Molecular Docking Studies of *Jasminium officinale* Compounds for Wound Healing Properties

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Abstract- **Wound healing is a complex biological process involving various cellular and molecular events. Natural compounds derived from medicinal plants have gained significant attention for their potential wound healing properties. *Jasminium officinale*, commonly known as jasmine, is a widely used traditional medicinal plant known for its therapeutic properties. In this study, we aimed to investigate the potential wound healing effects of compounds found in *Jasminium officinale* through molecular docking simulations. A comprehensive library of phytochemicals present in *Jasminium officinale* was constructed and their 3D structures were obtained using chemical databases and computational tools. Subsequently, the molecular docking approach was employed to evaluate the binding affinities of these compounds with key molecular target Matrix metalloproteinase (MMP) 13 involved in wound healing. The molecular docking studies revealed significant interactions between *Jasminium officinale* compounds and the target protein MMP-13. The compounds were also reranked on the basis of binding free energy calculated with MMGBSA method. Several compounds exhibited strong binding affinities, indicating their potential to modulate the activity of these proteins. Furthermore, the identified compounds were subjected to ADME (absorption, distribution, metabolism, and excretion) and toxicity predictions to assess their drug-like properties and safety profiles. Compounds exhibiting favorable pharmacokinetic and toxicological properties were prioritized for further consideration.**
These findings serve as a foundation for future *in vitro* and *in vivo* investigations to validate the efficacy of these compounds as wound healing agents.

Keywords: **Molecular docking, *Jasminium officinale*, wound healing, ligand-receptor interactions, bioactive molecules.**

1. Introduction

Jasminium officinale, commonly known as jasmine, is a flowering plant that has been traditionally used in various cultures for its medicinal properties. It belongs to the Oleaceae family and is native to regions of Asia and Europe. *Jasminium officinale* is known for its pleasant fragrance and is often cultivated for ornamental purposes (Ahmed et al., 2016; Pandey et al., 2020).

In traditional medicine, different parts of the *Jasminium officinale* plant, including the flowers, leaves, and stems, have been utilized for their therapeutic benefits (Maver et al., 2015). The plant has been traditionally employed to treat various ailments, including skin disorders, inflammation, and wound healing (Lordani et al., 2018). The wound healing properties of *Jasminium officinale* are attributed to its rich phytochemical composition, which includes flavonoids, phenolic compounds, and essential oils (Sahu et al., 2022). *Jasminium officinale* holds great promise as a natural source of compounds with wound healing properties.

This research has increasingly focused on exploring the potential wound healing properties of *Jasminium officinale* compounds. I*n silico* methodologies play a significant role in identifying potential bioactive compounds by facilitating the screening of compound libraries. Therefore, In this research work, a combination of two *in silico* methods molecular docking and MMGBSA has been used to screen the potential wound healing compounds of the *Jasminium officinale.*

2. Methodology

2.1 Ligand dataset

The IMPPAT 2.0 database is a comprehensive database of phytochemicals, which are the chemical compounds that give plants their medicinal properties. The database can be used to identify the compounds present in plants, herbs, and other natural products. In this study, the phytochemicals present in jasmine officinale were identified using the IMPPAT database. All of the compounds were then energy minimized and converted to pdbqt format using openbabel integrated with the PyRx module.

2.2 Protein preparation

The crystal structure of human MMP-13 was downloaded from the Protein Data Bank (PDB ID:). The protein structure was prepared using Chimera DockPrep module. In this step the hetero atoms, solvent was removed from the PDB file. Afterwards, hydrogen atoms were added to correct the ionization and tautomeric status of the amino acids. Charges were added where required using the CHARMM force field. FInally, the protein is loaded to PyRx software and converted to pdbqt format.

2.3 Molecular Docking

Molecular docking was performed to identify the hit compounds showing best orientations and maximum binding affinities with MMP-13 using AutoDock Vina (version 4, The Scripps Research Institute, USA) in PyRx platform. The performance of the docking protocol was evaluated by redocking the bound co-crystalised inhibitor to its binding site. After the molecular docking was completed, the poses of the docked complexes were visualized using Maestro, a free molecular modeling software provided by Schrödinger. The poses were originally in PDBQT format, which is not compatible with Maestro. Therefore, they were converted to PDB format using Open Babel, a free chemical file format converter.

2.4 MMGBSA

MMGBSA is a molecular modeling method that combines molecular mechanics (MM) and generalized Born surface area (GBSA) solvation models. MM is used to calculate the non-polar interactions between the ligand and the receptor, while GBSA is used to calculate the polar and solvent-accessible surface area (SASA) interactions. The MMGBSA method has been shown to be a reliable and accurate method for predicting the binding affinities of ligands to proteins. The poses which showed highest binding free energy were selected as potential hit compounds.

2.5 ADMET property calculation

SwissADME is a web-based platform that provides a comprehensive overview of the absorption, distribution, metabolism, and excretion (ADME) properties of small molecules. The platform includes data from a variety of sources, including published literature, clinical trials, and in vitro studies. SwissADME is a valuable resource for researchers and drug developers who are interested in understanding the ADME properties of small molecules. In this study we used SwissADME database to calculate ADMET properties of the identified hits.

3. Results

3.1 Dataset of *Jasmine officinalis* phytochemicals

A total of 47 phytoconstituents were collected from the IMPAAT database. The name of the phytoconstituents is provided in **Table 1.**

Table 1: Phytoconstituents of *Jasminium officinale* plant.

S. No.	Code	Chemical constituents
1.	IMPHY014882	(+)-Linalool
2.	IMPHY007223	(2-Nitroethyl)benzene
3.	IMPHY007358	1,5,9,13-Tetramethyl-1-vinyltetradecyl acetate
4.	IMPHY007293	2-[(Z)-but-2-enyl]-3-methyl-6-oxabicyclo[3.2.0]hept-2-en-7-one
5.	IMPHY006597	2-Methylquinoline
6.	IMPHY006136	2-Vinylpyridine
7.	IMPHY001135	6,10,14-Trimethylpentadecan-2-one
8.	IMPHY012160	alpha-Terpineol
9.	IMPHY005706	Anthranilic acid
10.	IMPHY006362	Ascorbic acid
11.	IMPHY009946	Benzaldehyde
12.	IMPHY002962	Benzoic acid
13.	IMPHY008991	Benzyl acetate

14.	IMPHY002915	Benzyl Alcohol
15.	IMPHY010097	Benzyl benzoate
16.	IMPHY011588	cis-3-Hexen-1-ol
17.	IMPHY003689	cis-3-Hexenal
18.	IMPHY011804	cis-3-Hexenyl acetate
19.	IMPHY011696	cis-3-Hexenyl benzoate
20.	IMPHY004428	cis-3-Hexenyl isobutyrate
21.	IMPHY003536	Eugenol
22.	IMPHY011632	Farnesol
23.	IMPHY014923	Geraniol
24.	IMPHY006176	Geranyllinalool
25.	IMPHY006981	Indole
26.	IMPHY000112	Isophytol
27.	IMPHY001068	Jasminine
28.	IMPHY001555	Jasmone
29.	IMPHY012058	Linalool
30.	IMPHY007067	Linalyl acetate
31.	IMPHY006890	Methyl (1R-trans)-3-oxo-2-pentylcyclopentaneacetate
32.	IMPHY007137	Methyl 2-(methylamino)benzoate
33.	IMPHY006968	Methyl anthranilate
34.	IMPHY006700	Methyl benzoate
35.	IMPHY003691	Methyl jasmonate
36.	IMPHY004225	Methyl linoleate
37.	IMPHY006971	Methyl palmitate
38.	IMPHY003485	Myrcene
39.	IMPHY012654	Nerol
40.	IMPHY015022	Nerolidol
41.	IMPHY007356	Nicotinate
42.	IMPHY003113	p-Cresol
43.	IMPHY006941	Phenylacetonitrile
44.	IMPHY012712	Phytol
45.	IMPHY011523	Salicylic acid
46.	IMPHY003358	Stachyose
47.	IMPHY001931	Vanillin

3.2 Molecular docking study

The molecular docking study performed in this study showed that stachyose had the highest binding affinity for MMP-13, with a binding free energy of -42.406 kcal/mol, which is significantly higher than the standard inhibitor (-28.93 kcal/mol). This suggests that stachyose is a promising candidate for further development as a wound healing agent. The docking results also showed that stachyose forms five hydrogen bonds with MMP-13 at the following residues: Gly173, Asp198, His200, and Asn194. These residues are located in the active site of MMP-13 and are essential for its catalytic activity. The formation of hydrogen bonds between stachyose and these residues suggests that stachyose could inhibit the catalytic activity of MMP-13 and prevent the degradation of extracellular matrix proteins. In addition, the docking results showed that stachyose is stabilized within the binding pocket of MMP-13 through a combination of hydrogen bonds and hydrophobic interactions. In addition to this, Benzyl benzoate formed pi bonds with Phe175 and Tyr195. Methyl linoleate formed one hydrogen bond with Asn194. Myrcene stabilized itself within the hydrophobic pocket of MMP-13. 2-Methylquinoline formed a hydrogen bond with Gly173. This suggests that identified hits has a high binding affinity for MMP-13 and is unlikely to dissociate from the enzyme easily. Overall, the results of the molecular docking study suggest that the hits represent a promising starting point for further development as a wound healing agent. However, further studies are needed to confirm the in vitro and in vivo efficacy of stachyose.

3.3 MMGBSA study

The results of the MMGBSA studies showed that stachyose had the highest binding affinity for MMP-13, with a binding free energy of -42.406 kcal/mol. The standard inhibitor had a binding free energy of -28.93 kcal/mol.

3.4 Interaction of the hits with MMP-13

The binding poses of the top-5 compounds are shown in **figure 1**. It had observed that, stachyose formed five hydrogen bonds with MMP-13 at the following residues: Gly173, Asp198, His200, and Asn194. Benzyl benzoate formed pi bonds with Phe175 and Tyr195. Methyl linoleate formed one hydrogen bond with Asn194. Myrcene stabilized itself within the hydrophobic pocket of MMP-13. 2-Methylquinoline formed a hydrogen bond with Gly173. The results of the molecular docking study suggest that stachyose is a potential inhibitor of MMP-13. Further studies are needed to confirm the in vitro and in vivo efficacy of stachyose as a wound healing agent.

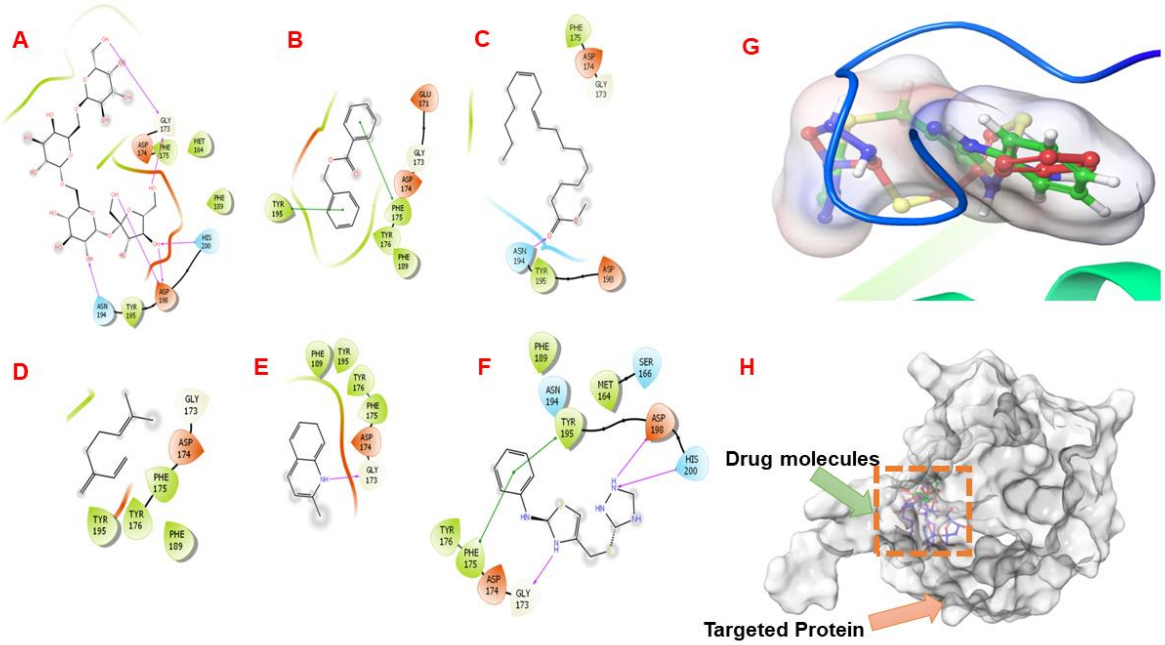

Figure 1: Binding poses of the top-5 compounds with the protein PDB ID.

3.3 ADMET Properties of the identified hits

The predicted ADMET properties from SwissADME showed that Stachyose, methyl linoleate, and 2-methylquinolin violate one or more of the criteria of Lipinski's rule of five. Stachyose has a molecular weight of 666.58 Daltons, which is greater than 500 Daltons. Methyl linoleate has a log P of 6.82, which is greater than 5 and 2-methylquinolin has a hydrogen bond donor count of 1, which is greater than 5. These violations of Lipinski's rule of five suggest that Stachyose, methyl linoleate, and 2-methylquinolin may have decreased oral bioavailability.

However, it is important to note that natural Lipinski's rule of five is not a perfect predictor of oral bioavailability. There are many exceptions to the rule. And even if a compound violates one or more of the criteria of the rule, it may still have good oral bioavailability.

Overall, Lipinski's rule of five is a useful tool for early drug discovery.

Table 2: ADMET properties of the chemical constituents present in *Jasminium officinale.*

Molecule	Formula	MW	Rotatable bonds	H-bond acceptors	H-bond donors	TPSA	XLOGP3	BBB permeant	Pgp substrate
Stachyose	C24H42O21	666.58	11	21	14	347.83	-7.99	No	Yes
Methyl linoleate	C19H34O2	294.47	15	2	0	26.3	6.82	No	No
Myrcene	C10H16	136.23	4	0	0	0	4.17	Yes	No
2-methyl quinoline	C10H9N	143.19	0	1	0	12.89	2.59	Yes	No

4. Discussion

In the current study, molecular docking studies have been performed of *Jasminium officinale* compounds for wound healing properties. After docking studies 4 compounds (Stachyose, methyl linoleate, Myrcene, and 2-Methylquinoline) have been selected on the basis of best binding energy.

Stachyose is an oligosaccharide which can help to improve gut health by increasing the populations of beneficial bacteria in the large intestine. This can help to reduce inflammation and improve digestion. In a study it was found that stachyose reduced inflammation and increased blood flow to the wound site. It also improved the tensile strength of the wound. These studies suggest that stachyose may be a potential treatment for wound healing.

Methyl linoleate is a fatty acid methyl ester of linoleic acid. Various studies have been published which have shown to have a number of medicinal properties in methyl linoleate, including anti-inflammatory effects, antioxidant effects, immunomodulatory effects, wound healing, etc. So, methyl linoleate may be a safe and effective topical treatment for wound healing.

Myrcene is a terpene found in a variety of plants, including hops, cannabis, and mangoes. It is a major component of the essential oil of hops, and it is responsible for the characteristic aroma of beer. Myrcene has been shown to have a number of medicinal properties, including anti-inflammatory effects, antioxidant, immunomodulatory effects, antimicrobial effects and wound healing effects. Myrcene has been shown to promote wound healing in a number of animal models. For example, it has been shown to increase the rate of wound healing and reduce the size of the scar. Therefore, this drug may be a good choice of treatment for wound healing.

2-Methylquinoline is a chemical compound that has been shown to have medicinal and wound healing properties. It is a derivative of quinoline, which is a naturally occurring compound found in plants. Overall, 2-Methylquinoline is a promising new compound with a wide range of medicinal and wound healing properties. It is a safe and effective treatment for a variety of conditions, including chronic wounds, burns, and infections.

There are some limitations of our study. First, we have only studied the in vitro effects of these compounds. It is important to confirm their efficacy in vivo. Second, we have not studied the long-term safety of these compounds in clinical models. It is important to assess their potential toxicity before they can be used in humans. Despite these limitations, our study provides promising evidence that *Jasminium officinale* is a valuable source of natural compounds with wound healing potential. Further studies are needed to confirm these findings and to develop these compounds into new therapeutic agents.

5. Conclusion

In this study, we have performed molecular docking studies of *Jasminium officinale* compounds for wound healing properties. We have identified four compounds (stachyose, methyl linoleate, myrcene, and 2-methylquinoline) that have the potential to inhibit MMP-13, a key enzyme involved in wound healing. These compounds have also been shown to have other beneficial properties, such as anti-inflammatory, antioxidant, and immunomodulatory effects. Further studies are needed to confirm the in vitro and in vivo efficacy of these compounds as wound healing agents. The results of this study suggest that *Jasminium officinale* is a promising source of natural compounds with wound healing potential. These compounds could be developed into new therapeutic agents for the treatment of a variety of wound-related conditions.

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Conflict of interest

Authors have no conflict of interest.

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