Molecular Docking: A dynamic procedure for structure-based pharmaceutical analysis.

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Abstract

Docking studies of metabolites Lupeol from *Alhagi maurorum* to receptor tyrosine kinase (3GQL) and Urospermal-A-15-O-acetate from *Dicoma tomentosa* to receptors GABA (6D6U) and 5HT3 protein (4PIR) were performed.

Introduction

Molecular docking is computer based technology. The goal of this technology is interpretation of 3D structure of particular molecule. This software mainly helpful in drug discoveries. This technique is interpretation a collection of expensive technology for drug formation and identification. The main crucial advantage of molecular docking is virtual screening. A quality of this technique was used to photos the 3D structure of the protein molecule and docking gain can also be identification. This technique is a crucial tool in computer-assist drug design. Docking can be worn to execute virtual screening on large libraries of compounds, rank the results, and suggest structural hypotheses of how the ligands reduce the target, which is precious in lead optimization.

Materials and Methods

To study the interaction of our compounds with receptor molecules we performed molecular docking of the metabolites in the binding sites of drug target protein molecules i.e. Tyrosine kinase (3GQL), GABA (6D6U) and 5HT3 protein (4PIR). Structure files of chemical compounds lupeol and Urospermal-A-15-O-acetate were downloaded from pubchem and receptor protein molecules 3GQL, 6D6U and 4PIR of *Homo sapiens* were downloaded from Protein Data Bank. Molecular docking studies were performed by using PyrX for docking, Lupeol was docked with tyrosine kinase of *Homo sapiens* (3GQL) and Urospermal-15-o-acetate with 5HT3 (4PIR) and

GABA receptor (6D6U). Both the compounds were docked on their respective receptor molecules. Pymol was used for visualization of the docked structures and Ligplus was used for studying ligand-protein interactions in the docked structures.

Results

ΔG was used to score different orientation of ligand molecules in the domain of receptor molecules and to calculate affinity of the ligand molecule with the receptor molecule. ΔG scores of the best poses are presented in Table 1, Table 2 and Table 3. It was analyzed that the ligand molecules bound within the domain of the protein where the native ligand was present in the crystallized structure. Fig 1 shows docked structure of lupeol with receptor tyrosine kinase, Fig 2 shows docked structure of Urospermal-A-15-O-acetate with GABA and Fig 3 shows docked structure of Urospermal-A-15-O-acetate with 5HT3. Binding of the ligand molecules within the active site of the molecules suggests that protein activity will be inhibited after binding of the ligand molecule.

Table 1

S. No	Ligand molecule	Drug Target PDB id	Binding affinity Estimated Free Energy ΔG (Kcal/mol)	Rmsd/ub	Rmsd/lb
1	Lupeol	3GQL	-8.8	0	0
2	1b	3GQL	-7.9	3.758	1.556
3	1c	3GQL	-7.9	62.813	60.016
4	1d	3GQL	-7.8	44.058	41.207
5	1e	3GQL	-7.6	49.473	46.556
6	1f	3GQL	-7.6	48.789	45.614

Table 2

S. No	Ligand molecule	Drug Target PDB id	Binding affinity Estimated Free Energy ΔG (Kcal/mol)	Rmsd/ub	Rmsd/lb
1	Urospermal-A-15-O-acetate	6D6U	-7.5	0	0
2	2b	6D6U	-7.1	86.254	83.504
3	2c	6D6U	-7	10.714	7.509
4	2d	6D6U	-6.9	4.532	2.504
5	2e	6D6U	-6.9	4.666	2.079
6	2f	6D6U	-6.7	5.642	2.458

Table 3

S. No	Ligand molecule	Drug Target PDB id	Binding affinity Estimated Free Energy ΔG (Kcal/mol)	Rmsd/ub	Rmsd/lb
1	Urospermal-A-15-O-acetate	4PIR	-7.7	0	0
2	3b	4PIR	-7.5	46.54	44.003
3	3c	4PIR	-7.5	50.445	47.347
4	3d	4PIR	-6.9	51.421	48.076
5	3e	4PIR	-6.6	58.234	56.278
6	3f	4PIR	-6.6	55.551	53.12

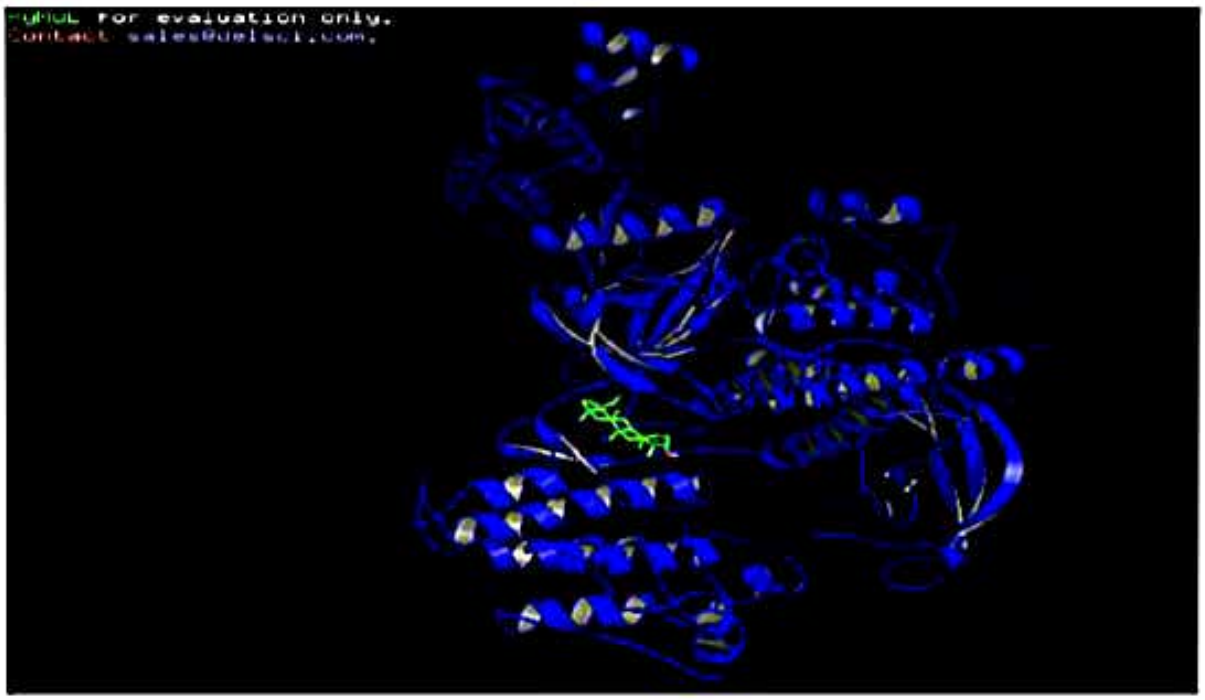
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Fig 1a

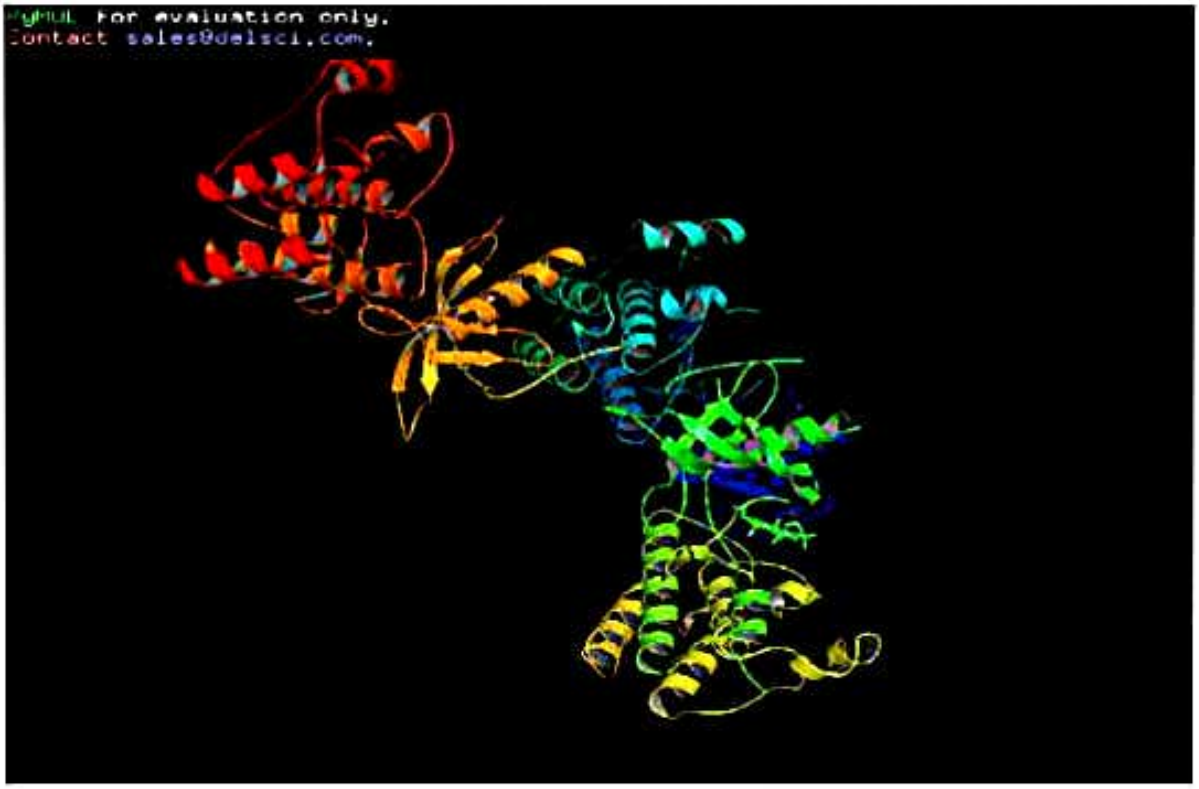
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Fig 1b

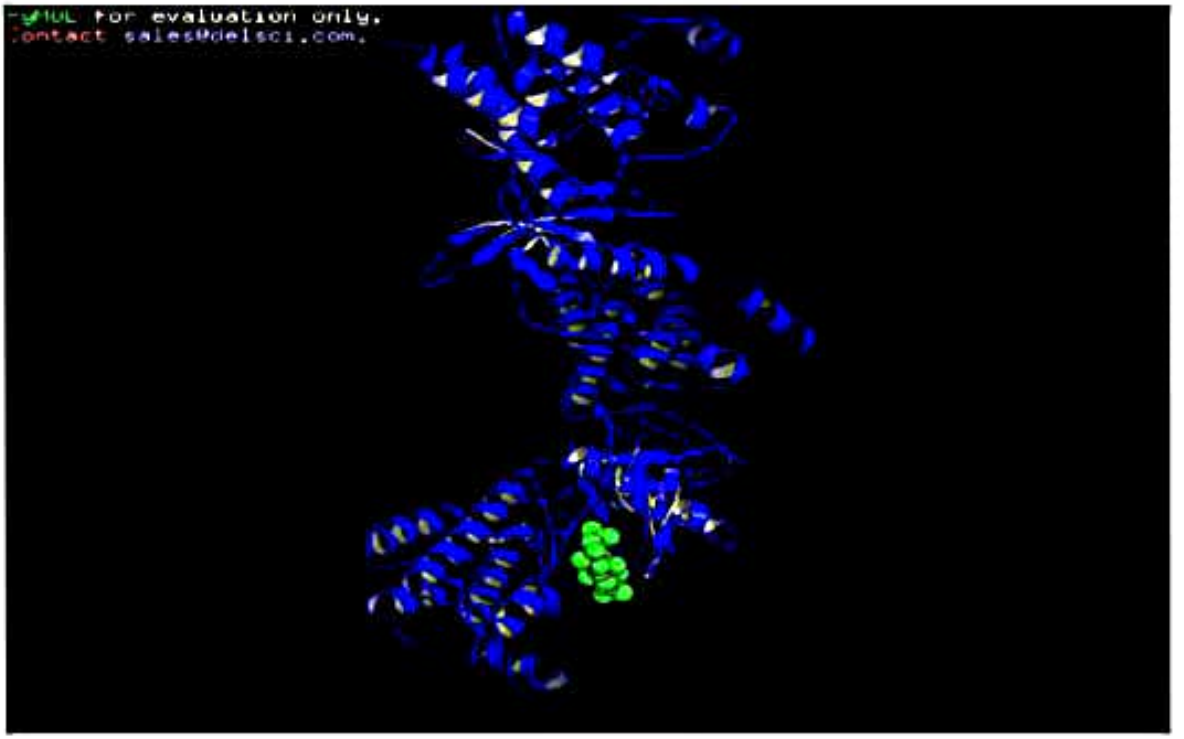


Fig 1c

Fig 1d

Fig 1. Receptor tyrosine kinase (3GQL) with Lupeol

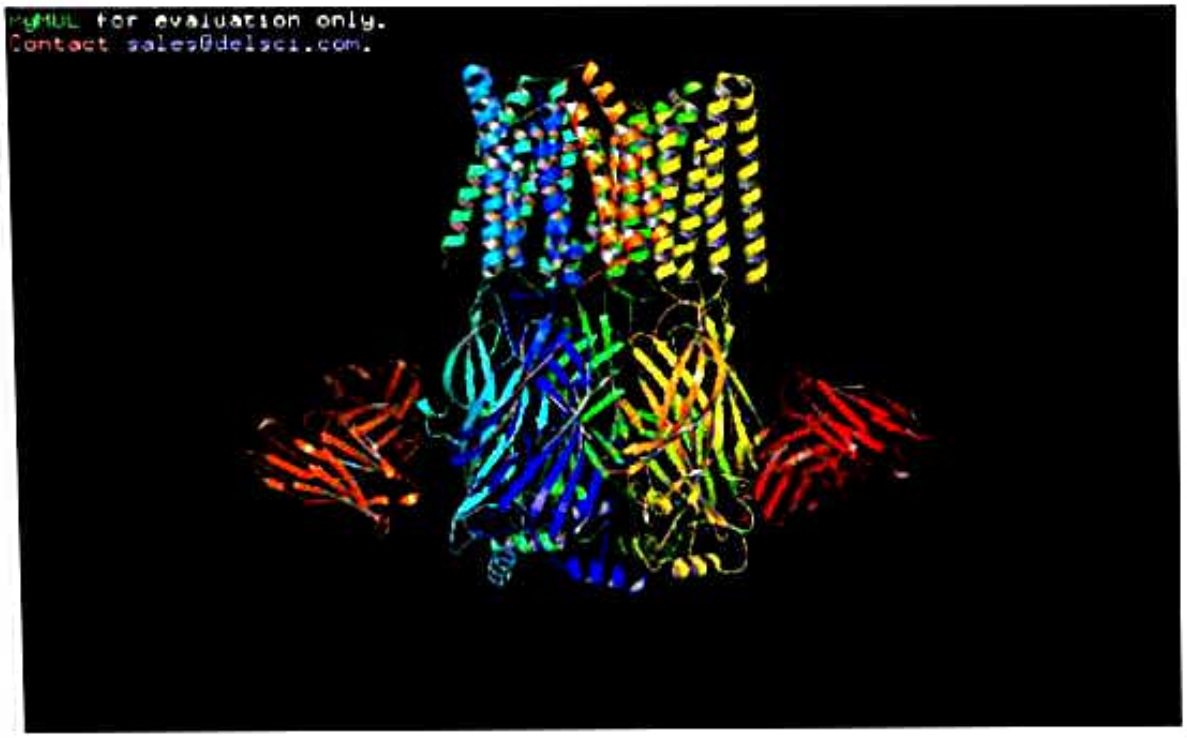


Fig 2 a

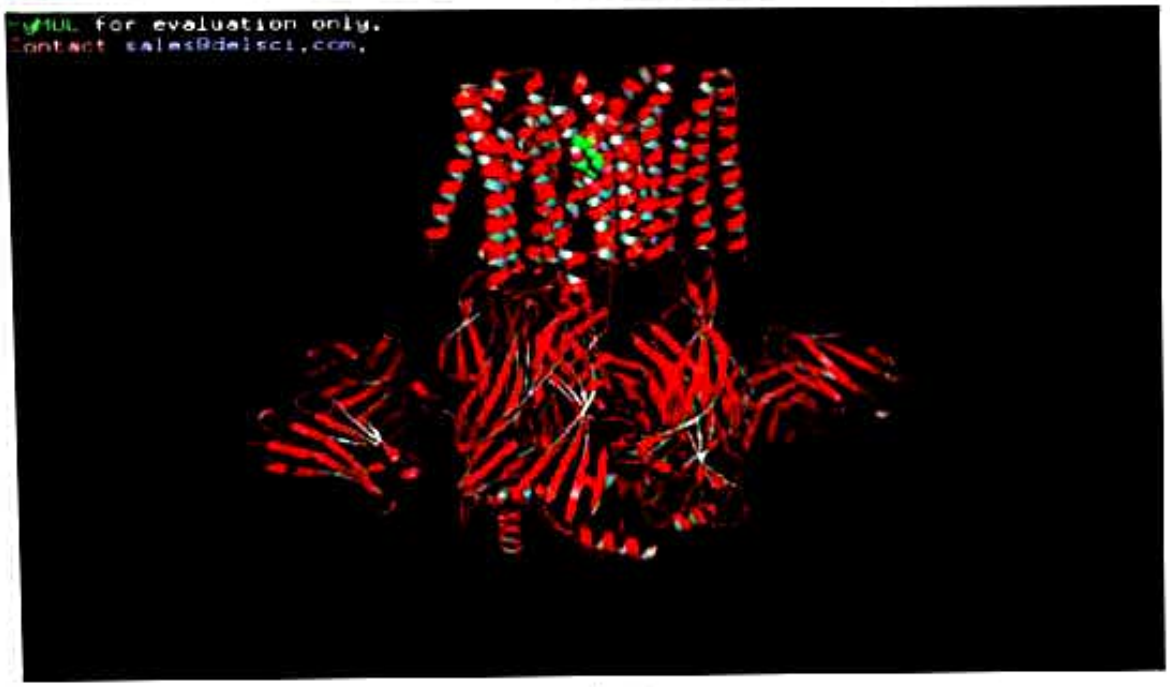
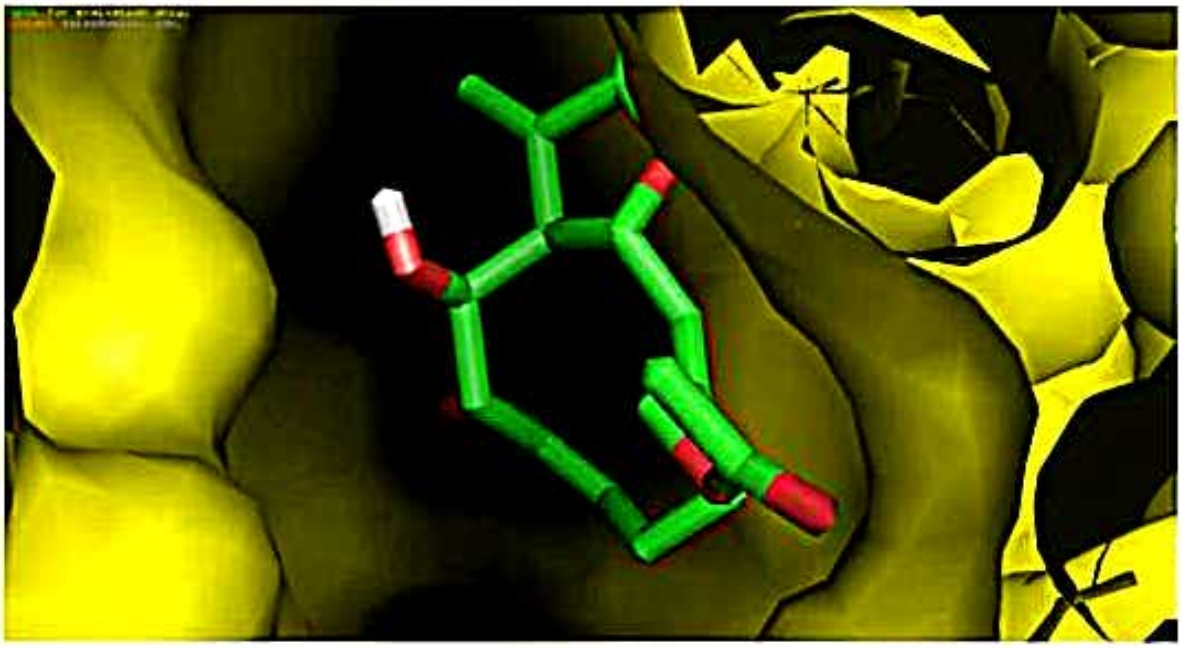


Fig 2b



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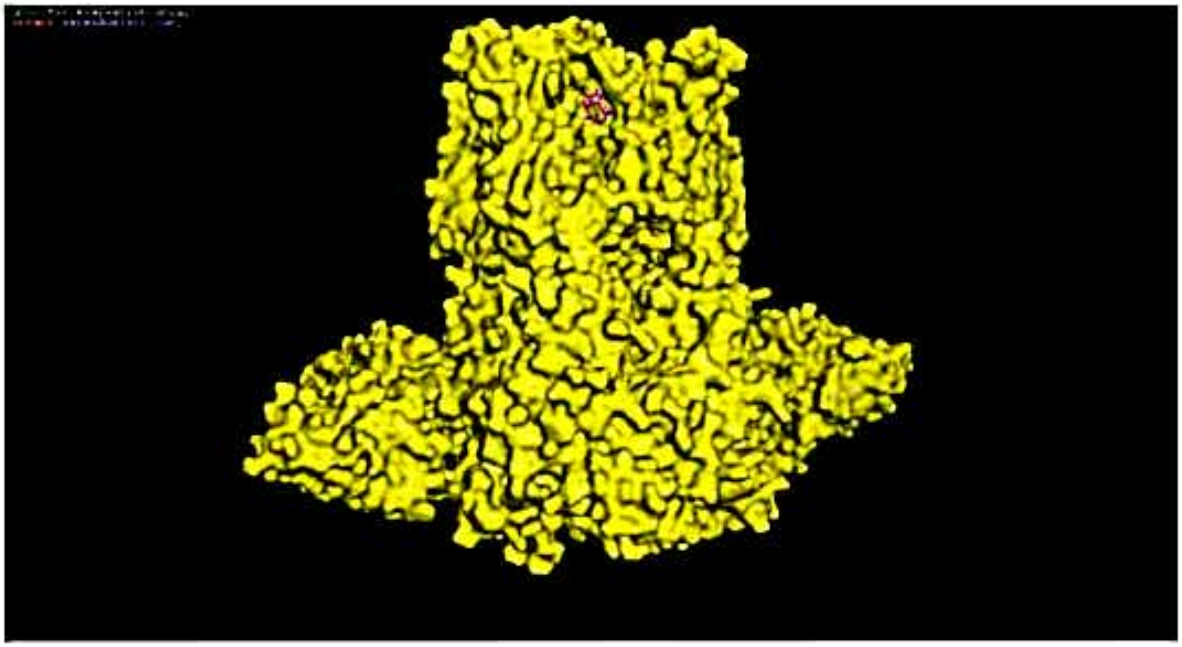

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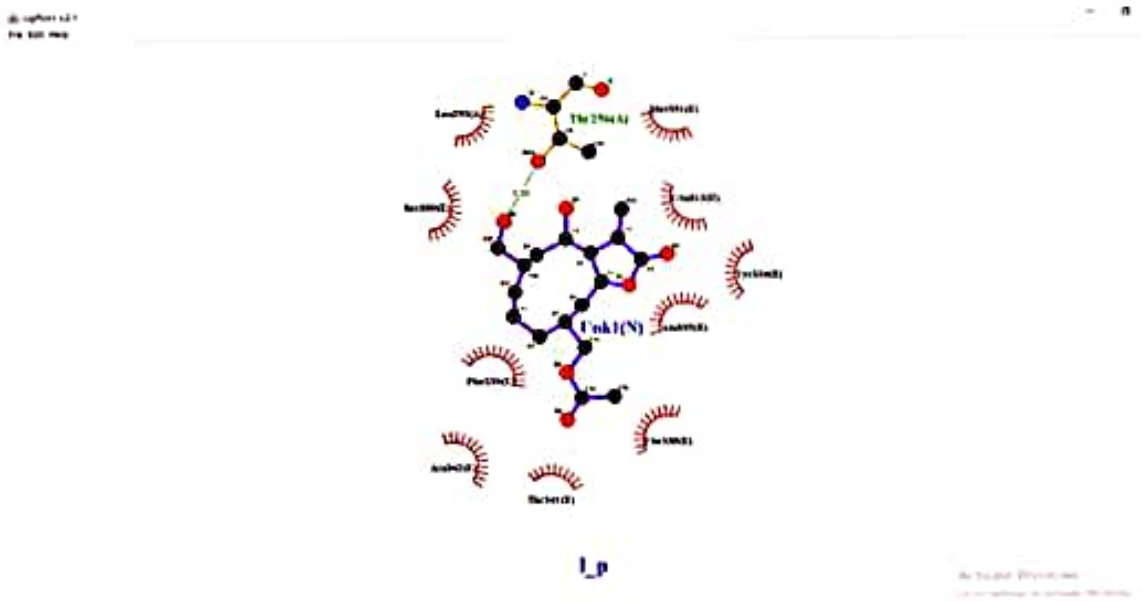

Fig 2e

Fig 2. Urospermal-A-15-O-acetate with GABA (6D6U)

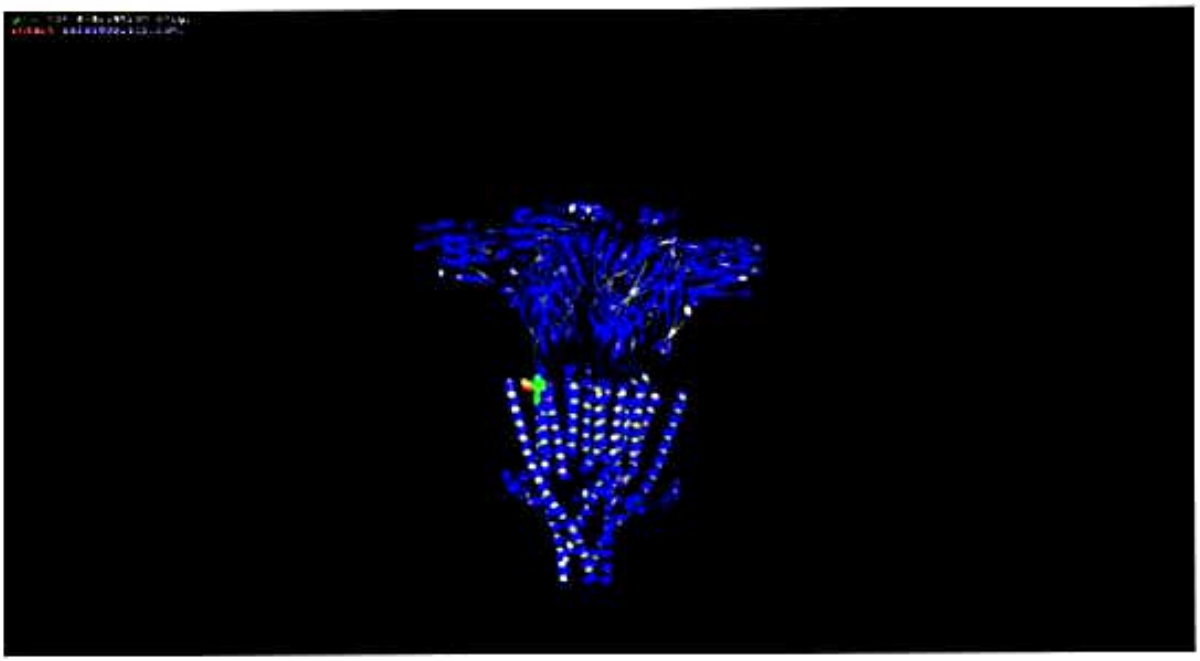

Fig 3a

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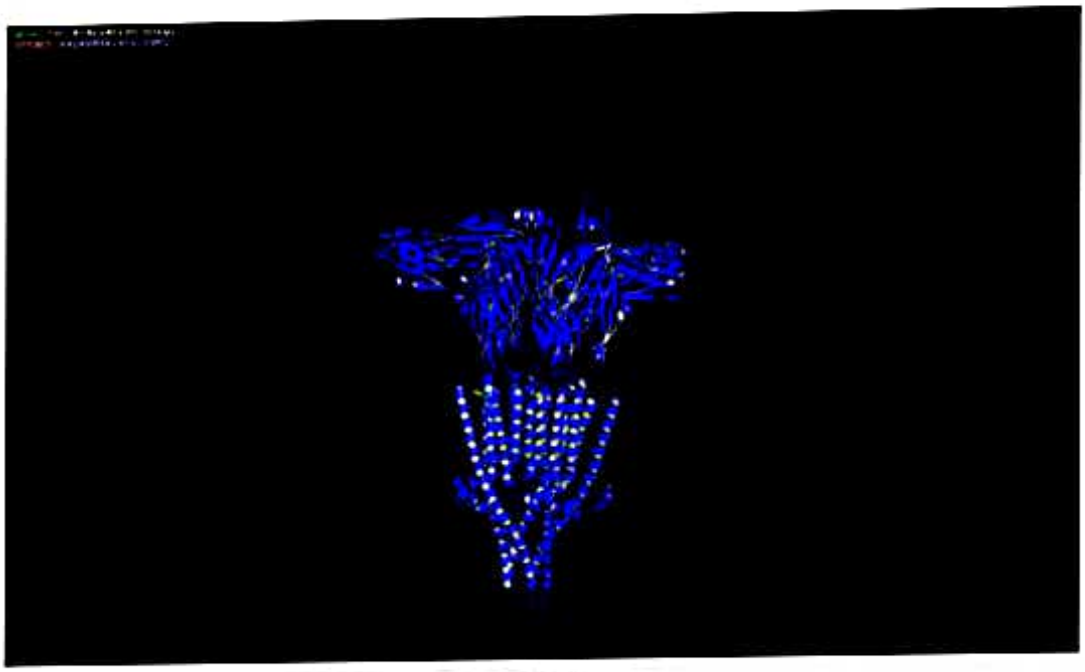

Fig 3b

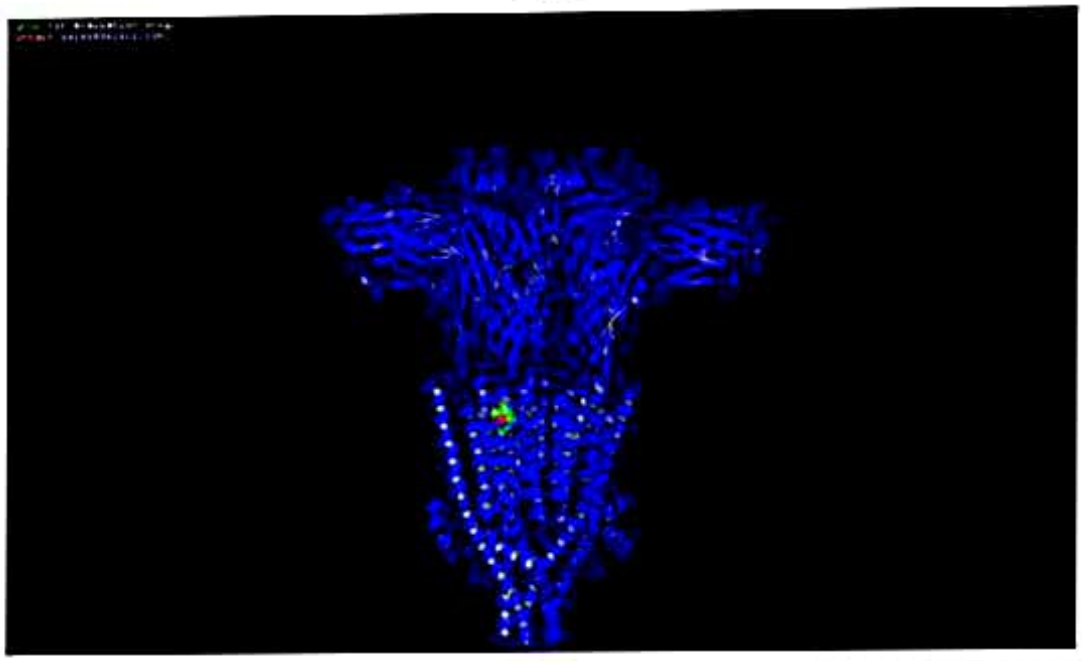

Fig 3c

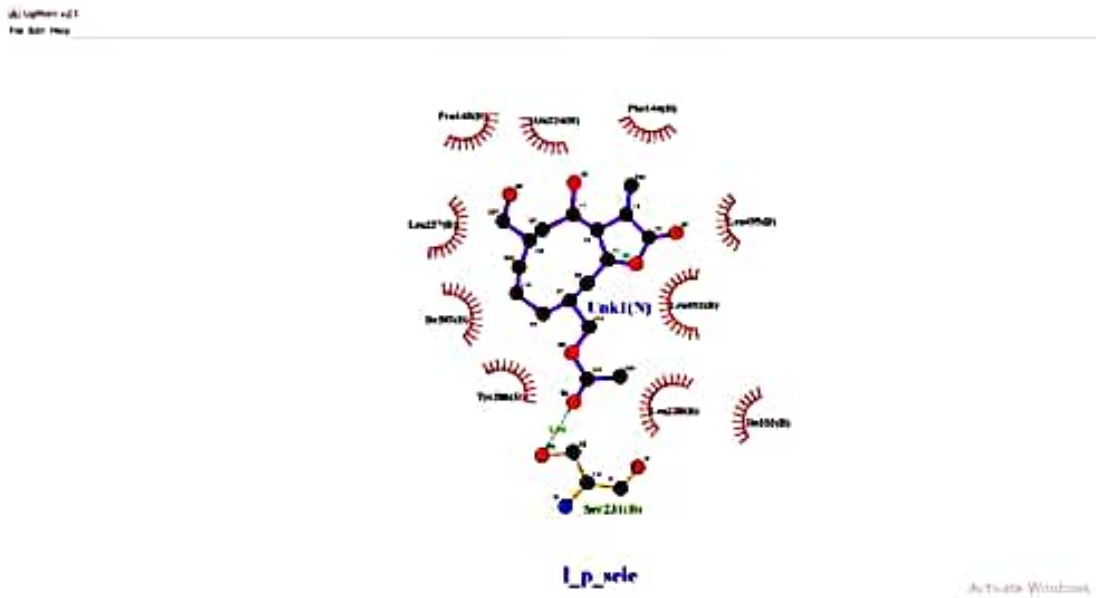

Fig 3d

Fig 3. Urospermal-A-15-O-acetate with 5HT3 (4PIR)

Discussion

Docking studies are required to analysis the interaction of ligand molecule with the receptor molecules. Through docking technique we can analysis the orientation of ligand molecules according to their least ΔG, which can help us in calculating prolong binding of the protein molecule with the receptor molecule. Orientation of ligand molecules according to prolong binding are analyzed in the three tables. ΔG change i.e. maximum value in negative will be considered as the orientation having maximum prolong binding.. All the three molecules showed to bind within the binding domain where the native ligand was present (ligand present in the crystal structure of the protein molecule). Docking was performed PyrX software. Molecular visualization was done by Pymol and for studying protein-ligand interaction Ligplus was used.

References

Laskowski R A, Swindells M B (2011). LigPlot+: multiple ligand-protein interaction diagrams for drug discovery. *J. Chem. Inf. Model.*, 51, 2778-2786. [PubMed id: 21919503]

Dallakyan S., Olson A. J. (2015). Small-molecule library screening by docking with PyRx. *Methods Mol. Biol.* 1263 243–250. 10.1007/978-1-4939-2269-7_19

The Pymol Molecular Graphics System, Version 2.0 Schrodinger, LLC