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Docking of Hematoporphyrin on various Anticancer Drugs targeting enzymes

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ABSTRACT

The present study deals with docking of Hematoporphrin with various anticancer drugs targeting enzymes. The targets used were PDB-ID 2Y3I, PDB-ID 3OZZ, PDB-ID 3UEN and PDB-ID 4O33. Hematoporphyrin docked with these enzymes and interactions between the enzyme and compound were measured and compared with standard Paclitaxel. The study concluded that, the compound (Hematoporphyrin) isolated from plant were high interactions with PDB-ID 4O33 when compared to standard.

Keywords: Docking, Hematoporphyrin, Paclitaxel, Protein Data Bank, Interactions.

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INTRODUCTION

Docking is the technique which envisages the preferred orientation of one molecule to a second when bound to each other to form a stable complex in three dimensional spaces. In cell biology, the function of proteins is a result of its interaction (i.e. docking) with other proteins as well as other molecular components. Thus the results of the docking are exceptionally beneficial in finding drugs which are effective against particular disease. Knowledge of the favored orientation in turn may be used to predict the strength of association or binding affinity between two molecules using scoring function.

Docking tools are based on the search, algorithm and the scoring function. A search algorithm finds the best docking pose measured by the scoring function. A scoring function differentiates correct docking poses from incorrect ones.

The quality of any docking results depends on the reasonable starting structures of both the protein and the ligand. The protein and ligand structures require preparation before docking in order to achieve the best docking results.

Docking analysis of bioactive compounds i.e. ligands was carried out by Argus lab docking software. Docking virtually screen a set of compounds and predict the strongest binding capacity based on various scoring function. It explores ways in which two molecules such as ligand and receptor (protein) fit together and docks to each other well. The molecule binding to a receptor inhibits its function and thus acts as drug.

Argus lab 4.0 distributed freely for windows platforms by planaria software. It is an introductory molecular modeling package with academics. Argus docking engine implementry in Argus lab approximates an exhaustive search method which is similar to DOCK and GLIDE. Flexible ligand docking is possible with Argus lab, where the ligand is described as torsion tree and grids are constructed that overlay the binding site. The accuracy of the Argus lab docking algorithm takes into account, the key features such as the nature of the binding site and the number of rotatable bonds to the ligand.

Molegro molecular viewer: Molegro molecular viewer is an application which helps in analyzing the energies and interaction of the binding site.

MATERIALS AND METHOD

Biological Target

There are various biosynthetic enzymes that are essential for the survival of the human and are considered as potential drug targets. Some of the targets are

- Human PGK in complex with L-ADP, 3PG And TSA Aluminium tetrafluoride (2Y3I)[2-4]
- Cytochrome b5 core swab mutant (3OZZ)
- Top BP1 BRCT4/5 domain (3UEN)[5,6]
- Human PGK1 3PG and tetrazosin (TZN ternary complex, 4O33)[7]

Ligand preparation

- Draw the structure from chem. Sketch and save as MDL mol format.
- Import the ligand into workspace of Argus lab.
- Clean geometry → clean hybridization.
- Select the ligand, right click on the mouse → make a group from the residues → give name→ ligand→ OK.

Protein preparation

Step 1:

- Enter protein PDB-ID (2Y3I, 3OZZ, 3UEN, 4O33) in the protein data bank.
- Go to download files and select pdb as text file.
- Save the downloaded pdb text file to desktop.

Step 2:

- Open Argus lab file → open → Import pdb file from the desktop.
- 3D structure of the protein will appear in the workspace of Argus lab.
- Left side of the screen shows molecular tree view.
- Open pdb → open 'Residues' → open 'Misc'.
- From 'Misc' delete the inhibitor and hetero residues, do not delete cofactor.
- Open water press shift, select all water molecules and delete.
- Add hydrogen atoms.
- Go to calculation on toolbar → energy by UFF method → start.
- Save the prepared protein as *.agl file format in the desktop.

Docking Parameters

- Select calculation from the toolbar → Dock a ligand
- 'Argus Dock' as the Docking engine
- 'Dock' was selected as calculation type
- 'Flexible' for the ligand
- Ascore as the scoring function
- Calculation size

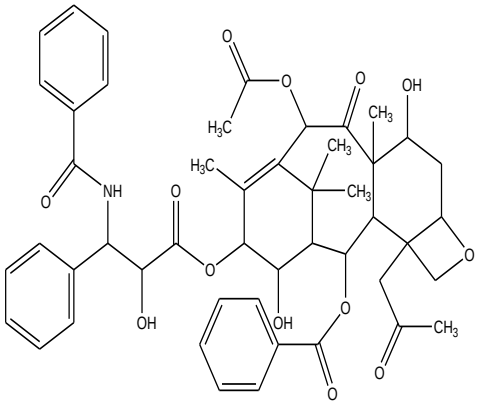
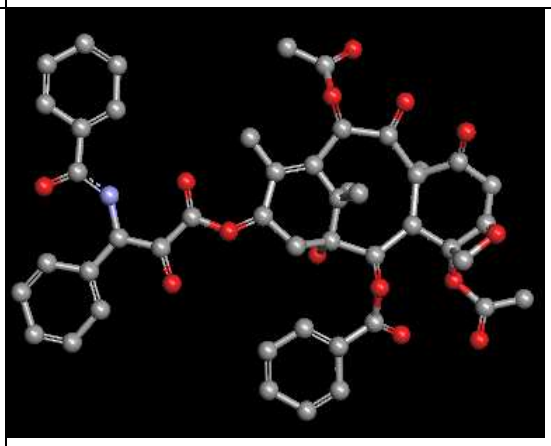
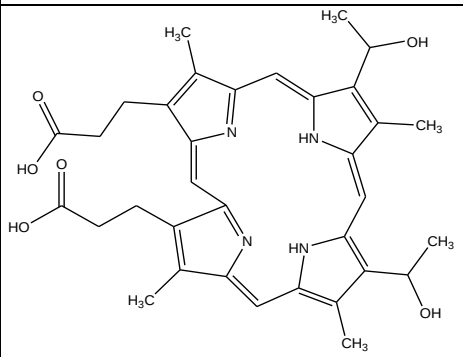
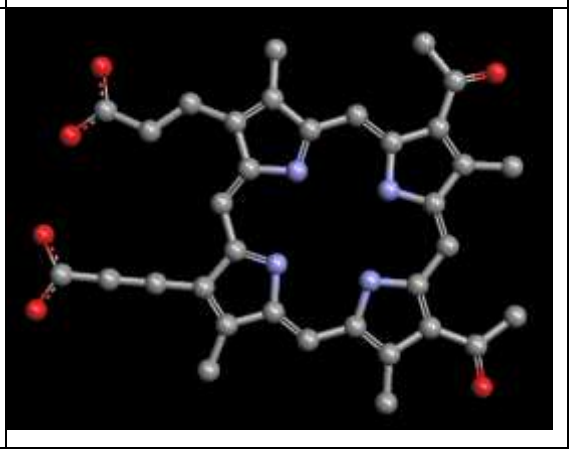
- Start docking
- Save the Docked protein Ligand complex as Brookhaven pdb files (*.pdb)

Visualization/ Interpretation of Docking

Molegro molecular viewer will help in analyzing the energies and interaction of the binding.

RESULTS AND DISCUSSION

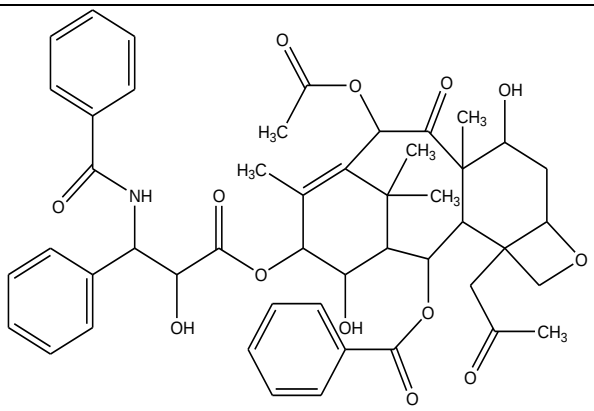
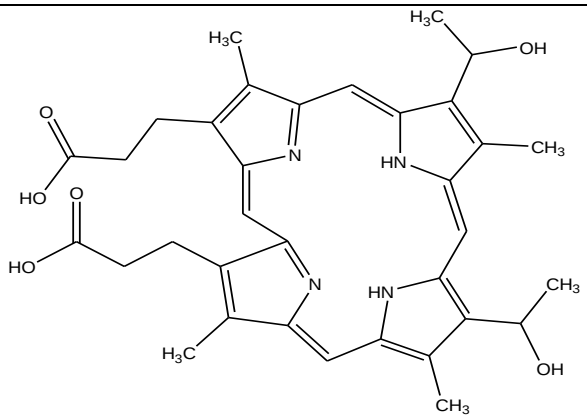
Table 1: 2D and energy minimized 3D structures of standard and IBC32

Ligand code	2D structure	Energy minimized 3D structure
PAC		
IBC32		

Docking scores of compounds against multiple target enzymes

The docking scores of the compounds ranges from -12.79 to-8.92 kcal/mol on all the target enzymes and were summarized in Table 2, 3, 4 and 5.

Table 2: Docking scores of compounds on PDB-ID 4O33

Ligand code	Structures	PDB-ID	Docking Scores (Kcal/mol)
PAC		4O33	-11.0293
IBC32			-11.0687

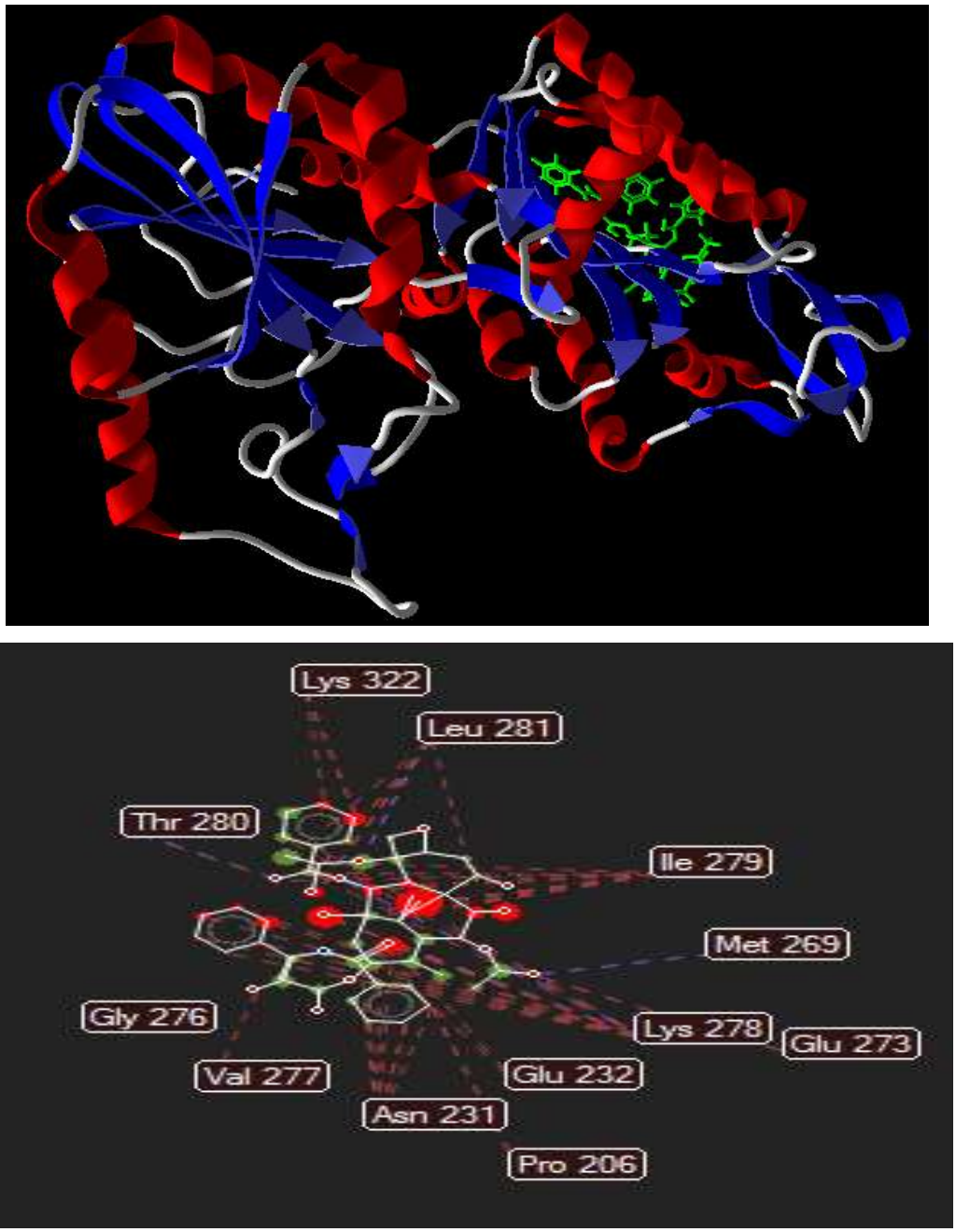


Figure 1: Paclitaxel docked with PDB-ID 4O33 and its interactions

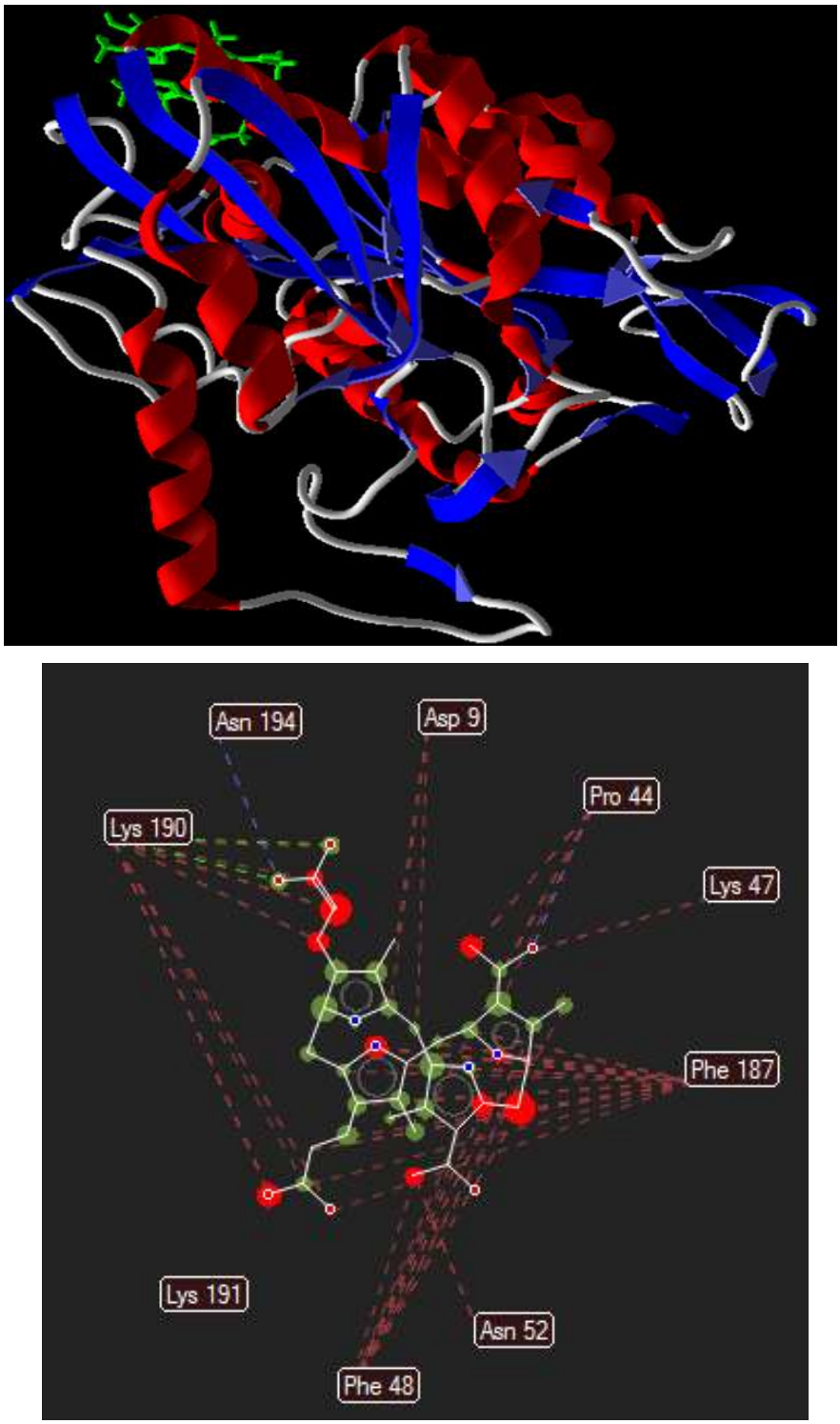
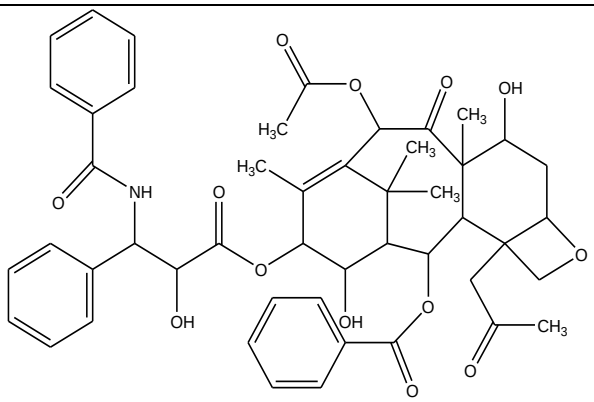
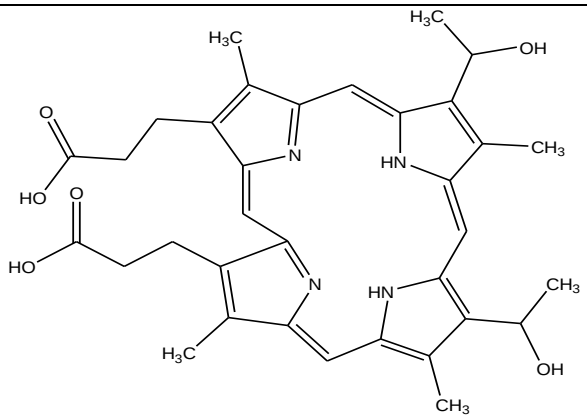


Figure 2: IBC32 docked with PDB-ID 4O33 and its interactions

Table 3: Docking scores of compounds on PDB-ID 2Y3I

Ligand code	Structures	PDB-ID	Docking Scores (kcal/mol)
PAC		2Y3I	-12.7911
IBC32			-10.7869

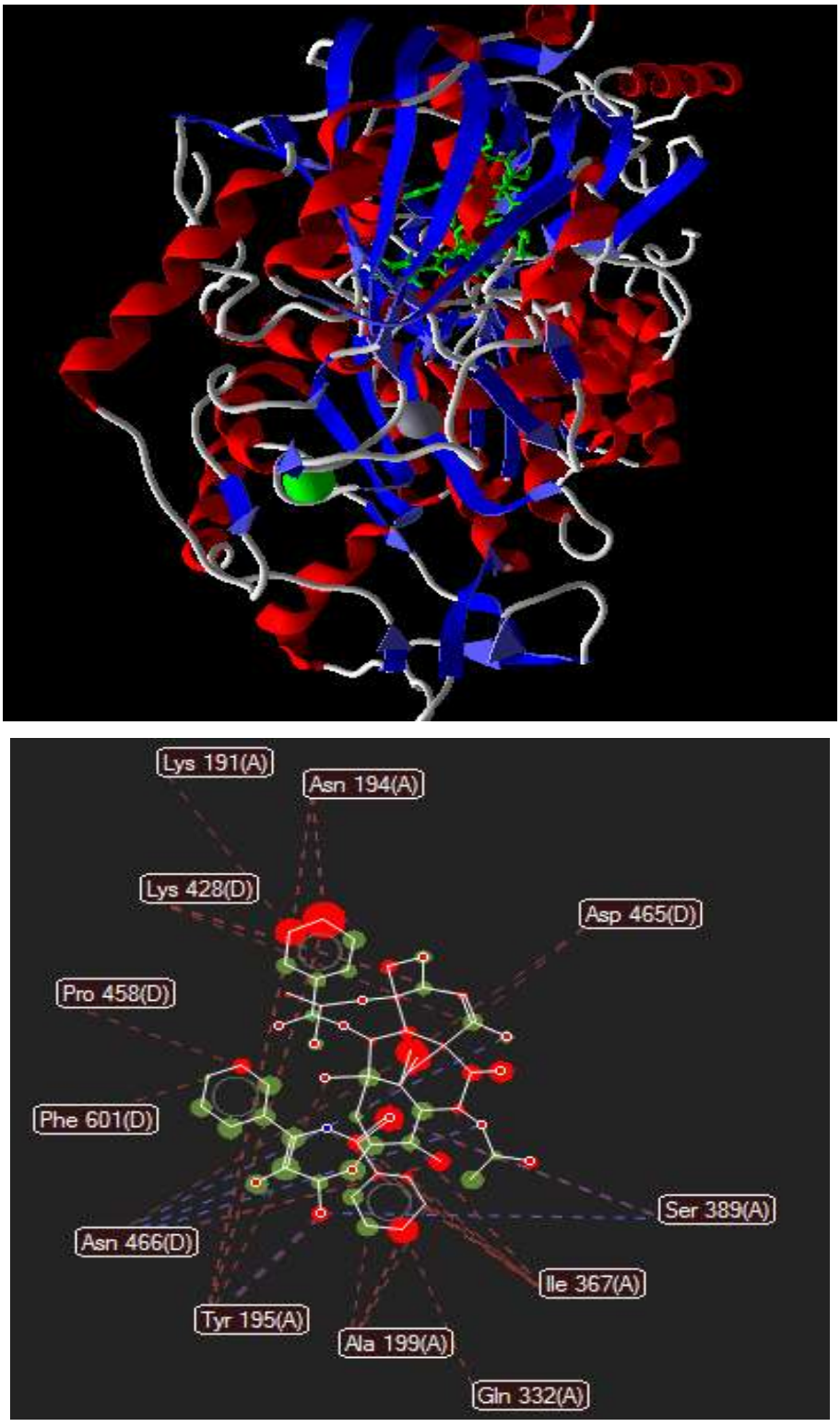


Figure 3: Paclitaxel docked with PDB-ID 2Y3I and its interactions

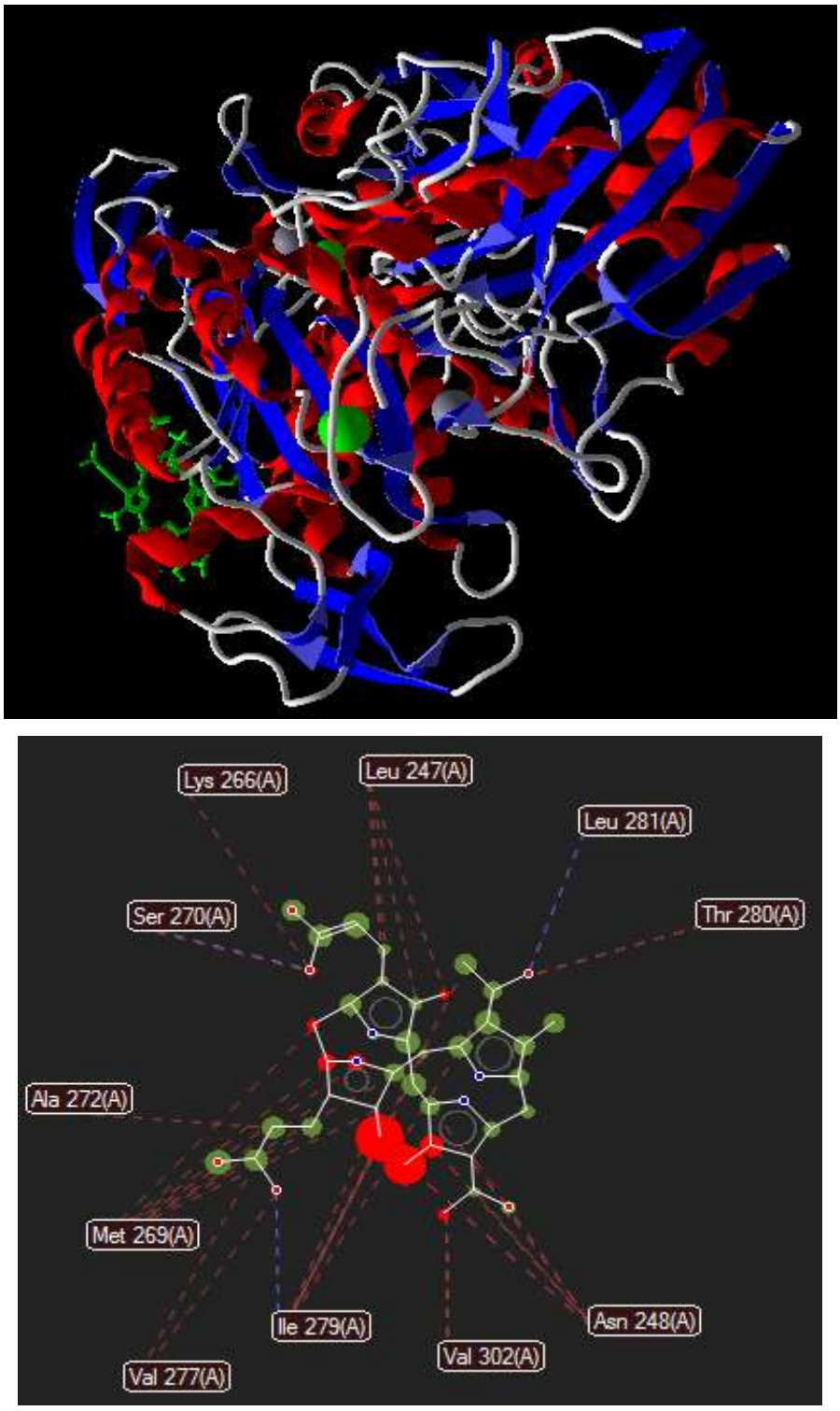
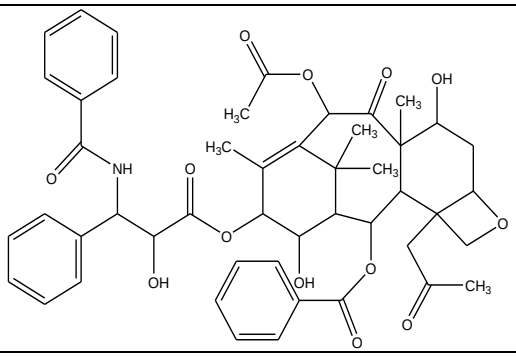
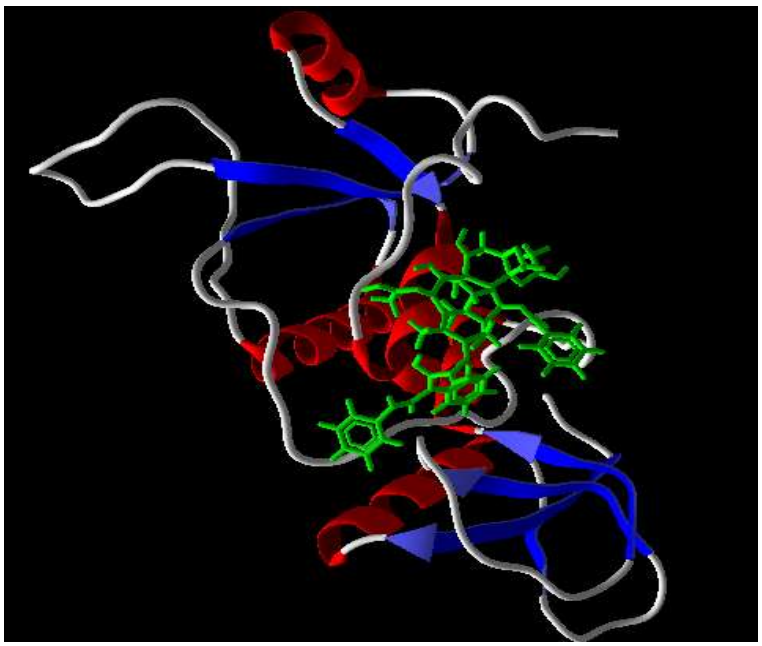


Figure 4: IBC32 docked with PDB-ID 2Y3I and its interactions

Table 4: Docking scores of compounds on PDB-ID 3UEN

Ligand code	Structures	PDB-ID	Docking Scores(kcal/mol)
PAC		3UEN	-11.1698



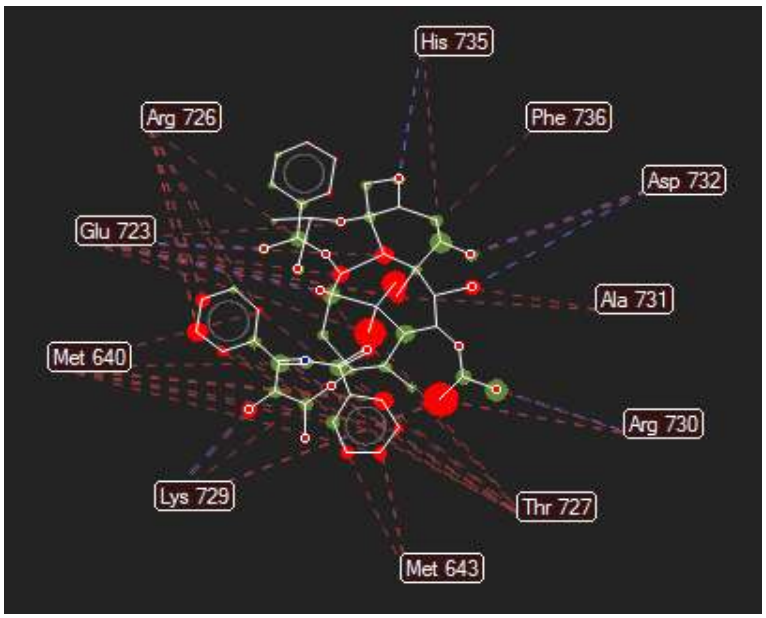


Figure 5: Paclitaxel docked with PDB-ID 3UEN and its interactions

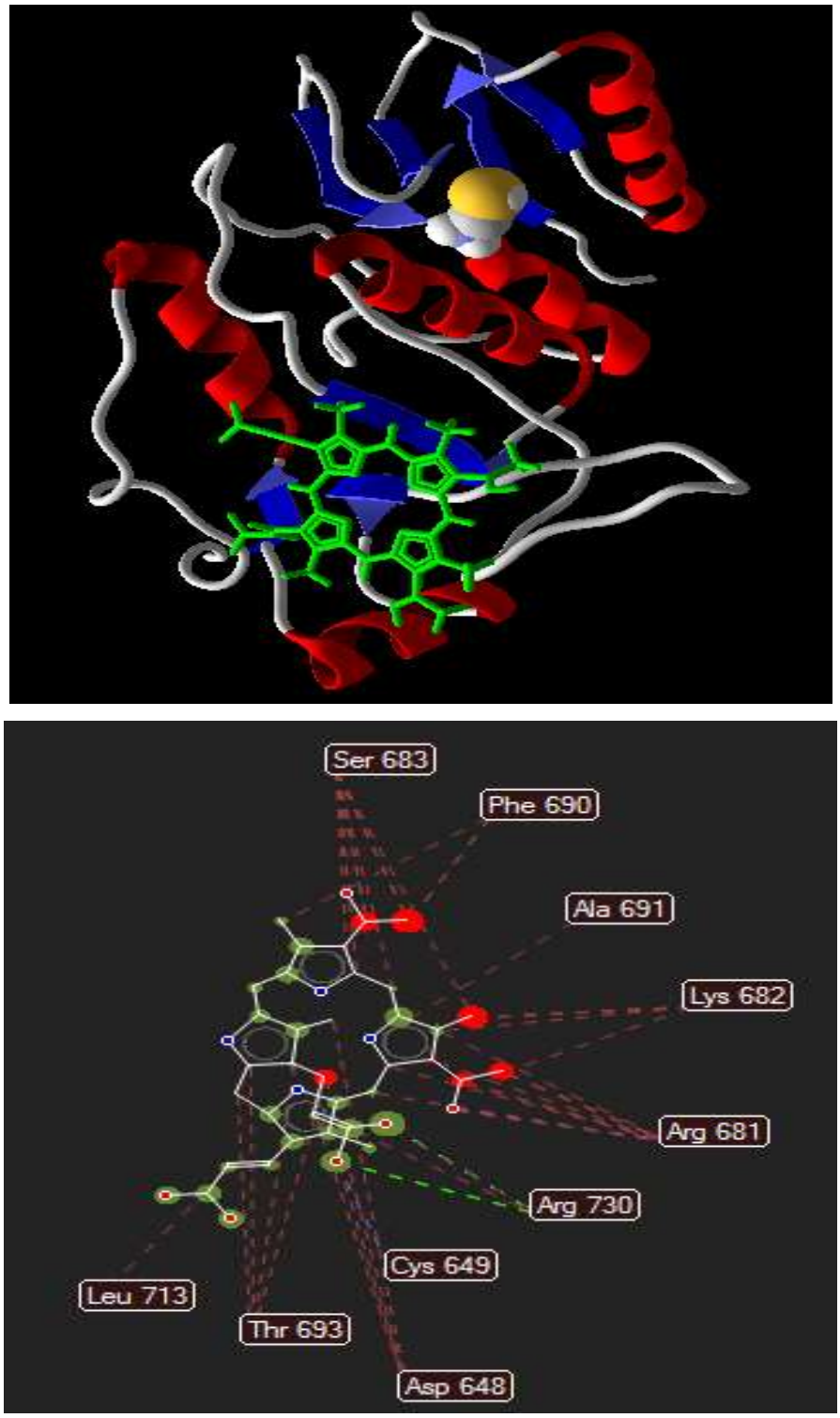
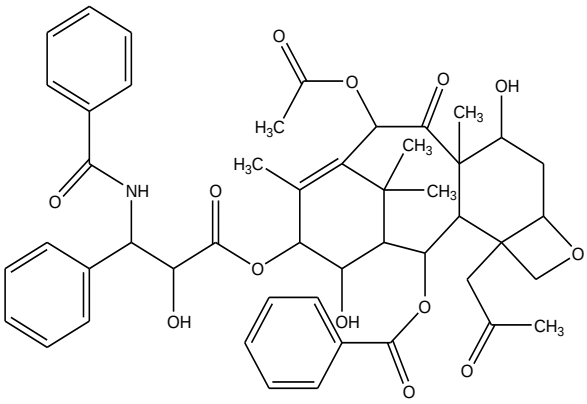
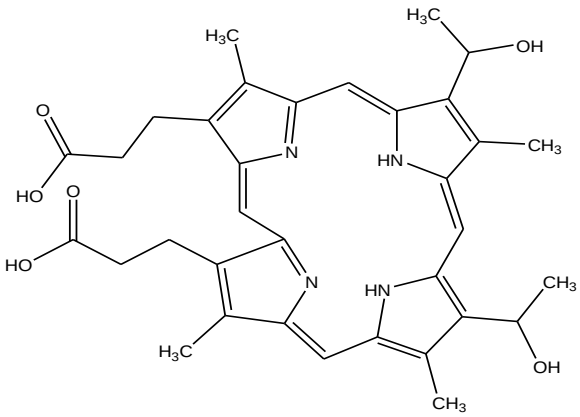


Figure 6: IBC32 docked with PDB-ID 3UEN and its interactions

Table 5: Docking scores of compounds on PDB-ID 3OZZ

Ligand code	**Structures**	**PDB-ID**	**Docking Scores (kcal/mol)**
PAC		3OZZ	-11.6924
IBC32			-10.0192

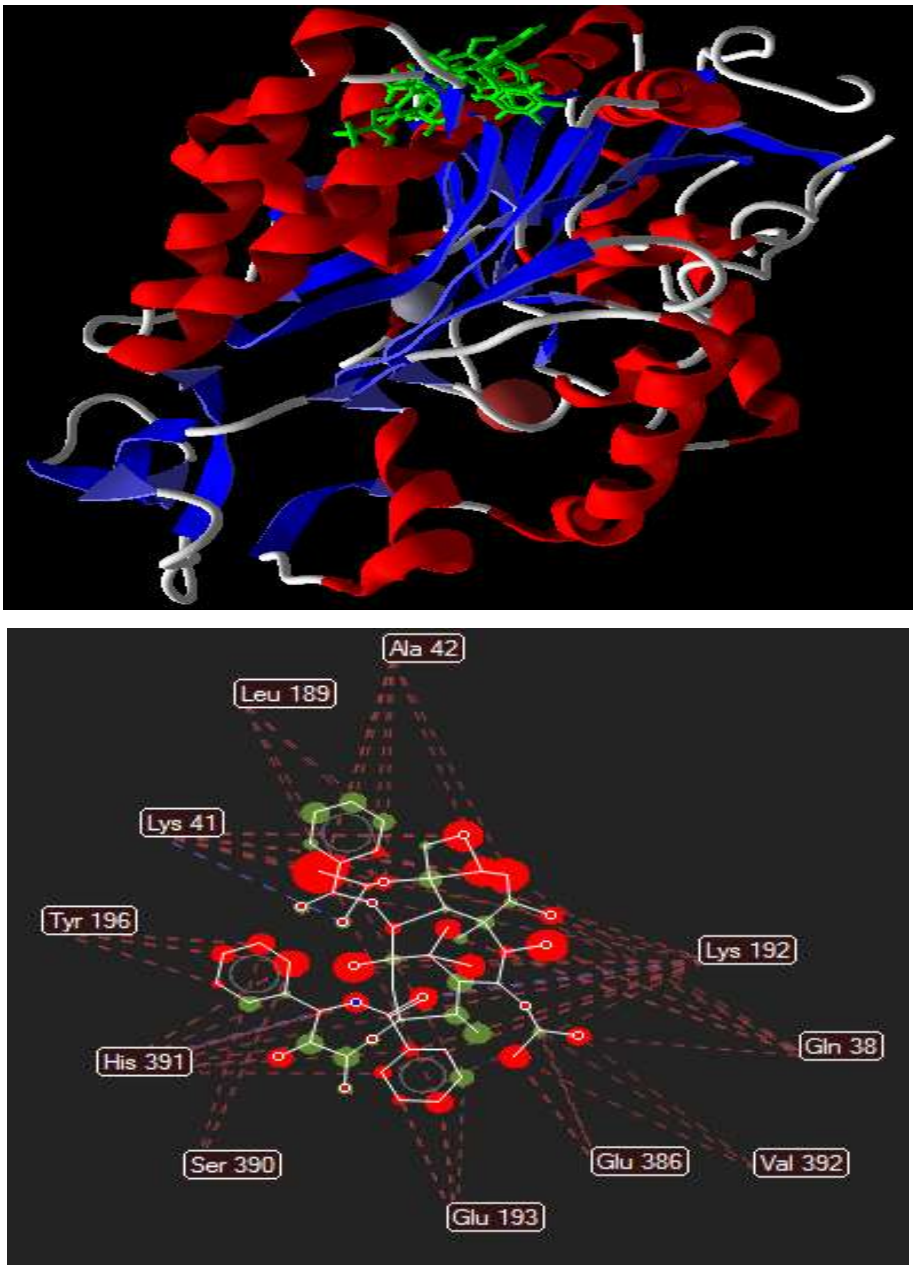


Figure 7: Paclitaxel docked with PDB-ID 3OZZ and its interactions

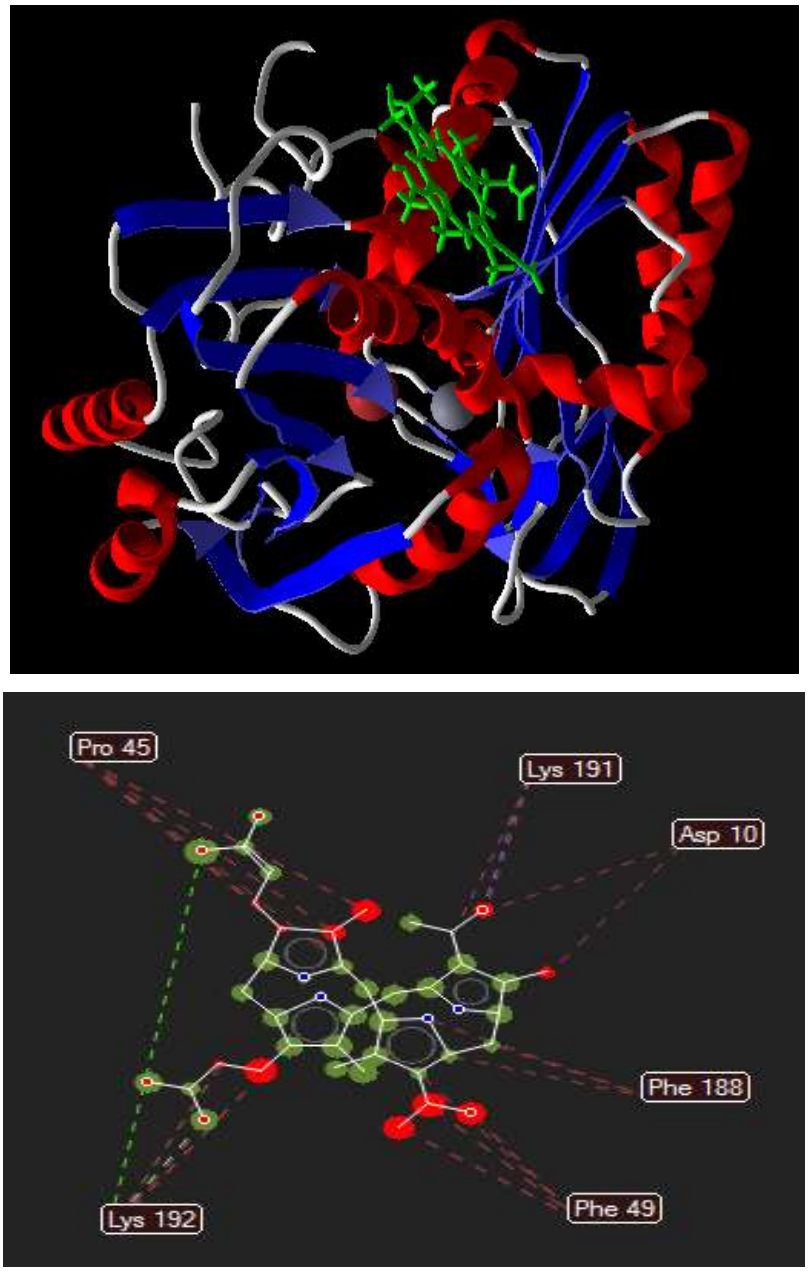


Figure 8: IBC32 docked with PDB-ID 3ZOZ and its interactions

DISCUSSION

CADD computational tools and software are used to simulate drug receptor interactions. Computational drug discovery helps scientists to get an insight into the drug- receptor interactions and also helps to reduces the time and cost.

Hematoporphyrin compound was predicted to be effective against cancer through computational studies. This was achieved by the molecular docking studies against the target enzymes such as (PDB ID- 4O33, 2Y3I, 3UEN, 3ZOZ) of cancer. Hematoporphyrin scored-11.0687kcal/cal when docked with PDB-ID 4O33 whereas the standard (Paclitaxel) scored -11.0293kcal/mol. Docking of

Hematoporphyrin on other enzymes (PDB-ID 2Y3I, 3UEN and 3OZZ) also showed relatively nearer scores with that of standard.

CONCLUSION

The docking study of Hematoporphyrin was performed by Argus lab 4.0 software and the result concluded that has good binding interaction with biomarker enzyme and proved for its anticancer activity in molecular modeling study. It was also interesting to notice that, the Hematoporphyrin showed good docking scores when compared to standard paclitaxel.

REFERENCES

1. Yamane K, Tsuruo T. Conserved BRCT regions of TopBP1 and of the tumor suppressor BRCA1 bind strand breaks and termini of DNA. Oncogene. 1999; 18 (37): 5194-203.
2. Liu K, Lin FT, Ruppert JM, Lin WC. Regulation of E2F1 by BRCT domain-containing protein TopBP1. Mol Cell Biol. 2003; 23 (9): 3287-304.
3. Liu K, Luo Y, Lin FT, Lin WC. TopBP1 recruits Brg1/Brm to repress E2F1-induced apoptosis, a novel pRb-independent and E2F1-specific control for cell survival. Genes Dev. 2004; 18 (6): 673-86.
4. Maeda M, Yoshida A. Molecular defect of a phosphoglycerate kinase variant (PGK-Matsue) associated with hemolytic anaemia: Leu----Pro substitution caused by T/A----C/G transition in exon 3. Blood. 1991; 77 (6): 1348-52.
5. Valentin C, Birgens H, Craescu CT, Brodum-Nielsen K, et al. A phosphoglycerate kinase mutant (PGK Herlev; D285V) in a Danish patient with isolated chronic hemolytic anemia: mechanism of mutation and structure-function relationships. Hum Mutat. 1998; 12 (4): 280-7.
6. Maeda M, Bawle EV, Kulkarni R, Beutler E, et al. Molecular abnormalities of a phosphoglycerate kinase variant generated by spontaneous mutation. Blood. 1992; 79 (10): 2759-62.
7. Chen X, Zhao C, Li X, Wang T, et al. Terazosin activates Pgk1 and Hsp90 to promote stress resistance. Nature Chemical Biology. 2014.