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In Silico N-Chloropicolinamide and Ascorbic Acid Molecular Docking with 1HD2 Protein

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Abstract: During the course of this *in silico* experiment, molecular docking with the 1HD2 protein was carried out using N-chloropicolinamide and ascorbic acid. *In silico* molecular docking is one of the most fascinating methods for discovering novel ligands for proteins whose structures are already well understood. As a result of this, the present work used *in silico* molecular docking to investigate the binding properties of peroxiredoxin 5 with N-chloropicolinamide and ascorbic acid. Docking tests, which used ascorbic acid as a point of reference, demonstrated that N-chloropicolinamide has the ability to activate the target protein peroxiredoxin 5, as well as its capacity to have an antioxidant effect (1HD2).

Keywords: CADD, Molecular docking, Ascorbic acid, N-chloropicolinamide, Peroxiredoxin 5

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Introduction

The field of Computer-Aided Drug Design (CADD) has advanced to become a useful tool in the search for potential lead compounds and in the development of potential treatments for a broad variety of diseases (Binkowski *et al*., 2003). Multiple computational methods are now being used to sift through enormous chemical libraries in search of potential lead compounds. Researchers employed a wide range of *in vitro*, *in vivo*, and computational methods to assess the antioxidant capability of drugs or substances. Among these methods, docking has seen extensive usage in the creation of drugs to combat free-radical-induced disorders including cancer and diabetes (Ghose and Crippen, 1987; Srivastava *et al.,* 2012). Discovering potential synergies between drugs and their goal receptors via molecular docking and modeling research

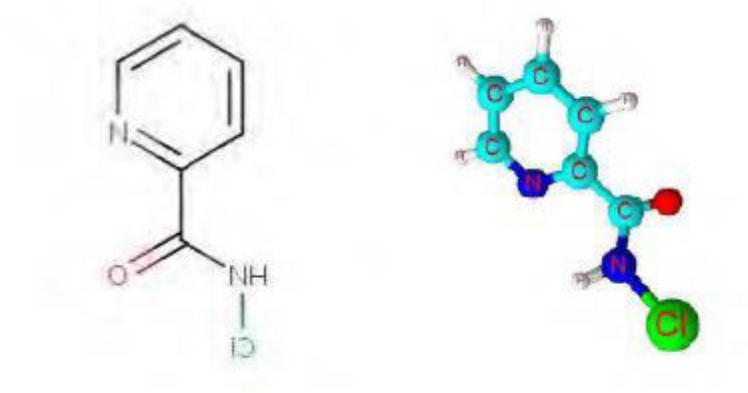


Fig. 1: N-chloropicolinamide 2D structure and 3D structure optimization.

improves the precision and reliability of organic assays. Therefore, N-chloropicolinamide and ascorbic acid, a gold-standard antioxidant, were docked against the antioxidant protein Peroxiredoxin 5(1HD2) in the present study.

Materials and Methods

Ligand and protein preparation:

The protein was collected from the PDB database, and the ligands (including N-chloropicolinamide and ascorbic acid as a reference) were drawn using the ACD/ChemSketch tool after being obtained from the Pubchem database. Water molecules and other Ligand molecules were often eliminated from 1HD2 proteins before docking.

Antioxidant Protein Peroxiredoxin 5 (*1HD2*):

The RCSB PDB, also known as the Exploration Collaboratory for Primary Bioinformatics, Protein Information Bank, is a repository for the three-dimensional structural information of important natural macromolecules such as proteins and nucleic acids. It provides what is need. It provides standard as well as complex searches that are based on the sequence structure and function annotations. The three-dimensional structure of the therapeutic target peroxiredoxin 5 was retrieved from the Protein Data Bank under the ID number 1HD2 (http://www.pdb.org).

In silico docking studies:

Protein structures were accessed using the PDB database, while ligands were located via the Pubchem database. Docking robots with graphical user interfaces were used to deploy frameworks, calculate dock scores, and evaluate activator-bound conformers in proteins as targets. An energy-minimization simulation was run in ChemDraw. After that, docking tests were performed on the simplified designs. To achieve this goal, the water atoms and other components that make up the hetero particles were removed from the proteins. Auto dock 4.1 was used to do the necessary calculations, which followed a Lamarckian hereditary approach. The energy of a communication may be calculated using this product, and the most adaptive ligand location can be located by minimising the amount of energy required to achieve the desired effect. The strength of scoring is determined by the intermolecular interaction formed between the ligand and protein during docking. In accordance with the inherited procedure, all twists were given free rotation during docking.

Results and Discussion

The antioxidant target protein human peroxiredoxin 5, an unique kind of mammalian peroxiredoxin, was docked against (PDB code: 1HD2) (Trott and Olson, 2010; Vidya *et al*., 2012; Tabassum *et al*., 2013). As a thioredoxin peroxidase present in mitochondria, peroxi-somes, and the cytosol, peroxiredoxin 5 (PRDX5) is ubiquitously expressed throughout the human

Ligand	Molecular formula	M. weight (g/mol)	H-bond acceptors / donors	Binding Affinity (kcal/mol)	1HD2 Amino acids binding
N-Chloropicolinamide	$C_6H_5ClN_2O$	156.57	2/1	-4.90	LYS 89, GLU 91, ARG 86, ALA 90, GLY 85, GLY 82, LEU 96, ARG 95, VAL 94.
Ascorbic acid*	$C_6H_8O_6$ or $HC_6H_7O_6$	176.12	6/4	-5.40	LYS 93, GLY 92, GLU 91, ALA 90, GLY 85, ARG 86, THR 81, GLY 82, GLU 83, GLY 17, LEU 96, GLU 16, ARG 95, VAL 94.

* Standard as Anti-oxidant

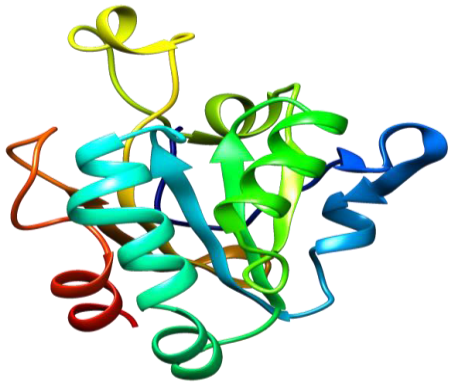
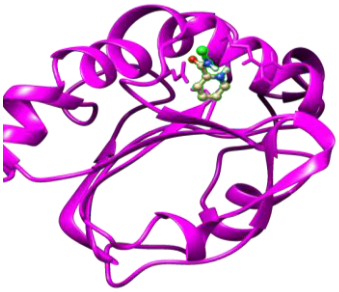


Plate 1: 3D Cartoon view of prepared 1HD2 protein.

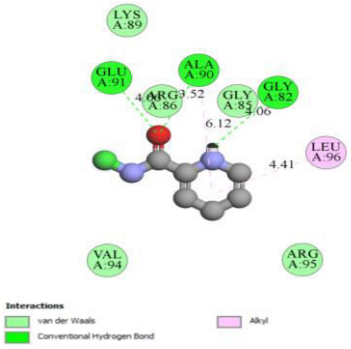
body. Rather than being a redox sensor, PRDX5 has been considered as a cytoprotective antioxidant enzyme that protects cells from endogenous and exogenous peroxide assaults. As a result, overexpression of the enzyme in several subcellular compartments protects cells from oxidative stress induced mortality. In order to explain *in silico* antioxidant investigations, molecular docking studies were conducted and a specific protein peroxiredoxin 5 (1HD2) (Sarkar, 2023; Sivajothi and Dakappa, 2014; Alam *et al*., 2022) was identified as the target for antioxidant substances. The docked ligand atoms were picked in light of their docking energy and capacity to tie well with dynamic site deposits, as demonstrated in Table 1. Plate 1 depicts a 3D cartoon representation of the produced 1HD2 protein. The docking of N-Chloropicolinamide and Standard ascorbic acid is shown in Plates 2 and 3. The hydrogen connection between the atoms was shown by a violet colour, whereas the rest of the interactions were hydrophobic. All of the chemicals binding interactions with the target protein showed strong hydrogen bonding and hydrophobic interactions. N-Chloropicolinamide had a docking value of 4.90 and normal ascorbic acid had a docking score of -5.40 Kcal/mol, respectively. The docking score was the most similar to the industry norm. The limiting system and connection energy of the hits were uncovered by means of sub-molecular docking. The antioxidant activity of NChloropicolinamide and conventional ascorbic acid was validated in docking studies, indicating that the target protein Peroxiredoxin 5 was activated through binding interactions.

Conclusion

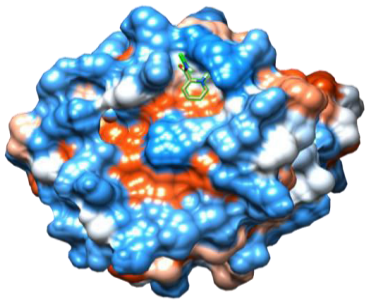
Finding novel ligands for proteins with known structures is a key step in developing structure-based medications, and *in silico* molecular docking is one of the most effective methods for



3D Cartoon view of N-Chloropicolinamide ligand binding with 1HD2 protein

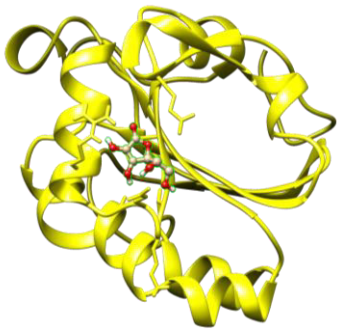


2D view of N-Chloropicolinamide ligand interaction with 1HD2 protein

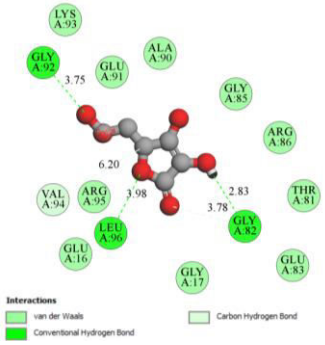


3D Surface view of N-Chloropicolinamide ligand binding with 1HD2 protein

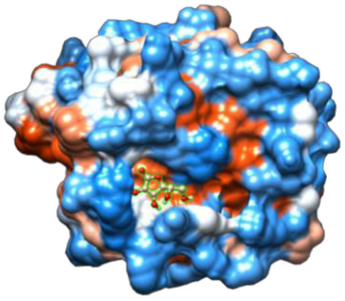
Plate 2: N-Chloropicolinamide ligand binding with 1HD2 protein



3D Cartoon view of Ascorbic acid ligand binding with 1HD2 protein



2D view of Ascorbic acid ligand interaction with 1HD2 protein



3D Surface view of Ascorbic acid ligand binding with 1HD2 protein

Plate 3: Ascorbic acid ligand binding with 1HD2 protein.

doing so. Peroxiredoxin 5's interaction with N-Chloropicolinamide and ascorbic acid was investigated using *in silico* molecular docking. Through binding interactions, N-Chloropicolinamide and ascorbic acid activate Peroxiredoxin 5 (1HD2), as shown in docking tests. Therefore, the present study's findings might provide evidence for the *in vivo* antioxidant activity of N-in Chloropicolinamide and facilitate the drug's commercialization.

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