in Iran. Main protein of Caviar is vitellogenin,a phospholipoglycoprotein which is synthesized in liver and secreted in to bloodstream for accumulation in oocyte in reproduction cycles. There is a little information on vitellogenin protein in Persian sturgeon fish. The aim of this study was to assess the size of vitellogenin protein in bloodstream, changes and cleavage during transportation into oocye in Persian sturgeon. Vitellogenin induction was detected after injection of 17 beta estradiol at concentration of at least 5 mg per kg of body weight. Immature sturgeons at juvenile stage do not naturally synthesize Vg, but strongly responded to exogenously injected hormone. After 3 injections, heparinated bloods were collected centrifuged in 4ºC and plasma was separated. Plasma was diluted and electrophored by SDS-PAGE method was showed molecular weight of vitellogenin in this species. Vtg is cleaved into three yolk protein components:lipovitellin, phosvitin and beta component. Beside injection of juvenile fish, oocyte protein was selected from ovulated fish and vitellogenin protein was purified. Serum of injected fish was dialysed against distilled water. The precipitate was separated by centrifugation at 10 000 g for 15min at 4ºC. The pellet was suspended in distilled water, recentrifuged and dissolved in 0.5 M Nacl. The solution was applied to a gel filtration column. Gel filteration with exact protein markers showed the size of this protein in blood. Gel preparation method was selected for purification of cleavaged Lipovitellin from vitellogenin in oocyte Antisera were raised in rabbits against purified vitellogenin in plasma and purified Lipovitellin(in oocyte) by intradermal injection of each sample emulsified in an equal volume of Freund complete adjuvant. Concentrations of proteins were 0.5 mg per kg body weight. Injections were conducted at four times. The Enzyme-linked immunosorbant assay for sturgeon vg was developed to quantify serum Vg, using purified sturgeon Vg and anti-Vg. At the end, this stage and western blotting were done for demonstrate induction of vitellogenin in blood.

Keywords: Acipenser Persicus, Phospholipoglycoprotein, Vitelogenin, Blood, Oocyte.

Abstract No.81

Stabilization of an Atypical Bacillus Amylase by Adding Extra DX unit in EF-hand Like Motif

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