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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