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RESEARCH ARTICLE

Molecular docking study of potential phytochemicals of *Malvastrum coromandelianum* and their effects on the complex of SARS-CoV2 spike protein and Human ACE2

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ABSTRACT

Seven different coronaviruses are currently known to cause human breathing disorders. The latest SARS-CoV-2 coronavirus outbreak in December 2019 is in the coronavirus 2B type, which is 80% identical to the SARS-CoV genome. In the future too, continuous mutation is likely. A variety of CoV therapies, such as immunomodulations, vaccines, antivirals specific to CoV and host-specific antivirals are being developed. Many people with COVID-19 have severe breathing problems. Human ACE2 receptor (PDB ID-1R42) is considered as receptor protein for molecular docking study of spike protein fragment with its receptor in human host. The study of in-silico docking was performed using Molegro virtual docker (MVD). In-silico docking studies have taken the place of the new version of GLIDE Software v5.5, built by Schrödinger. These findings showed that the binding energy in all active components ranged from -4.2 to -8.4 kcal/mol. If compared to the standard (-8.6 kcal/mol). It was found that, as opposed to the standard drugs, the investigated phytoconstituents showed potent inhibiting activity as the MolDock score directly represents possible binding to the enzyme.

INTRODUCTION

Coronaviruses are a group of enveloped viruses named for their coronary appearance with positive single-stranded RNA genomes [1], in addition to six well-known strains of human-infectious coronaviruses. Two other particularly pathogenic SARS-CoV and MERS-CoV-viruses, SARS-CoV-2 also causes major respiratory failure and death. Furthermore, the populations have become vulnerable to highly pathogenic coronaviruses and have grown into events of public health, thereby increasing the need to prepare a possible reappearance or to produce new viruses [2]. COVID-19 is hard to foresee before the end of the pandemic; high-death coronavirus [3-4].

An annual or perennial herb or shrub native to North and South America, *Malvastrum coromandelianum* is also known as threelobe false mallow [5-6]. It has been applied in many other parts of the world, including Australia, Africa, and South and East Asia [7, 8]. Molecular docking is an appealing scaffold for understanding medicinal biomolecular interactions in rational drug design as well as in the mechanical analysis in order, primarily non-covalently, to insert the molecule (ligand) into the favorite binders of the particular target area of the DNA/protein (receptor) [9, 10]. The information gathered from the docking method can be used to demonstrate the binding energy, free energy and complex stability. The docking are currently used to forecast the preliminary ligand-receptor complex binding parameters [11]. The present study aims to carry out a reverse pharmacological assessment of the antiobesity impact of selected phytoconstituents of medicinal plants suggested in folk medicine. Furthermore, in Ayurvedic literature, the routine use of coriander seed decoction is considered to be effective in reducing the amount of blood lipids [12-15].

MATERIALS AND METHODS

Molecular Modeling Studies:

The GLIDE software v5.5 built by Schrödinger on the Red Hat Enterprise Linux5 workstation has also been used for molecular modeling studies. For all steps involved in ligand preparation, protein preparation, HTVS, Maestro v9.5 Graphical User Interface (GUI) workspace was used (High Throughput Virtual Screening) [16].

Ligand Preparation:

The ligands used in this study have been developed with the Schrödinger Suite 2013 LigPrep module v2.3. LigPrep follows the energy minimization force fields in OPLS-AA (Optimized Potential Liquid Simulations for All Atoms) [17].

Protein Preparation:

Human ACE2 receptor (PDB ID-1R42) is considered as receptor protein for molecular docking study of spike protein fragment with its receptor in human host. Only high atoms, water, cofactors and metal ions can be used in a standard PDB structure, and multimerical structures can be used. These entities are not familiar with bond instructions, topologies or formal atomic costs. The raw PDB structure should therefore be prepared for docking in a suitable way. GLIDE software protein preparation Wizard for the processing and preparation of protein was used. This is also in line with the optimized power potentials in the energy reduction fields for liquid simulations-all atoms (OPLS-AA) [18].

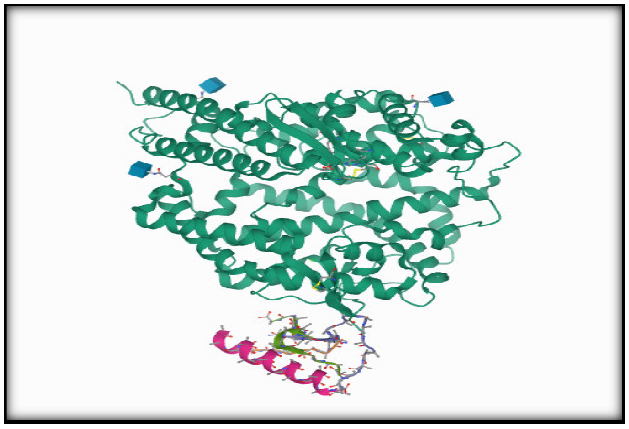

Figure 1: 3D View of Human ACE2 receptor (PDB ID-1R42)

Docking Protocol:

The GLIDE Extra Precision (XP) mode was used for all docking calculations. The position of the bond for the different energy networks is defined in two concentration-cubed terms: the bounding box with the center of every appropriate ligand pose and the enclosing box with a Root Mean Square Diversion (RMSD) of less than 0.5 Å and a maximum atomic displacement of less than 1.3 Å The binding site for which various energy grids have been determined and stored. For those atoms with absolute partial loads below 0.15 (scale factor of 0.8) and 1.0 electrons of the ligand and proteins respectively, the scale factor for Van der Waals radii was added. In the initial calculation process, the maximum number of poses produced by the max keep variable was set at five thousand and the best hold variable was set at one thousand, which determines the number of poses per ligand in the energy minimum. Energy minimization protocol includes dielectric constant of 4.0 and 1000 cycle of conjugate gradient. At most 100 poses per ligand were produced when each docking calculation was completed. A GLIDE (Gscore) function was used to choose the best docked structure. The E-model, which comes from a combination of g score, coulombic, Van der Waals and the ligand strain energy, is another scoring feature used by GLIDE [18].

RESULTS AND DISCUSSION

The docking outcome of the ligands is shown in Table 1. The interaction energy comprises van der Waal's energy, electrostatic energy, and intermolecular hydrogen bonding for each of the reduced complexes. The GLIDE norm score for hydroxychloroquine was found to be -8.6. This demonstrates that potential drugs for the production of anti-diabetic activity drugs could be the chemical component of the plant. The GLIDE score may be used as a semi-quantitative descriptor to describe ligands which bind to a certain conformation of a protein receptor. In general, a high affinity of the ligand to the receptor for a low GLIDE score can be predicted. In particular, with a docking score of -8.4 and -4.2 respectively, the compounds Malvalic acid and Stigmasterol was found to be potent. The role of the docking inhibitor and the crystal protein structures is well decided upon. Compliance studies of various docking complexes have also shown that protein residues (ALA 307, ASP 197, HIS 20, ILE 232, GLU233, LYS 200, ALA 307, ALA 122, HIS 305, ALA 307 and GLU233) play a significant role. GLIDE-led docking studies have confirmed that the inhibitors referred to above fit into the protein binding site. The findings show that for active

docking, intermolecular hydrogen and liphophilic interactions between the ligand and the receptor are very important. The main reason why the GLIDE score has increased is because of intra-ligand sanctions. The phytoconstituent that are responsible for the highest MolDock ranking, namely Malvalic acid and Stigmasterol.

Table 1: Glide score of Phytoconstituents of *Malvastrum Coromandelianum*

Sr. No	Phytochemical constituents	Glide score
1	Palmitoleic acid	-4.2
2	Stearic acid	-6.5
3	Palmitic acid	-4.6
4	Linoleic acid	-5.9
5	Malvalic acid	-8.4
6	Stigmasterol	-7.7
7	Lutein	-5.2
8	Hydroxychloroquine	-8.6

CONCLUSION

The attraction of the ligand's binding affinity towards protein is determined by the force between the S-protein fragment, ACE2 and Malvalic acid. Protein-ligand binding strength is known as binding affinity. This affinity specifies whether a ligand can eventually bind or separate from the surface of the protein and return to its unbound state. Docking servers calculate the binding affinity of various docking structures in the absence and presence of spike protein for non-competitive modulators.

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