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Short Communication

IN-SILICO ANALYSIS OF BIOACTIVE COMPOUNDS FROM ROOT EXUDATES OF *ALLIUM CEPA*

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ABSTRACT

The aim of our study was to analyze the isolated Steroidal Glycoside against Human Angiotensin receptor. In this study, the steroidal glycoside was isolated from the root exudates of tissue cultured *Allium cepa* and subjected to various spectroscopic analyses. The steroidal glycoside was also docked with cardiac protein using reliable bioinformatics tool and found that the steroidal glycoside have a very good control against the cardiac pain. The interesting result we got from this study shows the importance of the unstudied part of the root exudates of medicinal value herb in Therapeutic area especially in Biopharmaceuticals.

Keywords: *Allium cepa*, Root, Root Exudates, Steroidal Glycoside

1. INTRODUCTION

Cardiovascular diseases have been considered a serious health problem worldwide. The major risk factors for heart diseases include family history, hypercholesterolemia, hypertension, obesity, cigarette smoking, and other lipid abnormalities. It has been documented that various medicinal plants such as *Digitalis purpurea,* [1-3] *Crataegus monogyna,* [4-6] *Allium sativum* [7-9] and *Rauwolfia serpentine* [10-12] have been used for the treatment of cardiovascular disease and the natural remedies are considered to be effective and safe alternative treatment for disease. The aim of the present study was to assess the cardiovascular activity of the identified compound from the tissue cultured *Allium cepa* L. roots through docking studies.

2. MATERIAL AND METHODS

2.1. Ligand preparation

The ligands were initially drawn using chemsketch tool and the chemical language format is converted in to protein data bank format for the docking.

2.2. Protein preparation

The drug target protein preparation is done with auto dock 4.02 v software, The polar hydrogen's were added along with kollmann charges and the respective drug target protein was saved in current mode of protein data bank.

2.3. Auto Grid calculation

AutoGrid is a program that pre-calculates grid maps of interaction energies for various atom types, such as aliphatic carbons, aromatic carbons, hydrogen bonding oxygens, and so on, with a macromolecule such as a protein, DNA or RNA. These grid maps are then used by AutoDock docking calculations to determine the total interaction energy for a ligand with a macromolecule. Doing this pre-calculation saves a lot of time during the docking, primarily because we do not have to update non-bonded lists during the calculation. Also, what was a calculation with order N-squared complexity is reduced to one that is order N, where N is the number of atoms interacting. The Grid is placed in equal dimensions 50X50X50 in XYZ dimensions with 0.5 spacing in angstroms along box is placed in -35.508 X, 64.91 Y, 25.87 Z directions respectively.

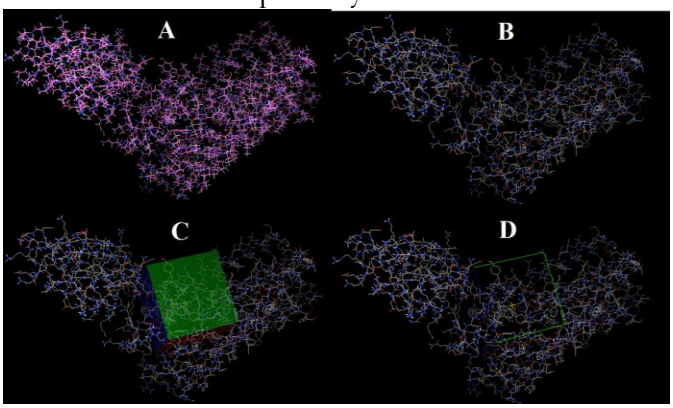

Fig. 1: Grid before and after calculation

A: Before grid calculation, B: After grid calculation, C&D: Grid map

2.4. Molecular docking

Molecular docking is a key tool in structural molecular biology and computer-assisted drug design. The goal of ligand-protein docking is to predict the predominant binding mode(s) of a ligand with a protein of known three-dimensional structure. Successful docking methods search high-dimensional spaces effectively and use a scoring function that correctly ranks candidate docking. The Crystal Structure of Human Angiotensin Receptor of PDB:4ZUD was chosen and docked with isolated compounds

3. RESULTS

3.1. Receptor-ligand interaction

The isolated ligand and the Human Angiotensin Receptor as a drug target protein are docked using Autodock4.02v. Docking is carried out with genetic algorithm mode with population size of 150 and 2500000 maximum number of energy evaluations, 27000 maximum numbers of generations with 10 runs. The best run with negative binding energy is considering best results. The interaction results are visualized using acclerys discovery studio 4.05 visualizer.

Steroidal glycoside - Drug target protein(Human Angiotensin Receptor)

Docking results

Estimated Free Energy of Binding = -3.23 kcal/mol [=(1)+(2)+(3)-(4)]

Estimated Inhibition Constant, Ki = 4.39 mM (millimolar) at temperature = 298.15 K

(1) Final Intermolecular Energy = -5.32 kcal/mol

vdW + Hbond + desolv Energy = -5.29 kcal/mol

Electrostatic Energy = -0.02 kcal/mol

(2) Final Total Internal Energy = -0.42 kcal/mol

(3) Torsional Free Energy = +2.09 kcal/mol

(4) Unbound System's Energy [=(2)] = -0.42 kcal/mol

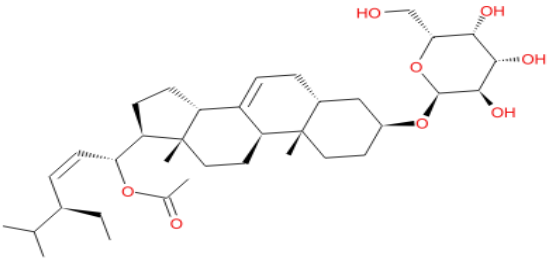

Fig. 2: Steroidal Glycoside

No of Atoms- 44

Molecular Composition- C: 0.699, H: 0.094, O: 0.207

Molecular weight- 618.86

Molecular Formula- C_{36} H_{58} O_8

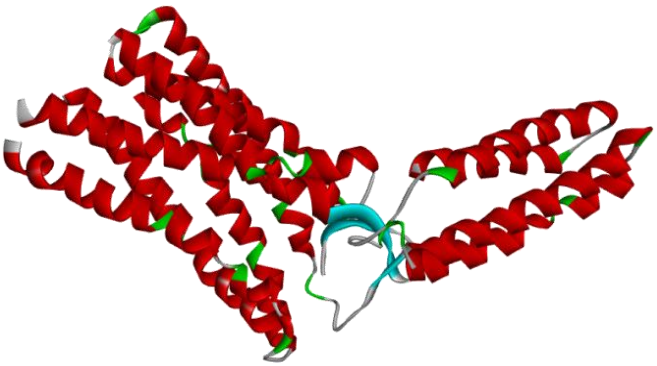

Figure 3: Human Angiotension Protein

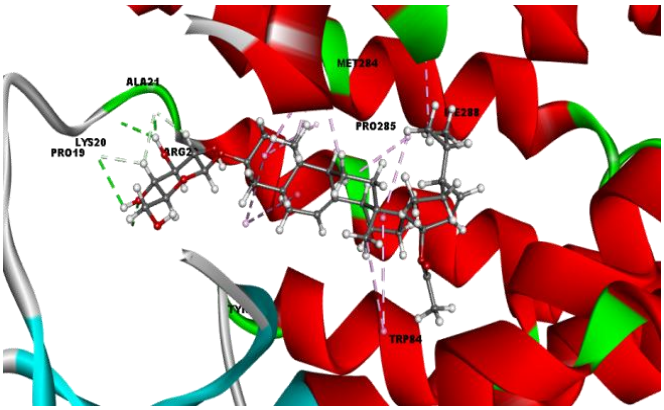

Fig. 4: Binding of compound to active site of drug target protein

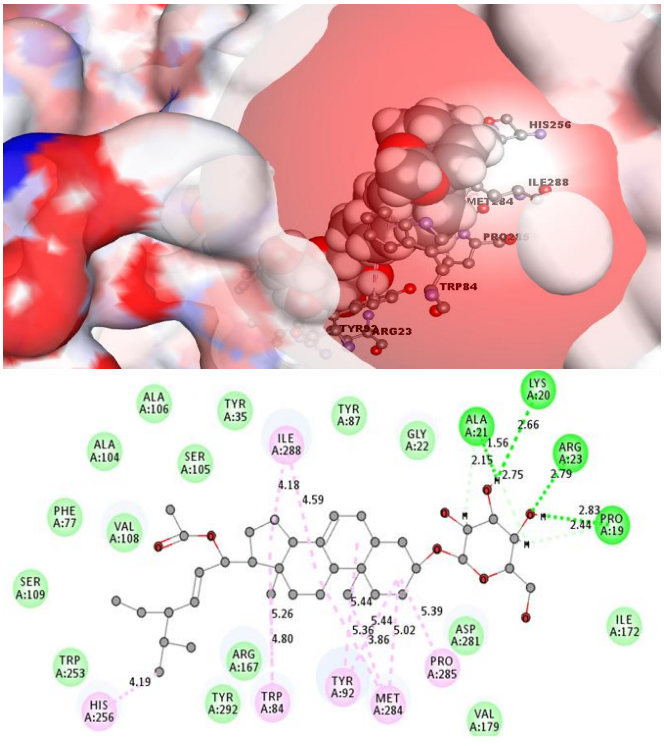

Fig. 5: Active site amino acid and compound binding interaction

Table 1: Interaction and binding energy of ligand to the active site of the protein molecule

Receptor and Ligand	Amnio acid Binding	Distance in Å	Free Energy of Binding kcal/mol
Human Angiotensin Receptor with Steroidal glycoside	HIS 256	4.19	-3.23
	ILE 288	4.18,4.59	
	TRP 84	5.26,4.80	
	TYR 92	5.44,5.44	
	MET 284	5.36,3.86,5.02	
	PRO 285	5.39	
	ALA 21	2.15,1.56,2.75	
	LYS 20	2.66	
	ARG 23	2.79	
	PRO 19	2.44,2.83	

4. DISCUSSION

The present results revealed that the isolated Steroidal glycoside and drug target protein , shows ten amino acid interaction with estimated free energy of binding of -3.23 kcal/mol and favors for conventional bond interaction indicates that good binding interaction between the active site and compound. Other type of interaction includes Pi-alkyl, alkyl and vanderwaals interaction are also observed after docking. Likewise in the previous *in-silico* study it was concluded that the steroidal glycosides from *Dregea sinensis* Hemsl. had the strong ability to dock with tumor associated proteins [13]. Thus the bioactive compounds from the *Allium cepa* L. root exudates were interacting with the Human Angiotensin Receptor (Target protein) will have a very good control against the cardiovascular problems.

5. CONCLUSION

The molecular docking studies showed that the identified compound docks well with Human Angiotensin Receptor (Target protein) and it might act as potential bioactive compound for treatment of the cardiovascular problem. Thus the selected compounds can be verified at the clinical-level drug examinations and made into an effective drug against cardiovascular diseases. Hence, Steroidal glycoside can be drug candidate for treating the cardiac related problem but *in vitro* and *in vivo* study need to prove the bio efficacy of the same.

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