"Molecular Docking and ADMET study of Terminalia chebula's seed as an inhibitor of Nipah virus Glycoprotein (PDB id: 2vsm)"

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Abstract

PDB ID: 2vsm the glycoprotein of Nipah virus take a vital role in viral attachment to take entry into host cells, making them most desired pin points for antiviral drug development. In this study, an integrated in silico approach was created for evaluation purposes for the antiviral potential of selected secondary metabolites (phytochemicals) from the seeds of *Terminalia chebula*, namely β-sitosterol, linoleic acid, oleic acid, and palmitic acid. Molecular docking of receptor and ligand, analysis was taken to investigate binding interactions with the 2vsm and ligand using SwissDock , followed by druggabilty (ADME) assessment using SwissADME and toxicity prediction done by using ProTox-3.0.

Docking results showed that all compounds were stable binding within the active binding site. β-sitosterol exhibits the highest binding affinity for its rigid sterol chemical structure. However, in ADME analysis showed that β-sitosterol has multiple drug-likeness violations, poor gastrointestinal absorption, low solubility, and In contrast, oleic and palmitic acids exhibited favorable druggabilty profiles, they have high gastrointestinal absorption with acceptable bioavailability, while linoleic acid showed moderate performance followed by limitations in flexibility and solubility. In toxicity predictions revealed that none of the compounds are mutagenic or carcinogenic, although β-sitosterol displayed neurotoxicity and immunotoxicity, whereas fatty acids showed relatively safer profiles.

Overall, oleic acid had a profile of the most promising candidate, exhibited a balanced image of binding affinity, druggabilty, and less toxicity. These study marked up the fatty acid based phytochemicals established as potential compounds for the development of antiviral agents targeting glycoprotein (2bsm). Further experimental validation is warranted to confirm these computational insights.

Keywords: Nipha virus, Glycoprotein, Terminalia chebula, molecular docking, ADME, toxicity prediction, phytochemicals

1. Introduction

Viral contamination continues pose significantly global health challenges, specifically with the rise of novel and re-rise of pathogens that have lack of potential therapeutic interventions. In this situation, Nipha virus belongs to an important group of viruses, they can able of infecting the host cells through their highly specialized surface glycoproteins. These glycoproteins play a vital part in mediating viral attachment, membrane fusion, and entry into host cells. Because of their direct participation in the beginning stages of infection, Nipha virus glycoproteins are considered crucial targets for antiviral drug development. Inhibiting these proteins can efficiently block viral contamination and blocks its subsequent replication, making them a strategic views in computational and experimental drug discovery.

In recent days, herbal products have increased their considerable opinion as potential resources of antiviral materials due to their structural diversity, biological activity, and relatively low toxicity. Medicinal plants have been huge explored in terms of traditional medicinal systems for their therapeutic benefits [1,2]. *Terminalia chebula* [3] (commonly known as Haritaki) is very well-known medicinal plant and widely used in Ayurvedic, Unani, and traditional Chinese medicine. It is reported to show a broad spectrum of pharmacological movements, including antioxidant, antimicrobial, anti-inflammatory, and antiviral properties.

According to Dr. Duke's Phytochemical and Ethnobotanical databases those compounds chosen whose activity was not 0 and have 3D structure in PubChem such as β-sitosterol, linoleic acid, oleic acid, and palmitic acid, which are present in *Terminalia chebula* seeds. B-Sitosterol, a plant sterol, is known for its immunomodulatory and anti-inflammatory ability, whereas fatty acids like oleic and linoleic acid have showed antiviral and membrane-interacting properties that may disrupt virus entry mechanisms. Despite these promising attributes, the molecular interactions between these phytochemicals and Nipha virus glycoproteins have not been thoroughly investigated previously.

Advanced stage in computational biology has switched on the vivid screening and examined of bioactive essentials through in- silico method. Molecular docking by SwissDock [4,5] took part to predict of binding affinity and transaction patterns between ligands and target macromolecule (proteins), providing a clear view of their inhibitory efficiency. In addition, druggabilty profiling using tools such as SwissADME [6] helps the examined of absorption, distribution, metabolism, and excretion (ADME) properties, which are vital for exhibits drug-likeness. Furthermore, toxicity prediction platforms like ProTox-3.0 [7] enable early exhibits of toxicity analysis.

Therefore, the present study aims to systematically exhibition of selected phytochemicals from *Terminalia chebula* seeds as efficient inhibitors of Nipha virus glycoprotein using a compact computational method.

2. Materials and Methods

2.1 Selection of Phytochemicals

Dr. Duke's Phytochemical and Ethnobotanical database helps here to get the phytochemicals of *Terminalia chebula* seeds. The selection was made upon their biological activity excluding biological inactive phytochemicals. smiles and 3d structure was retrieved from PubChem database.

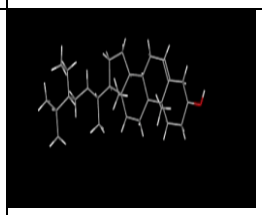
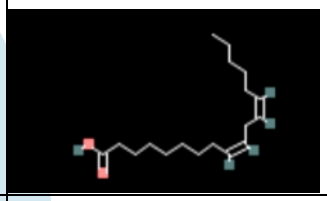
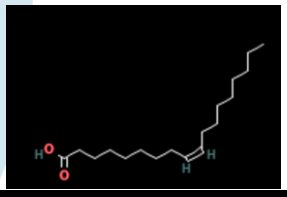
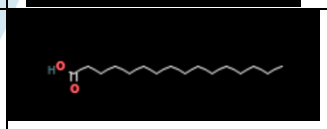
Sl. No	Compound Name	Smils	2D Structure
1	B-Sitosterol	CC[C@@H](C©C)CC[C@H]([C@H]1CC[C@@H]2[C@]1©CC[C@H]1[C@H]2CC=C2[C@]1©CC[C@@H](C2)O)C	
2	Linoleic acid	CCCCC/C=C\C/C=C\CCCCCCCC(=O)O	
3	Oleic acid	CCCCCCCC/C=C\CCCCCCCC(=O)O	
4	Palmitic acid	CCCCCCCCCCCCCCCC(=O)O	

Table 1. Selected Phytochemicals

2.2 Target Protein Preparation

The Nipha virus human glycoprotein (PDB ID: 2VSM) contains Chain A and the human surface control protein ephrinB2. PDB 2vsm was imported into Discovery Studio, where the human surface control protein heparinB2 was removed, and water and other heteroatoms were deleted. After that by adding hydrogen atoms, and optimizing the structure for docking.

2.3 Molecular Docking

Docking was performed using SwissDock [8] to evaluate ligand–protein interactions. Binding affinity was assessed using AC scores and Swiss-Param.

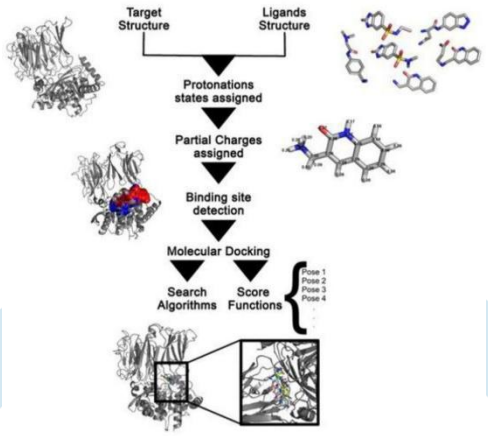


Figure : 1 Molecular docking

2.4 ADME Analysis

SwissADME was used to examine:

Lipophilicity (LogP): It showed the logarithm of the ratio of concentration in lipid phase (generally 1-octanol) to its concentration in aqueous phase. 0 means the phytochemicals distribute well in lipid and water, negative values indicate water, and positive values indicate lipophilic.

Solubility (Log S): it showed whether the phytochemicals were soluble in water or not

GI absorption: Solved whether a phytochemical was Gastro intestine absorb or not.

Drug-likeness rules: In this druggabilty filtration were checked like Lipinski [8] rule of 5, Ghosh, Veber etc. to examined phytochemicals were druggable or not.

Bioavailability score : Showed that the any could able to take the phytochemicals orally or not.

2.5 Toxicity Prediction

ProTox-3.0 was used to assess: It was used to judge a phytochemical or a compounds side effect of they have major toxic then it should be avoided.

Organ toxicity and toxicity endpoints was necessary to judge the phytochemicals have ability to damage major organs or not

CYP450 interactions was to tested to see phytochemical has ability to pass the test of metabolites or not.

Results and Discussion

4.1 Molecular Docking Analysis

For Molecular docking analysis the results of SwissDock was acted to find out the binding affinity of selected phytochemicals toward Nepha virus glycoprotein. All four compounds proof their eligibility as a stable binding within the binding active site, primarily binding done by hydrophobic interactions due to their long hydrocarbon chains.

Among the docked phytochemicals, β-sitosterol showed the strongest affinity, for its rigid sterol backbone structure and showed stability for van der Waals interactions within the hydrophobic pocket. However, its bulky structure l hydrogen bonding transactions.

Oleic acid and linoleic acid showed moderate binding affinities, with both by hydrophobic residues and limited polar interactions by their carboxyl group. The presence of double bonds in these fatty acids gave conformational flexibility, enhancing binding stability.

mediated Palmitic acid, being fully saturated, showed comparatively lower binding affinity due to elements flexibility and fewer interaction points within the binding cavity.

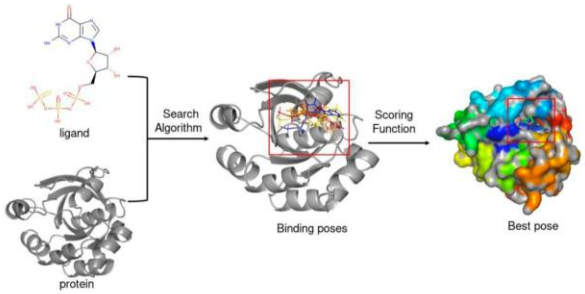


Figure 1: Protein-ligand docking process.

Figure : 2 Protein and Ligand docking process

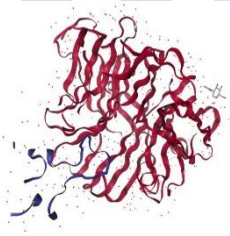


Figure: 3 Complex structure with Oleoc acid

Overall, docking results leaded that binding affinity was influenced by structural rigidity, chain length, and degree of unsaturation, with β-sitosterol showing the strongest interaction but fatty acids offering better adaptability.

ADME (Pharmacokinetic) Analysis

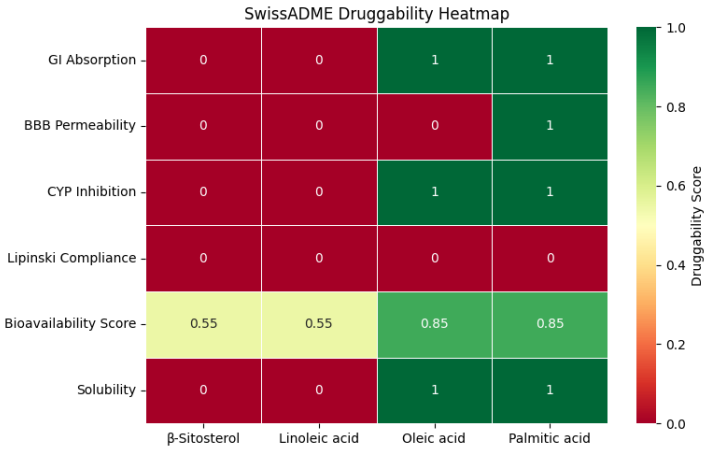


Figure: 4 Heatmap of essential properties of ADME

The druggability profiles of the phytochemicals were examined using SwissADME attributes, including Lipinski's rule, bioavailability radar, and solubility predictions.

B-Sitosterol exhibited low gastrointestinal (GI) absorption and poor solubility, due to its excessive molecular weight and high lipophilicity (consensus Log P > 7). It violated multiple drug-likeness filters (Ghose and Muegge), showed limited oral bioavailability.

Linoleic acid also exhibited poor GI absorption and low solubility, with excessive flexibility (rotatable bonds) poor impacting drug-likeness despite acceptable molecular weight.

Oleic acid exhibited high GI absorption, moderate solubility, and fewer rule violations, suggesting a favorable druggable profile in terms to other compounds.

Palmitic acid exhibited high GI absorption and optimal drug-likeness, satisfying most rules (Lipinski, Ghose, Egan), along with a high bioavailability score (0.85), indicating good oral absorption potential.

The bioavailability radar plots revealed that oleic acid and palmitic acid fall largely within the optimal physicochemical space, whereas β-sitosterol and linoleic acid deviate significantly, particularly in lipophilicity and flexibility.

4.3 Toxicity Prediction Analysis

Toxicity profiles predicted using ProTox-3.0 demonstrated distinct toxicity patterns among the phytochemicals.

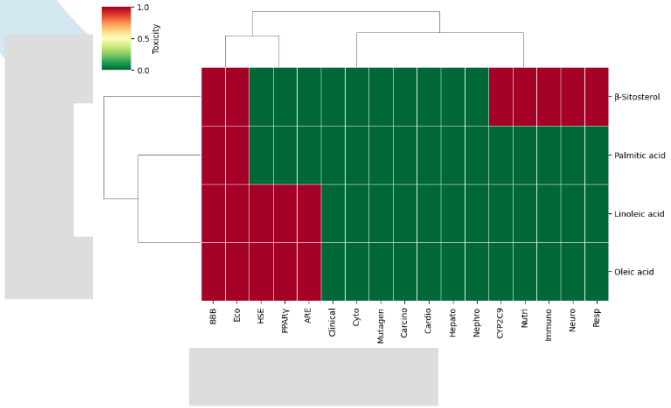


Figure: 5 Heatmap of Toxicity.

B-Sitosterol exhibited active for neurotoxicity, respiratory toxicity, immunotoxicity, and BBB permeability, indicating potential safety concerns despite its strong binding affinity. It also exhibited CYP2C9 inhibition, suggesting possible drug–drug interaction risks.

Linoleic acid demonstrated a favorable toxicity profile, with most endpoints predicted as inactive. However, it showed activity in BBB permeability and ecotoxicity, along with activation of stress response pathways (nrf2/ARE, HSE), indicating potential oxidative stress involvement.

Oleic acid showed a toxicity profile similar to linoleic acid, with minimal organ toxicity and no major mutagenic or carcinogenic risks, supporting its safety as a drug candidate.

Palmitic acid exhibited low toxicity across all major endpoints, with no significant organ toxicity or mutagenicity. However, its BBB permeability and ecotoxicity signals suggest limited but notable biological interactions.

Importantly, none of the compounds showed carcinogenicity or mutagenicity, reinforcing their general safety.

4.4 Integrated Analysis of Drug Potential

Combining docking, ADME, and toxicity results provides a deep exhibition:

B-Sitosterol: Strong binding but low druggabilty and high toxicity concerns limit its drug potential.

Linoleic acid: Moderate binding and good safety but limited by poor absorption and high flexibility.

Oleic acid: Balanced profile with good binding, favorable ADME, and low toxicity—emerges as a promising candidate.

Palmitic acid: Excellent ADME and safety but weaker docking interactions compared to others.

4.5 Overall Conclusion of Results

Among the studied phytochemicals, oleic acid demonstrates the most desired balance between binding affinity, druggabilty, and safety, this makes it a strong candidate for further desired validation against 2vsm .

Conclusion

This study exhibited an explored computational details conglomerate molecular docking, ADME, and toxicity profiles to examined selected phytochemicals from *Terminalia chebula* seeds as vital inhibitors of nipha virus glycoprotein.

The findings showed that all four phytochemicals—β-sitosterol, linoleic acid, oleic acid, and palmitic acid—explored the binding affinity within the active site of the target macromolecule, showing their vital antiviral relevance. As a promising phytochemical of the seeds of *Terminalia chebula*, oleic acid exhibited a well-balanced result, combining acceptable binding affinity with good gastrointestinal absorption, well pharmacokinetic properties, and satisfied toxicity concerns. This this study showed that the seeds of *Terminalia chebula* has the efficiency to be a potential inhibitor against 2vsm.

Further in vitro studies are needed to explain these computational interaction and to exhibit structural optimization strategies for balanced drug efficacy and bioavailability.

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