TRANS-DISCIPLINARY PROTEIN BINDING OF DRUG: DOCKING APPROACH

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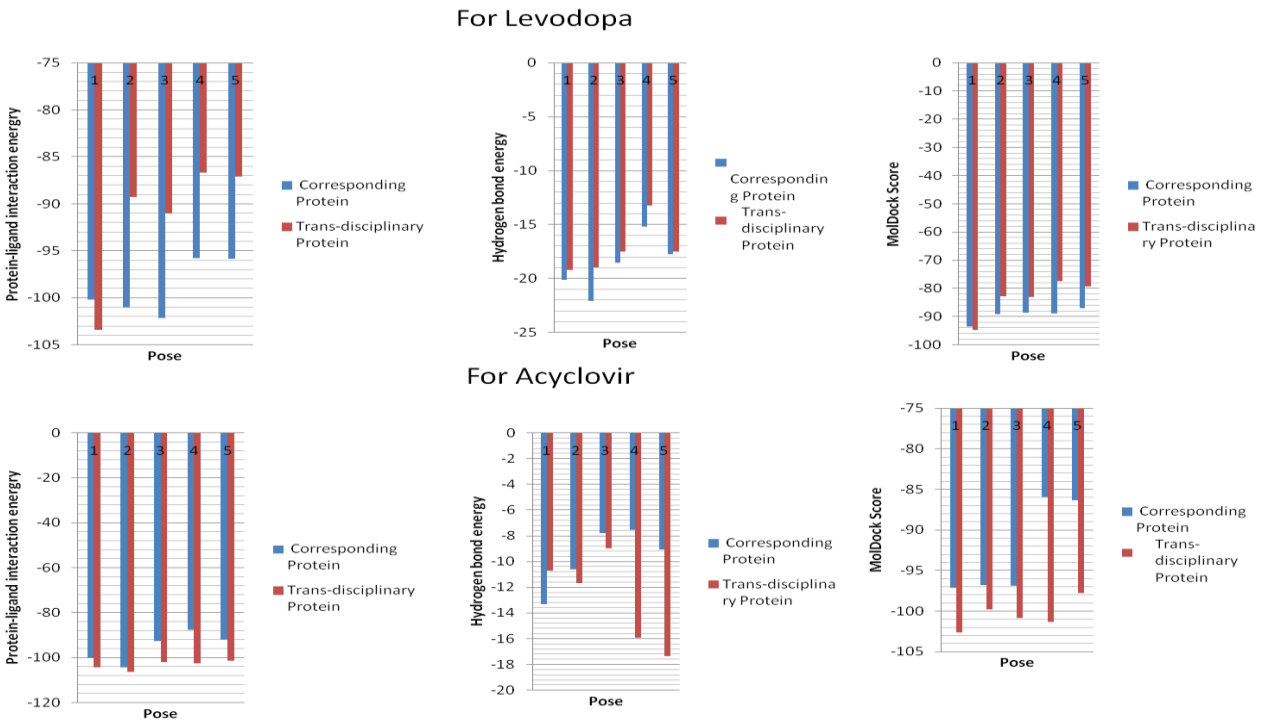
Abstract

The purpose of present work is to introduce the binding of existing drugs to the trans-disciplinary protein with the help of docking procedures. Docking procedures allows 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 two drugs are 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 legands (Levodopa and Acyclovir) and trans-disciplinary proteins have been equivalent or even better than that of between legands and corresponding proteins.

Key words: *Docking; Protein-ligand interaction energy; hydrogen bond energy; Phenylalanine Hydroxylase; Deoxycytidine kinase*

Graphical abstract



Introduction

Docking procedures permits virtually screening a database of compounds and predict the strongest binder on various scoring functions. It finds ways 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].

Till date docking procedures have been used with legand to their corresponding proteins, but in this work it is being used with legands to trans-disciplinary proteins. Here trans-disciplinary reveals just the recognized proteins of another legand.

Here two legands have been taken for carrying out this work, which are Levodopa and Acyclovir. Levodopa (**CID no. 6047**) has been recognized for anti-parkinsonism drug, whereas Acyclovir (**CID no. 2022**) as 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 [4]. 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, Levodopa has been docked with Deoxycytidine kinase and Acyclovir with Phenylalanine Hydroxylase.

Materials

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**[5] have been used.

Method

Levodopa (**CID no. 6047**) and acyclovir (**CID no. 2022**) structure data files were downloaded from N.C.B.I. website and protein targets were downloaded from Protein Data Bank with **PDB ID 6PAH** and **3MJR** respectively.

Step 1-Docking of Legand (CID no. 6047) with corresponding target (PDB ID. 6PAH)

Step 2-Docking of Legand (CID no. 2022) with corresponding target (PDB ID. 3MJR)

Step 3-Docking of Legand (CID no. 6047) with trans-disciplinary target (PDB ID. 3MJR)

Step 4-Docking of Legand (CID no. 2022) with trans-disciplinary target (PDB ID. 6PAH)

Step 5-Comparing docking results of step 1 with docking results of step 3

Step 6-Comparing docking results of step 2 with docking results of step 4

Comparing parameters are-

- Protein-legand 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 1 and Table 2.

Table 1 Results of comparative parameters of docking of levodopa with corresponding and trans-disciplinary protein

	Pose	Protein-legand interaction energy	Hydrogen bond energy	MolDock score
Legand with corresponding protein	1	-100.193	-20.1122	-93.4740
	2	-101.056	-22.0621	-89.1538
	3	-102.171	-18.5133	-88.5731
	4	-95.7854	-15.1872	-88.8022
	5	-95.8473	-17.7596	-87.0943
Legand with trans-disciplinary protein	1	-103.437	-19.2082	-94.7161
	2	-89.2665	-18.9527	-82.7658
	3	-91.0131	-17.4927	-83.1425
	4	-86.6507	-13.2055	-77.5133
	5	-87.0945	-17.473	-79.3102

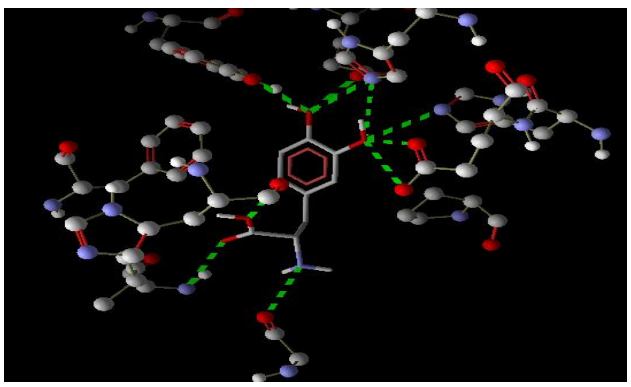
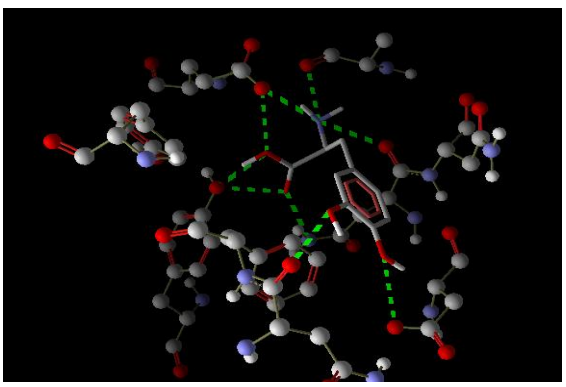
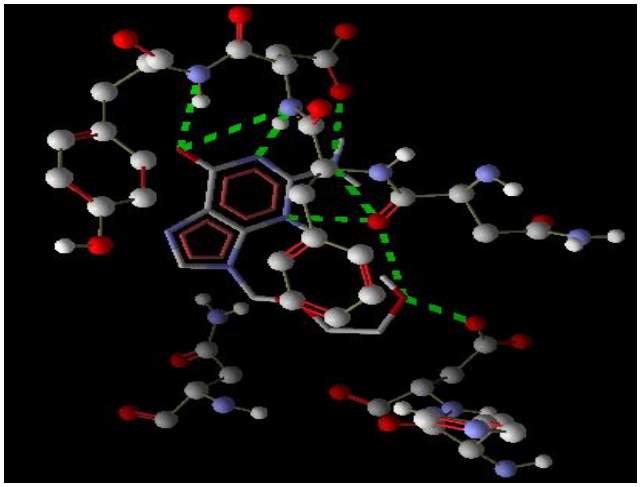
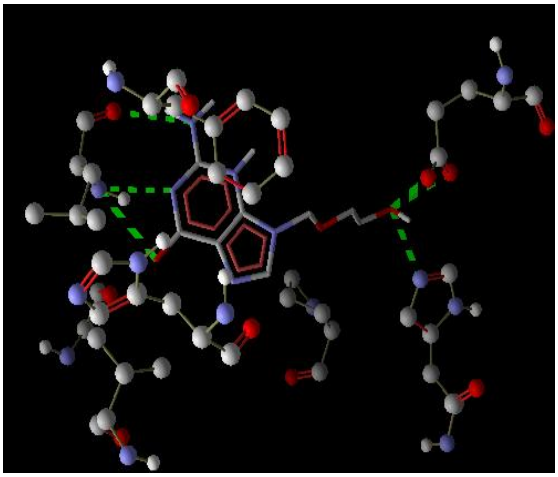
Levodopa docked with corresponding protein	**Levodopa docked with trans-disciplinary protein**
	

Table 2 Results of comparative parameters of docking of acyclovir with corresponding and trans-disciplinary protein

	Pose	Protein-legand interaction energy	Hydrogen bond energy	MolDock score
Legand with corresponding protein	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	-86.3360
Legand with trans-disciplinary protein	1	-104.315	-10.6867	-102.6410
	2	-106.293	-11.6564	-99.7742
	3	-102.057	-8.96364	-100.8510
	4	-102.62	-15.9242	-101.3580
	5	-101.294	-17.3413	-97.8042

Acyclovir docked with corresponding protein	**Acyclovir docked with trans-disciplinary protein**
	

Discussion

Results reveals that the protein-ligand interaction energy, hydrogen bond energy and MolDock scores provided by molegro virtual docker between legands (Levodopa/Acyclovir) and trans-disciplinary proteins (Deoxycytidine kinase/Human Phenylalanine Hydroxylase) have been equivalent or even better than between legands and corresponding proteins (Human Phenylalanine Hydroxylase/ Deoxycytidine kinase) respectively.

Conclusion

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 legand with the proteins that are not recognized for the stated legand, 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 because inside the body for a single legand all the receptor sites are available. The beneficial use of this concept may be made on further developments.

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References

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