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Research Article

TRANS-DISCIPLINARY RECEPTOR BINDING OF ACYCLOVIR TO HUMAN PHENYLALANINE HYDROXYLASE: DOCKING APPROACH

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ABSTRACT

The purpose of present work is to introduce the binding of Acyclovir to the trans-disciplinary protein with the help of docking procedures. Docking procedures allow virtually screening a database of compounds and predict the strongest binder based on various scoring functions. This work has been performed with the help of Molegro Virtual docker, in which a drug is docked with their corresponding and non-corresponding (trans-disciplinary) protein. Results reveals that the protein-ligand interaction energy, hydrogen bond energy and MolDock scores provided by Molegro virtual docker, between ligand (Acyclovir) and trans-disciplinary protein (Human Phenylalanine Hydroxylase, receptor protein for Levodopa) are better than that of between ligand and corresponding protein (Deoxycytidine kinase, receptor protein for Acyclovir).

Keywords: *Acyclovir; Docking; Protein-ligand interaction energy; hydrogen bond energy; Phenylalanine Hydroxylase; Deoxycytidine kinase.*

INTRODUCTION

Docking procedure permits virtually screening a database of compounds and predict the strongest binder on various scoring functions. It finds way in which two molecules, such as drugs and an enzyme and/or protein fit together and dock to each other well [1]. Molecularly, docking techniques have been used in modern drug designing to understand drug–receptor interaction. It has been stated in the literature that computational procedures strongly support more potent drugs by revealing the mechanism of drug-receptor interaction [2]. Rational Drug Design helps to facilitate and fasten the drug designing process, which involves various methods to identify novel compound, out of them one method is the docking of molecule of drug with the receptor [3]. The field of molecular docking has emerged during the last three decades and now is becoming an integral aspect in drug discovery and development area. It is utilized for the prediction of protein-ligand complexes which is composed of two components- a search algorithm, an algorithm that creates possible protein ligand complex geometries and a scoring function that predicts the binding affinity of ligand to the protein [4].

Flexible docking of ligand to receptor molecule is an emerging approach and is extensively used to reduce cost and time in drug discovery [5].

Till date docking procedures have been used with ligand to their corresponding proteins, but in this work it is being used with ligands to trans-disciplinary proteins. Here trans-disciplinary reveals just the recognized proteins of another ligand. Here two receptor proteins have been taken for carrying out this work, which are Phenylalanine Hydroxylase and Deoxycytidine kinase. Acyclovir (**CID no. 2022**) has been recognized for anti-herpes drug. Human Phenylalanine Hydroxylase (**PDB ID 6PAH**) is a recognized protein for Levodopa which catalyzes the hydroxylation of phenylalanine to tyrosine, which is a rate limiting step in catabolism of phenylalanine [6]. Deoxycytidine kinase (dCK) (**PDB ID 3MJR**) is a recognized protein for Acyclovir which includes different deoxyribonucleoside kinases including the cytoplasmic (TK1) and mitochondrial (TK2) thymidine kinases. The dCK enzyme is associated with drug resistance and sensitivity, as both dCK and TK2 phosphorylate several antiviral and chemotherapeutic nucleoside analogs. For trans-disciplinary binding, Acyclovir has been docked with Phenylalanine Hydroxylase.

MATERIALS AND METHODS

For carrying out this work, National Center for Biotechnology Information's **(NCBI)** website and Protein Data Bank's **(PDB)** website were used as chemical and protein data sources.

For docking studies**, Molegro Virtual docker**[7] have been used.

Acyclovir (**CID no. 2022**) structure data file was downloaded from N.C.B.I. website and protein targets were downloaded from Protein Data Bank with **PDB ID 6PAH** and **3MJR.**

Step 1-Docking of Ligand (CID no. 2022) with corresponding target (PDB ID. 3MJR)

Step 2-Docking of Ligand (CID no. 2022) with trans-disciplinary target (PDB ID. 6PAH)

Step 3-Comparing docking results of step 1 with docking results of step 2

Comparing parameters are-

- Protein-ligand interaction energy
- Hydrogen bond energy
- MolDock score (provided by Molgro virtual docker as its scoring function)

RESULTS

Comparison of parameters of docking result has been shown in Table.

Table 1: Shows results of comparative parameters of docking of acyclovir with corresponding and trans-disciplinary protein

	Ligand with corresponding protein		
Pose	**Protein-ligand interaction energy**	**Protein-ligand interaction energy**	**MolDock score**
1	-100.026	-13.3005	-97.1499
2	-104.416	-10.6236	-96.8315
3	-92.5594	-7.79648	-96.8769
4	-87.5527	-7.51684	-85.9688
5	-91.9402	-9.09093	-86.336
	Ligand with trans-disciplinary protein		
Pose	**Protein-ligand interaction energy**	**Protein-ligand interaction energy**	**MolDock score**
1	-104.315	-10.6867	-102.641
2	-106.293	-11.6564	-99.7742
3	-102.057	-8.96364	-100.851
4	-102.62	-15.9242	-101.358
5	-101.294	-17.3413	-97.8042

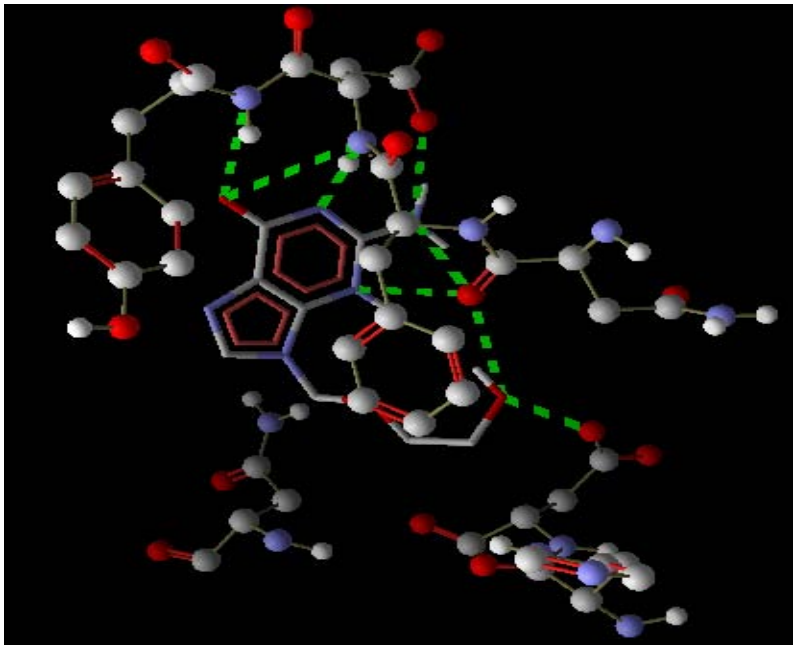

Fig. 1: It shows docking of Acyclovir with corresponding protein

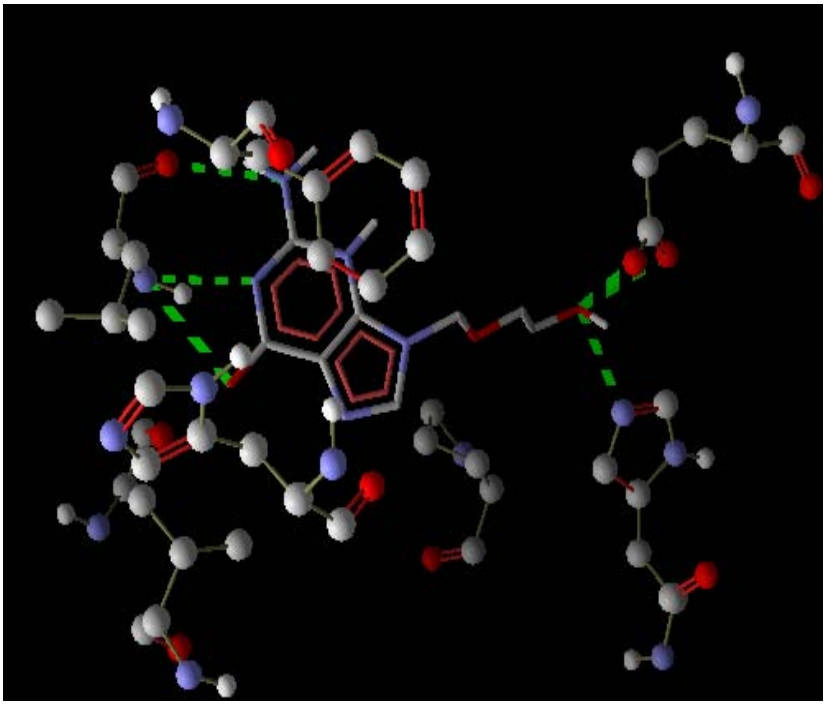

Fig. 2: It shows docking of Acyclovir with trans-disciplinary protein

Result reveals that the protein-ligand interaction energy, hydrogen bond energy and MolDock scores provided by Molegro virtual docker between ligand (Acyclovir) and trans-disciplinary proteins (Human Phenylalanine Hydroxylase) are better than between ligand and corresponding proteins (Deoxycytidine kinase).

DISCUSSION

Structural based drug designing is significantly based on the protein-ligand interaction. In this work docking procedures are used to predict the binding affinity of ligand with the proteins that are not recognized for the stated ligand, which reveals that this concept would be used to find out the alternatives of drugs or it may be used to retrieve the information regarding the undesirable effects of a drug as it clearly shows the other possibilities of binding of drug as inside the body all the receptor sites are available for a ligand. The beneficial use of this concept may be made on further developments. The result of this docking procedure reveals that the Acyclovir could be used instead of Levodopa as a better alternative.

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