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In Silico Molecular Docking of N-Halo Compounds with Proteins 1HD2 and 2CDU

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Abstract:

The fundamental step for drug discovery is the understanding of the protein-ligand interaction in numerous pharmaceutical applications. Molecular docking is one of the cuttingedge drugs planning techniques, which investigate the capability of a ligand by processing the base restricting energy. In the present study, *In Silico* N-chloronicotinamide and N-chloroisonicotinamide molecular docking with 1HD2 and 2CDU proteins have been carried out. *In silico* molecular docking is one of the most impressive strategies to find novel ligand for proteins of known construction and consequently assume a key part in structure-based drugs. Thus *in silico* atomic docking has been done to dissect the limiting properties of Peroxiredoxin 5 and water-shaping NAD(P)H oxidase from *lactobacillussanfranciscensis* with N-chloronicotinamide and N-chloroisonicotinamide. The docking studies confirm the antioxidant activity of N-chloronicotinamide and N-chloroisonicotinamide and thereby activation of target protein Peroxiredoxin 5 (1HD2) and water-forming NAD(P)H oxidase from *lactobacillussanfranciscensis*(2CDU) through the binding interactions.

Keywords*: InSilico* molecular docking, N-chloronicotinamide, N-chloroisonicotinamide, 1HD2 and 2CDU proteins

INTRODUCTION

Molecular Docking[1] is utilized in situating the PC created 3D construction of little ligands into a receptor structure in various directions, compliances and positions. This technique is helpful in drug revelation, giving bits of knowledge into atomic acknowledgment. PC Helped Medication Plan (CADD) has been created as an effective method for finding imminent lead compounds and for supporting the manifestations of potential drugs for a large number of problems[2]. To find possible lead molecules from large compound libraries, a variety of computer techniques are now being applied. Docking is one of these approaches that has been widely employed in drug development for diseases caused by free radicals, including cancer and diabetes[3,4]. Molecular docking research centers around computationally reenacting the molecular acknowledgment process. It plans to accomplish an enhanced conformity for both the protein and ligand and relative direction among protein and ligand to such an extent that the free energy of the general framework is limited. Molecular docking and modelling studies increase the precision and reliability of biological tests by revealing potential interactions between compounds and their target receptors.

In silico molecular docking studies has been used in the evaluation of cellulose/TiO2 nano composites[5]. Molecular docking studies of 1-arylsulphonylpyrazole derivatives has been studied[6]. *In silico* molecular docking studies has been done for evaluating antimalarial properties of naphthalene-sulfonic acid derivatives and for studying proteins and peptides[7,8]. Expected by a rising number of researchers, the in silico docking field is in full extension, new calculations and strategies are showing up at a dramatic rate[9-11]. The devices are assessed according to a few perspectives, as quantities of references, simplicity of use and PC necessities. At long last, the abilities and constraints as well as unambiguous utilizations of in silico docking methods can be determined[12,13]. Docking strategy predicts the exploratory restricting methods of

little particles inside the limiting site of specific receptor targets and is utilized as a standard computational device in drug plan and in virtual screening studies to find novel naturally dynamic molecules[14-16]. The essential devices of a mooring technique incorporate a quest of calculation and an energy scoring capability for creating and assessing ligand poses[17-19].

In the present study, N-chloronicotinamide and N-chloroisonicotinamide have been docked against Peroxiredoxin 5 (1HD2) and water-forming NAD(P)H oxidase from *lactobacillussanfranciscensis*(2CDU).

METHODOLOGY

Employing Autodockvina 1.1.2, molecular docking experiments were performed to examine the interaction and mechanism of binding among the substances N-chloronicotinamide and N-chloroisonicotinamide, with the proteins1HD2 and2CDU. For the purpose of antioxidant screening, the Protein Data Bank's Human Peroxiredoxin 5's (PDB ID: 1HD2) crystal structure and the gem construction of water-framing NAD(P)H oxidase from lactobacillus sanfranciscensis(2CDU) were recovered. ChemDraw Ultra 12.0 and Chem3D Expert 12.0 programming were utilized to make the 3D designs of the substances N-chloronicotinamide and N-chloroisonicotinamide.

Utilizing the AutoDock Tools 1.5.6 software package, the input files for AutodockVina were produced. The size x, y, z: 16, 16, 16 of the 1HD2 protein search grid were identified as center x: 7.657, center y: 42.687 and center z: 27.705 with spacing of 1.0. The size x, y, z: 20, 20, 24 of the 2CDU protein search grid were identified as center x: 0.755, center y: 7.447, and center z: 51.264 with spacing of 1.0. The value for exhaustiveness was set to 8. For Vina docking, the other parameters were left at their default values and unmentioned. The best-scoring molecule is the one with the lowest binding affinity value, and the data was visually assessed with the use of the Discovery studio 2019 application.

RESULTS AND DISCUSSION

The compounds **N-chloronicotinamide and N-chloroisonicotinamide,**exhibits equipotent binding affinity (-3.8 kcal/mol) to the 1HD2 protein. The stability of protein-ligand bonding is due to hydrogen bonding and the H-donor and H-acceptor atoms bond distance is less than 3.5. The inhibitor drugs have hydrogen bond distances in their respective proteins that were less than 3.5, which indicates strong hydrogen bonding.

N-chloroisonicotinamide compound and receptor 1HD2 creates a single hydrogen bond. In hydrogen bonding interactions, the amino acid residue Thr147 (bond lengths: 2.53) has been implicated. Hydrophobic interactions involve the amino acid residues Pro40, Gly46, Leu116, Phe120 and Arg127. With the receptor 1HD2, **N-chloronicotinamide** creates two hydrogen bonds. In hydrogen bonding interactions, the amino acid residue Thr44 (bond lengths: 2.05) and Cys47 (bond lengths: 3.56) has been implicated. Hydrophobic interactions involve the amino acid residues Gly46, Thr147 and Leu149.

Figures 1 and 2 demonstrate, respectively, the hydrogen bonding and hydrophobic interactions of amino acid residues in 1HD2 protein with substances N-chloronicotinamide and N-chloroisonicotinamide. The compounds N-chloronicotinamide, N-chloroisonicotinamide, exhibits equipotent binding affinity (-5.2 kcal/mol) to the 2CDU protein. N-chloroisonicotinamide compound and receptor 2CDU creates a single hydrogen bond. In hydrogen bonding interactions, the amino acid residue Val214 (bond lengths: 2.85) has been implicated. Hydrophobic interactions involve the amino acid residues Ile155, Ile178, Lys213 and Ile243. With the receptor 2CDU, N-chloronicotinamide does not create any hydrogen bonds. In hydrogen bonding interactions, the amino acid residue Ile178 (bond length: 2.21) and Asp179(bond length: 3.06) has been implicated. Hydrophobic interactions involve the amino acid residues Pro120, Lys213and Ile243. Figures 3 and 4 demonstrates the hydrogen bonding and hydrophobic interactions of amino acid residues in 2CDU protein with substances N-chloronicotinamide and N-chloroisonicotinamide

The findings demonstrate that the inhibitor drugs have a remarkable capacity to inhibit 2CDU protein than 1HD2 protein. Table 1 and 2 provides a summary of the findings.

Table 1: Molecular docking interaction of compounds N-chloroisonicotinamide and N-chloronicotinamide against protein 1HD2

Proteins	**Compound Name**	Binding affinity (kcal/mol)	No. of H-bonds	H-bonding residues
1HD2	N-chloroisonicotinamide	-3.8	1	Thr147
	N-chloronicotinamide	-3.8	2	Thr44, Cys47

Table 2: Molecular docking interaction of compounds N-chloroisonicotinamide and N-chloronicotinamide against protein 2CDU

Proteins	**Compound Name**	Binding affinity (kcal/mol)	No. of H-bonds	H-bonding residues
2CDU	N-chloroisonicotinamide	-5.2	1	Val214
	N-chloronicotinamide	-5.2	-	-

Figure 1: Docked complex (a), molecular surface (b), 3D (c), and 2D (d) interaction modes of compound **N-chloroisonicotinamide**within the binding site of 1HD2 protein.

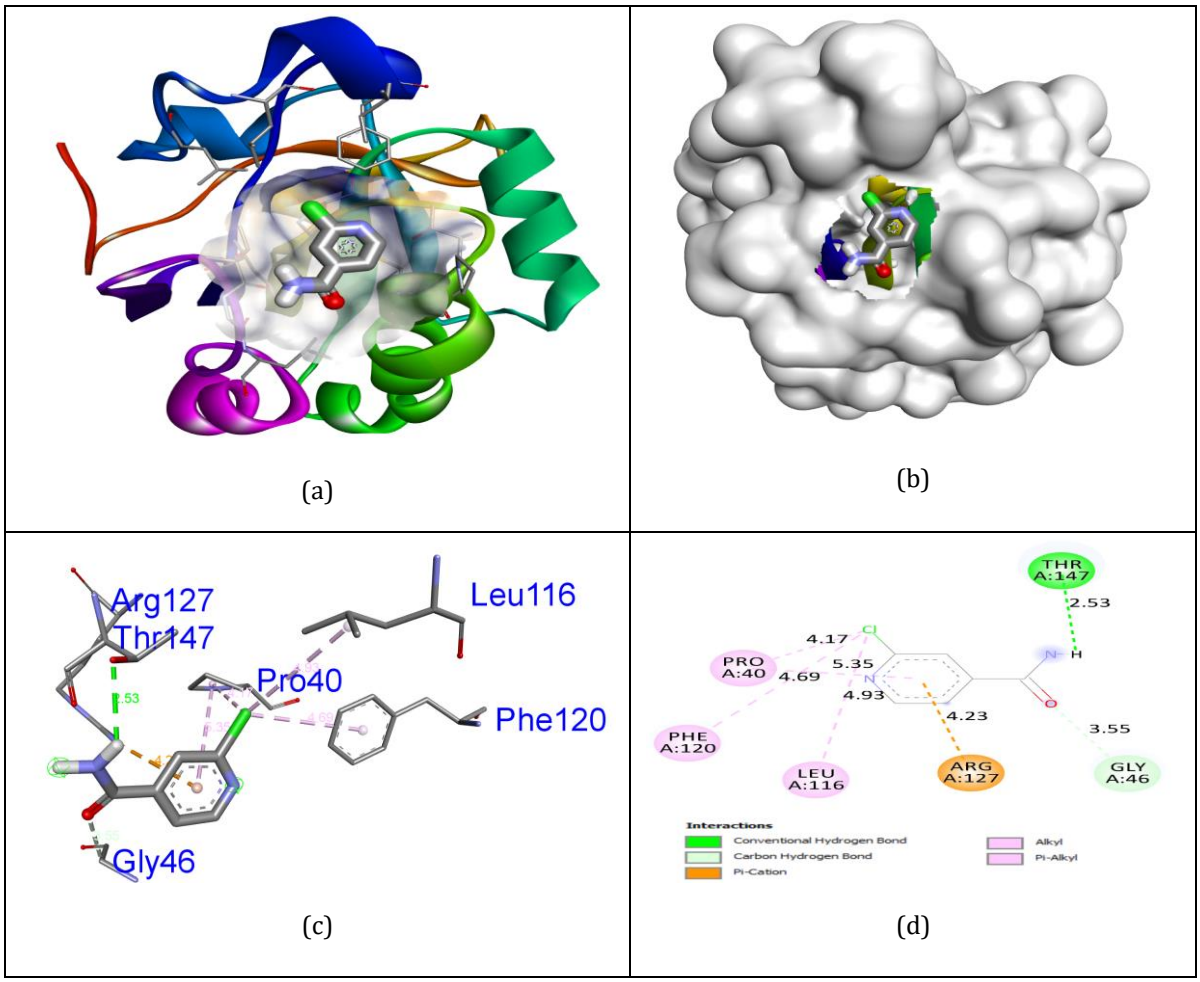


Figure. 2 Docked complex (a), molecular surface (b), 3D (c), and 2D (d) interaction modes of compound **N-chloronicotinamide** within the binding site of 1HD2 protein.

Figure3: Docked complex (a), molecular surface (b), 3D (c), and 2D (d) interaction modes of compound **N-chloroisonicotinamide** within the binding site of 2CDU protein.

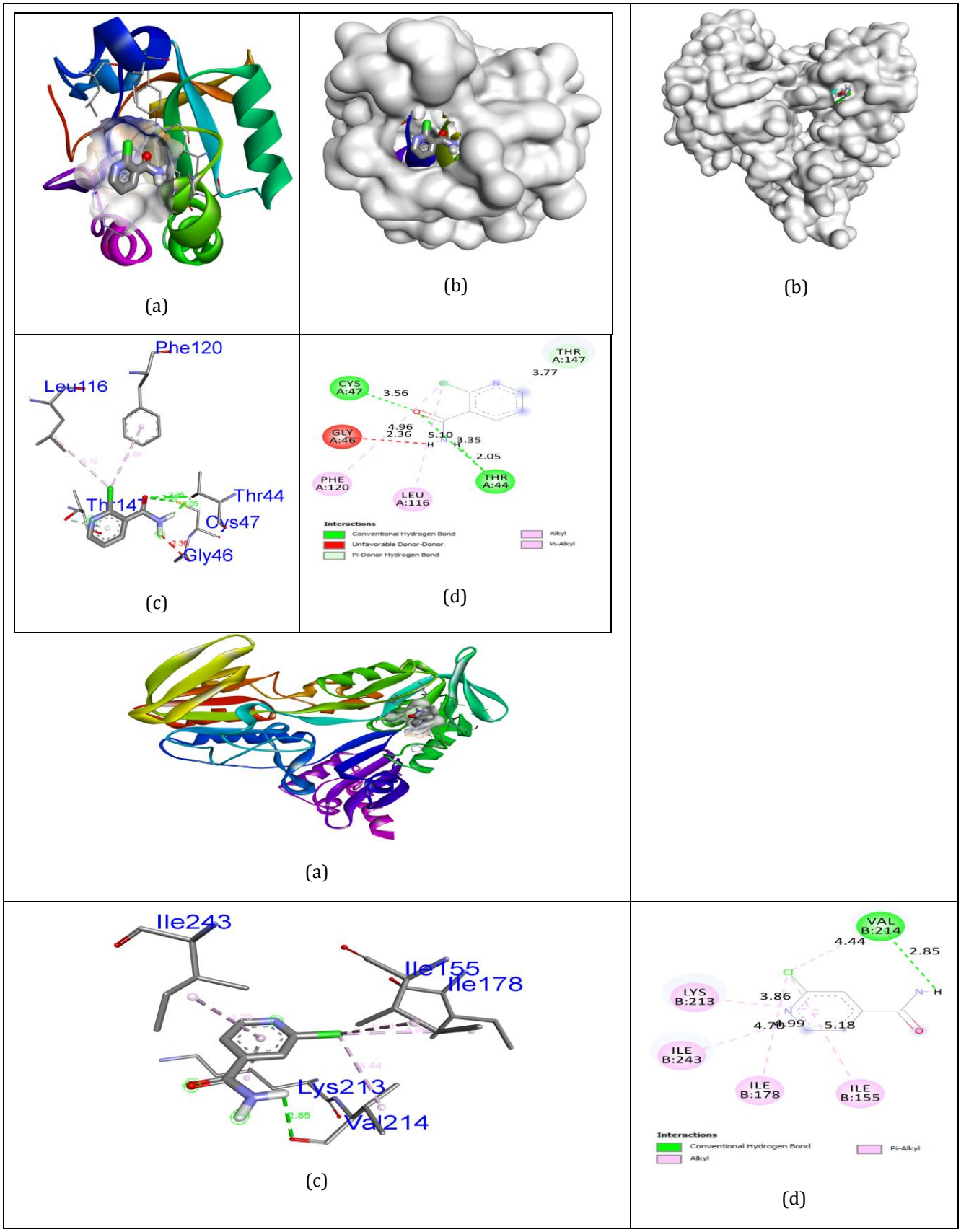
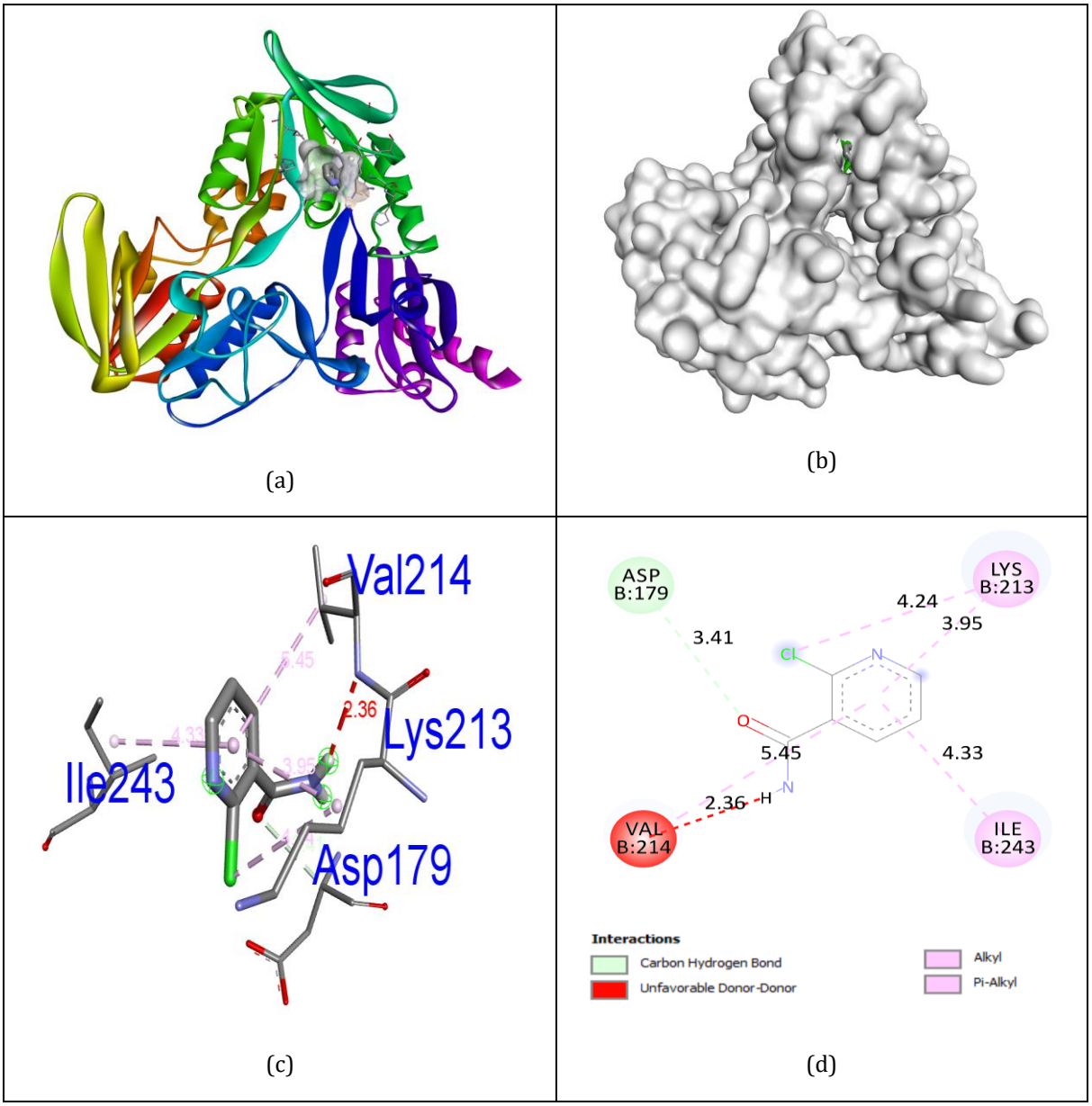


Figure4: Docked complex (a), molecular surface (b), 3D (c), and 2D (d) interaction modes of compound **N-chloronicotinamide** within the binding site of 2CDU protein.



CONCLUSION

In silico molecular docking is a computational method that plays a critical role in drug discovery and development. By using computer programs to predict the binding affinity and orientation of small molecule ligands to protein targets, *in silico* molecular docking can rapidly screen large databases of compounds to identify potential drug candidates, saving time and resources compared to traditional experimental methods. It can also be used to study protein-protein interactions and the effects of mutations on protein-ligand interactions. *In silico* molecular docking is just one tool in the arsenal of computational and experimental methods used in drug discovery, and it should be combined with other methods to maximize the chances of success in developing new therapies.

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