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Docking Analysis of *Tamilnadia uliginosa* Retz. Rirveng & Sastre (Rubiaceae)

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ABSTRACT

The development of a molecular docking tool usually starts with an efficient search algorithm, which places the ligand in the active site of the target protein in numerous different positions, orientations, and, in flexible docking, conformations. In the present study, fractionated methanolic extract was used for cytotoxic activity studies and found to be very effective. Detailed analysis of this fraction revealed that the major compound present in the fraction is quercetin, a flavanoid compound.

Keywords: Docking analysis, anti tumor activity, *Tamilnadia uliginosa*

Computer- aided drug design is a recent and emerging discipline. It uses computational chemistry to discover, enhance, study drugs and relate to biologically active molecules. The molecular designing of drug relies on knowledge of molecular properties, molecular structure, and functional groups present and molecular geometry. Drugs are small molecules that are designed to bind, interact and modulate the activity of specific biological receptors and are specifically known as "ligands". Receptors are proteins that bind and interact with these small molecules to perform the numerous functions vital for sustaining the life, and they are appropriately referred to as target molecules. (Rastogi *et al*. 2011). There are three basic approaches for computer aided drug designing, such as target-based drug design, ligand- based drug design and *de novo* approach. The target-based drug design approaches are a series of computational procedures, including visualization tools, to support the decision systems of drug design/discovery process. It includes different components such as target identification, protein modeling, molecular dynamics simulations, binding/catalytic sites identification, docking, virtual screening, fragment based strategies, substructure treatment of targets in tacking drug resistance and structural vaccinology. The ligand-based drug design relies on knowledge of other molecules that bind to the biological target of interest. In other words, a model of the biological target may be built based on the knowledge of what binds to it, and this model in turn may be used to design new molecular entities that interact with the target.

Drug design and discovery play a pivotal role in driving research in computational chemistry and biology (Cummings *et al*. 2005; Grzybowski *et al*. 2002; Schneider *et al*. 2002; Taylor *et al*. 2002; Warren *et al*. 2006; Kitchen *et al*. 2004). In computational drug design and discovery, it is often necessary to determine, as a first step, the binding of a ligand to a target protein. The computational scheme for predicting ligand binding occurrence, affinity, and

orientation is commonly referred to as "molecular docking", which has been a topic of intensive research for decades (Halperin *et al*. 2002). The development of a molecular docking tool usually starts with an efficient search algorithm, which places the ligand in the active site of the target protein in numerous different positions, orientations, and, in flexible docking, conformations. These are then evaluated by a scoring function to distinguish between good (near-native) and bad (decoy) docking solutions. The two aspects of searching and scoring can be, and usually have been, developed and evaluated separately, although one clearly affects the other and a balance is often sought to meet specific study aims Ferrara *et al*. 2004; Wang *et al* ; 2003).

MATERIALS AND METHODS

The data retrieved from Discovery studio, Protein data bank (PDB), and PubChem. Software were used for docking

Discovery Studio

Discovery Studio is a comprehensive software suite for analyzing and modeling molecular structure, sequence, and other relevant data. It is developed and distributed by Accelrys. It offers an interactive environment for viewing and editing molecular structure, sequence, x-ray reflection data scripts, and other data. A wide variety of tools are offered for working and visualizing data. It provides of ware applications including simulation, ligand design, Pharmacophore modeling, and structure based design, ADME (Absorption/ Administration, Distribution, Metabolism and Excretion). Sometimes, the potential or real toxicity of the compound is taken into account (ADME-Tox or ADMET). It makes use of software algorithms namely CHARMM, MODELLER, ZDOCK. It provides all the functionality required for docking ligand in to protein binding site from prepared input files.

Protein Data Bank (PDB)

The protein structure is relieved from Protein Data Bank. It is maintained by the organization Worldwide Protein Data Bank (wwPDB). The data obtained from X-ray diffraction, NMR, electron microscopy are submitted to PDB. Each entry in the PDB has a PDB ID which is an alpha numeric character. PDB data format is followed for downloading structures. Molecular structures are downloaded from PDB with an extension .pdb. BCL-XL was selected as the target and the structure was down loaded from the PDB with PDB ID 3SP7.

PubChem

PubChem is a database of chemical molecules and their activities against biological assays. Their structural and biological activity information is maintained by National Centre for Biotechnology Information (NCBI). It consists of 3 primary databases such as PubChem Compound which includes 54 million entries; PubChem Substance which includes 163.5 million entries and PubChem Bio Assay. Unique compound identification number is assigned for each entry in the PubChem data base. The SDF file of the 13 phytochemicals of *T. uliginosa* were retrieved and saved as SDF format.

RESULTS AND DISCUSSION

The 13 analyzed phytoconstituents of *T.uliginosa* showed good docking scores with hydrogen bond interaction, the docking score of quercetin being 103.874 with Arg 34 and Arg 6 (Table 1&2).

Out of the different phytochemicals of *T. uliginosa* subjected to docking, cynaroside showed better score though comparable scores were observed in others also. These compounds are flavonoids with reported antitumor activity. Major docking scores of the following phytochemicals such as vitexin (133.929), Nonacosane (135.184), Quercetin - 3-o- galactoside (129.272), Rutin (115.177), Quercetin (103.784), Myrectin (103.027), Luteolin (102.516), Kaemferol (102.13), and Isoramnetin (101.63). Nonacosane showed good libdock score but it has no active hydrogen bonding interaction. By analyzing the energy of the complex with target protein, ciscaffeic acid, ferulic acid, luteolin and nonacosaneare found showing least energy.

Table 1: Docking result of BCL XL apoptosis regulator protein with phytochemicals from *Tamilnadia uliginosa*

Sl. No.	Name of the Compound	Absolute Energy	Lib Dock Score	Interacting Residues
1	Apigenin	37.6335	98.4719	Val 10, Arg 34, Glu 32, Glu 36
2	Cis-Caffeic acid	31.083	62.0744	Asp 29
3	Cynaroside	66.3999	148.442	Glu 7, Glu 31, Glu 32, Thr 35, Asp 29
4	Ferulic acid	33.5314	91.2861	Thr 35, Asp 29
5	Isoramnetin	53.2131	101.63	Val 10, Arg 6, Arg 34
6	Kaempferol	40.3869	102.13	Arg 6, Arg 34
7	Luteolin	34.4521	102.516	Val 30, Trp 24, Glu 32
8	Myrectin	42.209	103.027	Trp 24, Glu 7, Arg 34
9	Nonacosane	16.9088	135.184	No residues
10	Quercetin-3-o-galactoside	56.8567	129.272	Ser 28, Trp 24, Thr 35, Arg 34
11	Quercetin	41.3176	103.784	Arg 6, Arg 34
12	Rutin	79.7624	115.177	Ser 28, Asp 29, Glu 32, Glu 3
13	Vitexin	59.3188	133.929	Glu 3, Glu 7, Arg 34, Glu 34, Glu 32, Trp 24

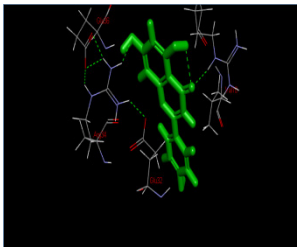

Fig. 1

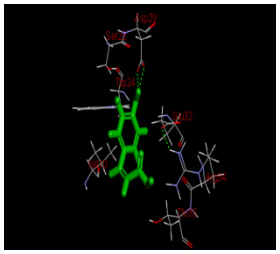

Fig. 2

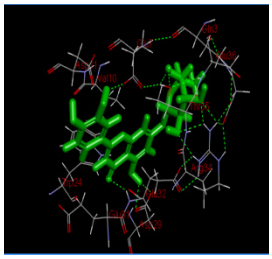

Fig. 3

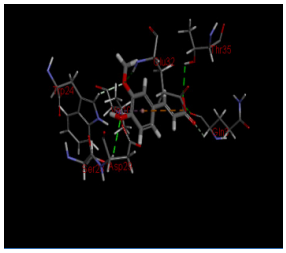

Fig. 4

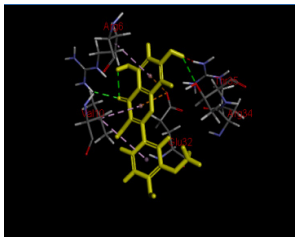

Fig. 5

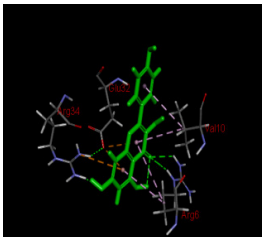

Fig. 6

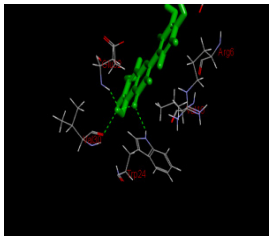

Fig. 7

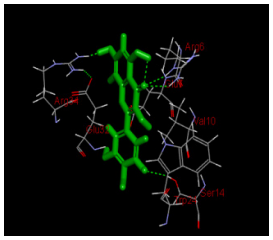

Fig. 8

Fig. 9

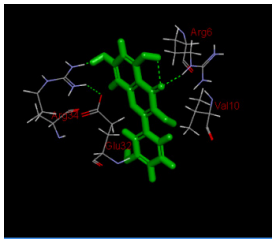

Fig. 10

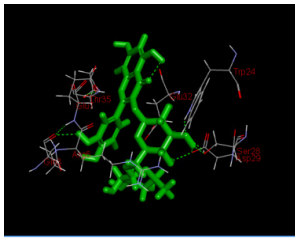

Fig. 11

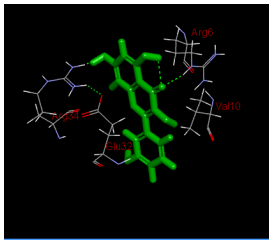

Fig. 12

In the present study, fractionated methanolic extract was used for cytotoxic activity studies and found to be very effective. Detailed analysis of this fraction revealed that the major compound present in the fraction is quercetin, a flavanoid compound. So the study concluded that activity of quercetin is responsible for the antibacterial, cytotoxic and anti-tumor activity of the plant extract. Docking study also confirmed antitumor activity of quercetin.

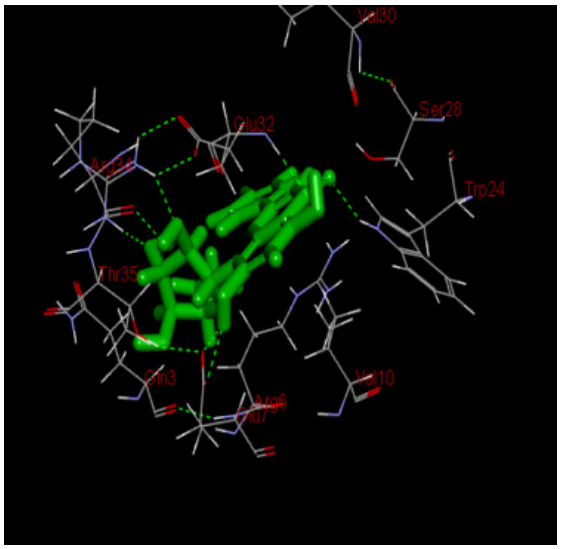

Fig. 13

Table 2.

Sl. No.	Name of the Compound
1	Interaction of aminoacids of Bcl Xl with apigenin
2	Interaction of aminoacids of Bcl Xl with cis Caffeic acid
3	Interaction of aminoacids of Bcl Xl with cynaroside
4	Interaction of aminoacids of Bcl Xl with ferulic acid
5	Interaction of aminoacids of Bcl Xl with Isoramnetin
6	Interaction of aminoacids of Bcl Xl with Kaempferol
7	Interaction of aminoacids of Bcl Xl with luteolin
8	Interaction of aminoacids of Bcl Xl with myrectin
9	Interaction of aminoacids of Bcl Xl with Nonacosane
10	Interaction of aminoacids of Bcl Xl with Quercetin 3 o galactoside
11	Interaction of aminoacids of Bcl Xl with Quercetin
12	Interaction of aminoacids of Bcl Xl with 5rutin
13	Interaction of aminoacids of Bcl Xl with vitexin

REFERENCES

1. Cummings, M.D., DesJarlais, R.L., Gibbs, A.C., Mohan, V. and Jaeger, E.P. 2005. Comparison of automated docking programs as virtual screening tools. *J. Med. Chem.,* **48**(4): 962–976.
2. Ferrara, P., Gohlke, H., Price, D.J., Klebe, G. and Brooks, C.L. 2004. Assessing scoring functions for protein-ligand interactions. *J. Med. Chem.,* **47**(12): 3032–3047.
3. Grzybowski, B.A., Ishchenko, A.V., Shimada, J. and Shakhnovich, E.I. 2002. From knowledge-based potentials to combinatorial lead design *in silico*. *Acc. Chem. Res.,* **35**(5): 261–269.
4. Halperin, I., Ma, B., Wolfson, H. and Nussinov, R. 2002. Principles of docking: An overview of search algorithms and a guide to scoring functions. *Proteins,* **47**(4): 409–443.
5. Kitchen, D.B., Decornez, H., Furr, J.R. and Bajorath, J. 2004. Docking and scoring in virtual screening for drug discovery: methods and applications. *Nat. Rev. Drug Discov.,* **3**(11): 935–949.
6. Rastogi, S.C., Mendiratta, N. and Rastogi, P. 2011. Bioinformatics: Methods and Applications, pp. 463-482.
7. Schneider, G. and Bohm, H.J. 2002. Virtual screening and fast automated docking methods. *Drug Discov. Today,* **7**(1): 64–70.
8. Taylor, R.D., Jewsbury, P.J. and Essex, J.W. 2002. A review of protein-small molecule docking methods. *J. Comput. Aided Mol. Des.,* **16**(3): 151–166.
9. Warren, G.L., Andrews, C.W., Capelli, A.M., Clarke, B., LaLonde, J., Lambert, M.H., Lindvall, M., Nevins, N., Semus, S.F., Senger, S., Tedesco, G., Wall, I.D., Woolven, J.M., Peishoff, C.E. and Head, M.S. 2006. A critical assessment of docking programs and scoring functions. *J. Med. Chem.,* **49**(20): 5912–5931.
10. Wang, R., Lu, Y. and Wang, S. 2003. Comparative evaluation of 11 scoring functions for molecular docking. *J. Med. Chem.,* **46**(12): 2287–2303.