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Molecular modelling studies of Oxazolidinone antibiotics in E.Coli ribosome

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Protein-Ligand docking has been used as an important tool in computer aided drug design and inhibitor design. The ribosome represents a major target for antibacterial drugs. Being a complex molecular machine, it offers many potential sites for functional interference. The high-resolution structures of ribosome in complex with various antibiotics provide a unique data set for understanding the universal features of drug-binding pockets on the ribosome. With the objective to design new chemical entities with enhanced inhibitory potencies against gram positive bacteria and multidrug resistant organisms. This study was designed to explore binding affinity and antibacterial activity of some newly synthesized 3,5-disubstituted oxazolidinone analogs in to the peptidyl transferase center of E.coli ribosome which was built from Schuwirth et al by using molecular modeling software Glide v 5.0 and the hydrogen-bonding interactions were observed between the inhibitors and the target ribosome. The structure-based drug design strategy described in this study will be highly useful for the development of new inhibitors with high potency and selectivity. From the docking result we can conclude that 3,5-disubstituted oxazolidinone analogs have showed good binding affinity towards the E.coli ribosome .

Interaction of Ru(II) & Co(III) complex of EHPIP with ds DNA – An experimental and computational approach

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DNA is an attractive target for the design of novel chemotherapeutics of cancer, as the cell cycle involves DNA replication during the S phase[1]. Metal complexes with aromatic ligand act as dual-function complexes i.e., they bind to DNA by metal coordination and intercalation of the aromatic ligand [2].Polypyridyl metal complexes, $[M(L)_2EHPIP](ClO4)_3$ where M = Ru(II) / Co (III); L = Phen / Bpy, EHPIP = 5-Ethoxy-(2-hydroxyphenyl) imidazo[4,5-f][1,10]phenanthroline,are synthesized and characterized.The low energy 3D conformer of the metal complex isgenerated and evaluated for discovering new drugs.

Binding of complexes with CT DNA has been investigated by absorption spectroscopy, luminescence titration, viscosity measurements, DNA cleavage assay [3]. The results show that metal complex binds to CT DNA by intercalation of EHPIP moiety and promote the cleavage of DNA.The computational studies involves the docking of the 3D conformer of the metal complexes were carried with DNA (PDB: 1FQ2) to identify the residues of binding [4]. The best docked complex with highest desolvation energy isconsidered and its binding energy calculated. The bases guanine and cytosine of the minor groove in DNA bind with EHPIP moiety which is a predominant feature of most of the anti-cancer drugs [5]. The computational methods compliment the experimental studies of DNA – metal complexes. The results confirm that minor changes of the ligand lead to profound influence on binding geometries. The metal complexes are projected to be potential cancer therapeutic molecules that interfere with DNA replication.

Keywords: Ru(II) and Co(III) complexes, DNA-binding, 3D Conformer, desolvation energy and Docking.