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# DOCKING SCORE OF THE ISOLATED COMPOUND: 19-HYDROXY LOCHNERICINE - WITH DIFFERENT PROTEINS

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***Abstract***

**It evaluates the inhibitory effect of the isolated compound with different drug targets for the anti-cancer activities. The present investigation analyses the docking score of the isolated compound with different proteins. Two types of proteins (Drug targets) were chosen against cancer namely Human Epidermal Growth Factor and Crystal structure of human placental aromatase cytochrome P450. This result reveals that the compound 19-Hydroxy lochnericine shows hydrogen interactions with the docking energy of – 7.41 and -7.15 –8.83 kcal/mol. This reveals a significant interaction between the target proteins and the selected compound. Hence, the compound may offer therapeutic advantages in the treatment and prevention of diabetes and breast cancer.**

**Keywords:** Isolated compound, C.roseus, Drug targets, cytochrome P450, ADMET, Docking scores.

## INTRODUCTION

Bioinformatics is the collection, classification, storage, and analysis of biochemical and biological information using computers especially as applied to molecular genetics and genomics. It is a management information system for molecular biology and has many practical applications. Bioinformatics organizes data in a way that allows researchers to access existing information and to submit new entries as they are produced, eg the Protein Data Bank for 3D macromolecular structures. While data-duration is an essential task, the information stored in these databases is essentially useless until analyzed. Bioinformatics also develops tools and resources that aid in the analysis of data.

Bioinformatics & Drug Design group [BIDD] is a research group based in Department of Pharmacy, Faculty of Science, National University of Singapore, which is active in computer-aided drug design, pharmainformatics and cheminformatics, computational biology and bioinformatics, herbal medicine, and art and sciences. This group maintains the Therapeutic Target Database from which the target proteins for Breast Cancer have been retrieved for this study [1- 4].

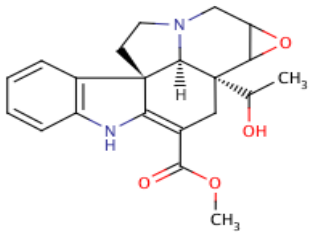
### *Selected proteins*

The present investigation analyses the docking score of the isolated compound with different proteins. Two targets were selected for this study, which are, TTDS00355, Human Epidermal Growth Factor and TTDS00252, Cytochrome P450 [5] Crystal Structure of Human Epidermal Growth Factor was retrieved from the PDB, bearing the ID 1JL9. Epidermal growth factor (EGF) is a typical growth-stimulating peptide and functions by binding to specific cell-surface receptors and inducing dimerization of the receptors. The crystal structure of human EGF has been determined at pH 8.1, having 2 chains, A and B ant of 51 Amino acid length [6].

The second target protein is the Crystal structure of human placental aromatase cytochrome P450 in complex with and rostenedione, bearing the PDB ID, 3EQM. Aromatase cytochrome P450 is the only enzyme in vertebrates known to catalyse the biosynthesis of all oestrogens from androgens. Aromatase inhibitors therefore constitute a frontline therapy for oestrogen-dependent breast cancer. The locations of catalytically important residues shed light on the reaction mechanism. The molecular basis for the enzyme's androgenic specificity and unique catalytic mechanism can be used for developing next generation aromatase inhibitors [7].

### *Structure of inhibitors*

Inhibitor has been selected for the docking analysis. Selected inhibitor was isolated from Catharanthus roseus. It has been confirmed by using different spectrometric methods. It is presented in Figure 1.



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Its molecular formula is C21H24N2O4 and the name is 19-Hydroxy lochnericine (Horhammericine). Its calculated molecular weight is 368.4 g/mol and the exact mass is 368 g/mol. PubChem CID: 443358, 19-Hydroxy lochnericine

## MATERIAL AND METHODS

The website http://www.swissdock.ch/ was used to perform the docking studies. It provides an access to: Swiss Dock, a web service to predict the molecular interactions that may occur between a target protein and a small molecule.

Swiss Dock is based on the docking software EA Dock DSS, whose algorithm consists of the following steps:

1. Many binding modes are generated either in a box (local docking) or in the vicinity of all target cavities (blind docking).
2. Simultaneously, their CHARMM energies are estimated on a grid.
3. The binding modes with the most favorable energies are evaluated with FACTS, and clustered. Aurélien Grosdidier
4. The most favorable clusters can be visualized online and downloaded on your computer.

SwissDock and S3DB are developed by, Vincent Zoete and Olivier Michielin, from the Molecular Modeling Group of the Swiss Institute of Bioinformatics in Lausanne, Switzerland.

Swiss dock review parameters are described below:

- PASSIVEFLEXIBILITYDISTANCE: 0.0
- WANTEDCONFS: 5000
- NBFACTSEVAL: 5000
- NBSEEDS: 250
- SDSTEPS: 100
- ABNRSTEPS: 250
- CLUSTERINGRADIUS: 2.0
- MAXCLUSTERSIZE: 8

## DOCKING RESULTS AND DISCUSSIONS

Docking of the 3D structure of EGF which is a successful target for Breast cancer, retrived from the PDB, bearing the ID 1JL9, with the ligand has revealed exemplenary binding energies. Figure 1 shows the binding of 1JL9 and Table 1 shows the best 10 docking scores measured in terms of binding energies or Gibb's Free Energy, ΔG.

**Table 1: Docking Results for 1JL4 (Epidermal Growth Factor)**

| Cluster | Element | Full Fitness (kcal/mol) | Estimated ΔG (kcal/mol) |
|---|---|---|---|
| 0 | 0 | -98.12 | -7.41 |
| 0 | 1 | -96.41 | -7.33 |
| 0 | 2 | -95.45 | -7.17 |
| 1 | 0 | -96.83 | -6.79 |
| 1 | 1 | -96.83 | -6.79 |
| 1 | 2 | -96.82 | -6.79 |
| 1 | 3 | -96.81 | -6.79 |
| 1 | 4 | -96.81 | -6.79 |
| 1 | 5 | -96.81 | -6.79 |
| 1 | 6 | -96.81 | -6.79 |
| 1 | 7 | -96.81 | -6.79 |

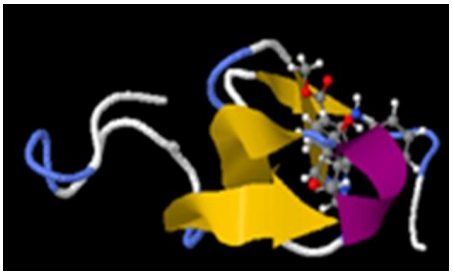

**Figure 2 Binding of IJL9**

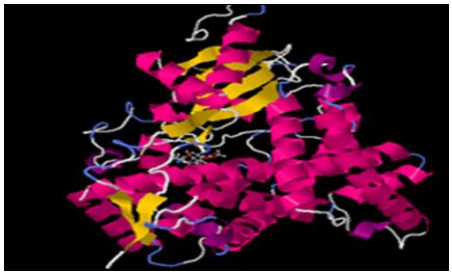

**Figure 3: Binding of 3EQM**

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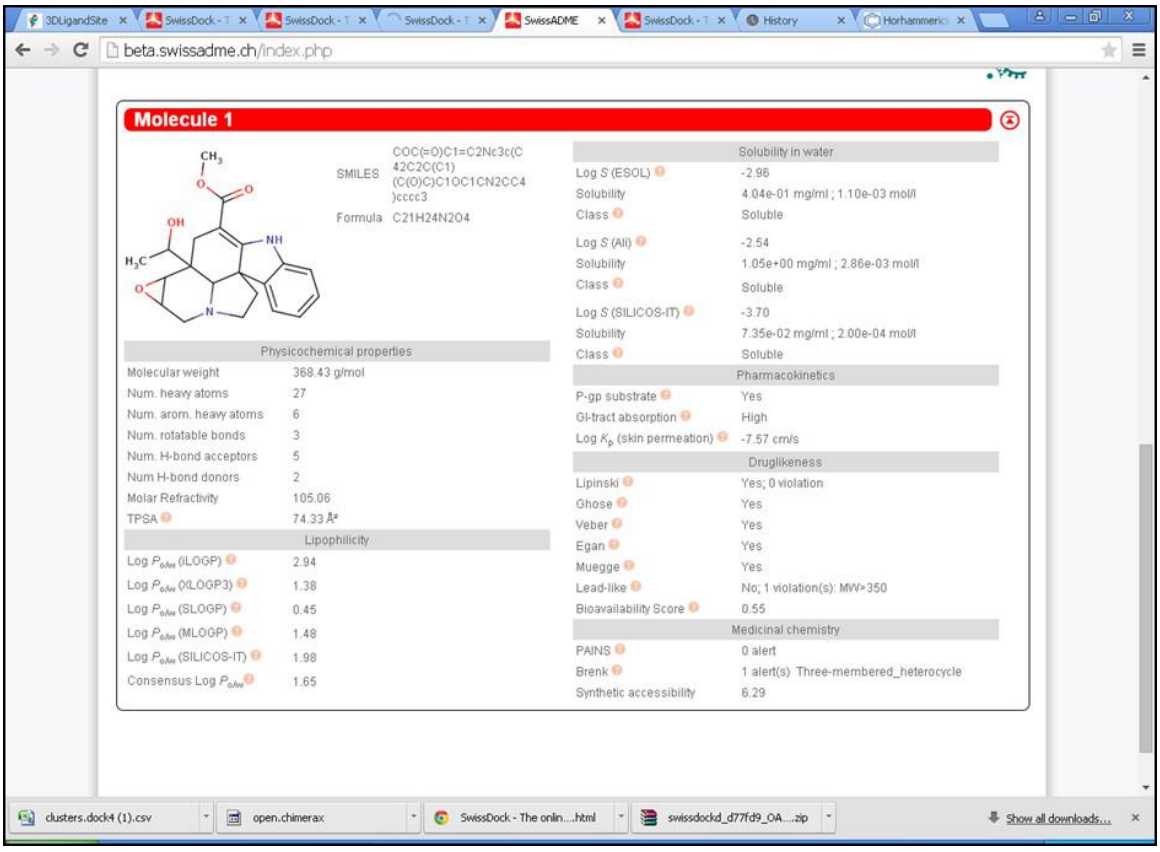
Docking of human placental aromatase cytochrome P450's 3D structure, retrieved from the PDB, bearing the ID 3EQM, with the ligand has revealed exemplenary binding energies. Figure 2 shows the binding of 3EQM and Table 2 shows the best 10 docking scores measured in terms of binding energies.

**Table 2: Docking Results for 3EQM (cytochrome P450)**

| Cluster | Element | FullFitness (kcal/mol) | Estimated ΔG (kcal/mol) |
|---|---|---|---|
| 0 | 0 | -1810.89 | -7.15 |
| 0 | 1 | -1809.68 | -7.03 |
| 0 | 2 | -1807.85 | -7.61 |
| 0 | 3 | -1807.85 | -7.61 |
| 0 | 4 | -1807.85 | -7.61 |
| 0 | 5 | -1807.85 | -7.61 |
| 0 | 7 | -1802.45 | -7.61 |
| 0 | 8 | -1797.80 | -7.28 |
| 0 | 9 | -1797.80 | -7.05 |
| 0 | 10 | -1791.63 | -7.05 |
| 0 | 11 | -1791.63 | -7.30 |

ADMET is an abbreviation in pharmacokinetics and pharmacology for "absorption, distribution, metabolism, excretion and Toxicity." It describes the fate of a pharmaceutical compound within an organism. This criterion influences the drug levels and kinetics of drug exposure to the tissues. A set of algorithms can predict the pharmacological activity of the compound as a drug.

In this study, the Swiss ADMET Tool, iLOG predictor, was engaged to predict the drug ability of the ligand. The website http://www.swissadme.ch/ hosts the iLOG predictor, which computes the physicochemical descriptors and predicts the pharmacokinetics properties and drug like nature of small molecules. It is developed and maintained by the Molecular Modeling Group of the Swiss Institute of Bioinformatics. The ADMET desctiptors of the ligand Horhamericine is described in the Table 3 below.



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Properties based on ADMET analysis assessed for their chemical properties of the ligand with its molecular weight being < 500 Daltons with < 5 hydrogen bond donors, < 10 hydrogen bond acceptors and QPlogPo/w < 5;

The n-octanol/water partition coefficient (log Po/w) is a key physicochemical parameter for drug discovery depicts lipophilicity indices of the ligand as within the range. The parameters measured for the ligand's solubility in water is proposes the ligand to be an ideal drug.

The Lipinski, Ghose, veber, Egan, Muegge rules for drug-like molecules have also approved the ligand. Bioavailability of the ligand resulted in the partition coefficient (QPlogPo/w) ranges from - 2.0 to 6.5 and water solubility (QPlogS), critical for estimation of absorption and distribution of drugs within the body, ranged between -6.5 and 0.5 and the Topological polar Surface Area of the ligand is also appreciable. All these pharmacokinetic parameters are within the acceptable range signifying the ligand to be a typical Drug molecule.

## CONCLUSIONS

The binding energies of the Breast Cancer targets, EGF and human placental aromatase cytochrome P450 with the ligand has been shown to be – 7.41 and -7.15 respectively. This is significant and in accord with the in vitro studies, revealed by cell line studies which also claim the ligand to be an effective anti-cancerous agent. The ADMET studies, carried out in the iLOG predictor, of the Swiss ADMET website also substantiate horhamerrcine to be a safe drug.

Therefore it is suggested that suitable Clinical research can be carried out with this molecule, and further studies would declare it to be a successful anticancer drug candidate.

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