International Journal of Pharmacy and Pharmaceutical Research (IJPPR)
Volume 30, Issue 12, December 2024 **ijppr.humanjournals.com** ISSN: 2349-7203

Phytochemical Analysis and Docking Study of Compounds Present in Polyherbal Preparations Used in the Treatment of Wound Healing

Shubhangi Mali, Aniket Gavade, Amol Patil, Sneha Tipugade, Vishal Patil

S.D. Patil Institute of pharmacy, Islampur ,India

Rajarambapu College of Pharmacy Kasegaon. India

S.D. Patil Institute of pharmacy, Islampur India

S.D. Patil Institute of pharmacy, Islampur India

Rajarambapu College of Pharmacy Kasegaon. India

Received: 2024-12-07 Revised: 2024-12-18 Accepted: 2024-12-24

ABSTRACT

The Asteraceae (sunflower family) species *Wedelia chinensis* is very significant in the Ayurveda, Siddha, and Unani Schools of Traditional Medicine. The leaf of *Wedelia chinensis* was examined for its phytochemical, cytotoxic, and antioxidant properties in the current study.[1]The current review article makes an effort to include medicinal plant *Wedelia chinensis* that have been said to be successful at treating wounds.[2] This review mainly focuses on phytochemicals and their role as antimicrobial, anti-oxidant and wound healing agent.[3]The phytochemical investigations of traditionally used medicinal plants have shown the diversified useful compound classes like alkaloid, phenolic, tannin, terpene, steroid, flavonoid, glycoside, and fatty acid.[3] 1FLS(MMP13) is a protein essential ion wound healing. Therefore, the present study is aimed to evaluate the inhibitory effect of phytoconstituents on MMP as a potential therapeutic target for wound therapy.[4] 1FLS showed binding affinity with different compounds. The binding energy of MMP13(1FLS) with phytochemicals are obtained as Beta-caryophyllene-7.1Kcal/mol, Thymol -6.6Kcal/mol, Alpha-phellandrene -6.3Kcal/mol, Alpha-terminene -6.2Kcal/mol. The presence of tannins and saponins in the leaf crude extract was confirmed. In the DPPH radical scavenging assay, both and methanol extract displayed more than 80% radical scavenging activity.[1]At the beginning of the drug development process, in silico methods are helpful. In this review the use of QSAR has been expanded to include molecular design, biological activity prediction, lead compound optimisation and virtual screening, categorization, diagnosis, and elucidation of drug action mechanisms, toxicity prediction of environmental toxicants, and drug-induced toxicity prediction.[3]

Keywords: Wound healing, phytochemicals, *Wedelia chinensis*, binding affinity, 1FLS protein.

INTRODUCTION:

Asteraceae is a family of flowering plants that includes the genus *Wedelia*. These belong to the genus known as "creeping oxeyes." *Wedelia* is known scientifically as sphagneticola. *Wedelia chinensis* (Asteraceae) is a perennial herb that grows to a height of between 0.3 and 0.9cm. The leaves are succulent, typically 4 to 9 cm long and 2 to 5 cm wide, irregularly toothed or serrated, and oval in form. The process of healing a wound that has been caused to the skin or other soft tissues. Inflammation, proliferation, and remodelling are the three phases of wound healing.[6] In order to restore the anatomical continuity and function of the damaged component, the primary premise of optimal wound healing is to minimise tissue damage while providing appropriate tissue perfusion and oxygenation, proper nutrition, and a moist wound healing environment.[7]

The skin serves as a crucial barrier to keep the body safe from external dangers such infections, radiation, and tissue damage. One of the common problems is a wound. When administered to wounds, phytochemicals, which are non-nutritive compounds found in plants, may improve tissue remodelling and function as proangiogenic agents to speed up the healing process. Here, we examine the data supporting their application to wound care. For the control and treatment of microbial infections and wounds, phytochemicals hold enormous potential.[8] Several active components, including flavonoids, diterpenes, triterpenes, saponins, and variety of medicinal plants that share the same phytochemicals as Alpha-pinene, Beta-pinene, Beta-caryophyllene, limonene, Alpha-

International Journal of Pharmacy and Pharmaceutical Research (IJPPR)
Volume 30, Issue 12, December 2024 ijppr.humanjournals.com ISSN: 2349-7203

phellandrene, camphor, Thujene, Alpha-thujene, sabinene, Gamma-terminene, Gallic acid, and Vanillic acid.[1] This study involves the use of docking study (Pass) for exploring the hidden pharmacological potential of selected traditional Indian medicinal plant *Wedelia chinensis* based on their main phytoconstituent.

Protein used for wound healing activity:

1FLS (Solution structure of the catalytic fragment of human collagen) is a protein essential in wound healing. The purpose of the current study is to assess 1FLS as a potential therapeutic target for wound therapy and the inhibitory effect of plants on it. Every phytochemical displayed a strong affinity for 1FLS. In order to meet the demand for wound healing goods, this Several phytoconstituents that have been previously reported to be identified from the extracts of *W. chinensis*, *W. Trilobata*, *W. Urticifolia*, *W. Gluca*, and *W. Prostrata* are the focus of the current work, which aims to target crucial proteins involved in the healing process of wounds. Molecular docking is an In-silico method for determining the optimal interactions between a protein and its ligand. Current work offers important insights into the molecular structure interaction and requirements of the phytoconstituents from *Wedelia chinensis*.

Role of Metalloproteinase in wound healing:

Protein is one of the most important nutrient factors affecting wound healing. Gelatin; fibronectin; laminin; tenascin; aggrecan; fibrillin; serpins; collagen I, II, III, IV, IX, X, and XIV through influencing wound contraction, indirectly promotes re-epithelialization. MMP- plays a crucial role in the maturation of granulation tissue by influencing myofibroblast activity, inflammation, angiogenesis, and matrix degradation. MMP-13 is expressed by fibroblasts deep in the chronic wound bed. Molecular docking is an in-silico method for determining the optimal interactions between a protein and its ligand. MMPs, or matrix metalloproteinases, are found in both acute and chronic wounds. At all stages of the healing process, MMPs must be regulated in order to promote wound healing process, MMPs must be regulated in order to promote wound healing.

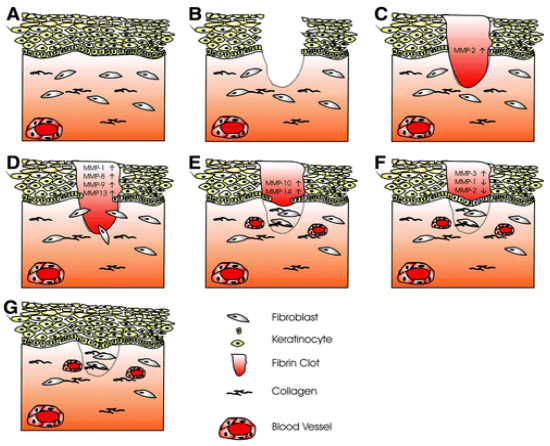


Fig.no. 1 stages of wound healing

Materials and method: [4]

1. **Protein preparation:** The three-dimensional structure of the selected 1FLS (MMP13) were retrieved from RCSB database **(**PDB DOI: 10.2210/pdb1FLS/pdb) in Protein Data Bank (PDB) format.

International Journal of Pharmacy and Pharmaceutical Research (IJPPR)
Volume 30, Issue 12, December 2024 **ijppr.humanjournals.com** ISSN: 2349-7203

Table. No 1. Phytoconstituents of WC

Beta caryophyllene: ID: 52811515	Mol: $C_{15}H_{24}$ Mol wt: 204.35g/mol
Alpha pinene: ID: 6656	Mol: $C_{10}H_{24}$ Mol wt: 136.23g/mol
Beta pinene: ID: 14896	Mol: $C_{10}H_{16}$ Mol wt: 136.23 g/mol
Alpha thujene: ID: 6451618	Mol: $C_{10}H_{16}$ Mol wt: 136.23 g/mol
Alpha phellandrene: ID: 7460	Mol: $C_{10}H_{16}$ Mol wt: 136.23g/mol
Limonene: ID: 22311	Mol: $C_{10}H_{16}$ Mol wt: 136.23g/mol
D-Limonene: ID: 440917	Mol: $C_{10}H_{16}$ Mol wt: 136.23g/mol
Camphor: ID:2537	Mol: $C_{10}H_{16}O$ Mol wt: 152.23 g/mol
Thujene: ID:520384	Mol: $C_{10}H_{16}$ Mol wt: 136.23 g/mol
Sabinene: ID:18818	Mol: $C_{10}H_{16}$ Mol wt: 136.23 g/mol
Gallic acid: ID: 370	Mol: $C_7H_6O_5$ Mol wt : 170.12 g/mol
Vanilic acid: ID: 8468	Mol: $C_8H_8O_4$ Mol wt: 168.15 g/mol
Beta phellandrene:ID:1142	Mol: $C_{10}H_{16}$ Mol wt: 136.23 g/mol
Myrcene: ID: 31253	Mol:$C_{10}H_{16}$ Mol wt: 136.23 g/mol
Camphene: ID: 6616	Mol: $C_{10}H_{16}$ Mol wt: 136.23 g/mol

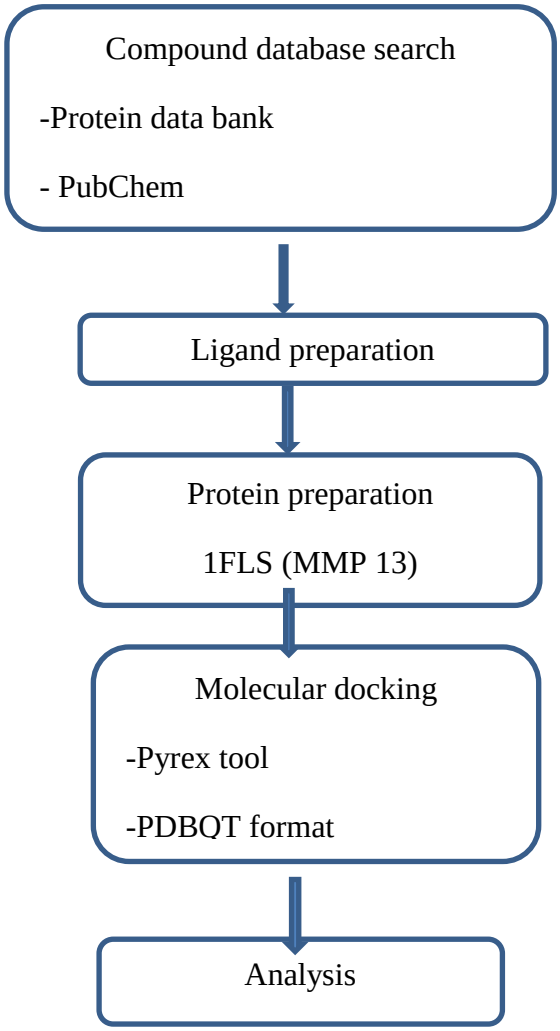
Ligand preparation: The three-dimensional structure of the phytochemicals was retrieved from PubChem database. The compound ID of all phytochemicals with molecular formula are given below:

2. Active Site of 1FLS: One of the key factors in docking research is the active site, where the ligand interacts with the protein's active site amino acid residues to produce powerful binding interactions. Based on reports in the literature, the experimentally confirmed active site residues of the chosen 1FLS (MMP 13) were taken into consideration in the current study.

4. Dock preparation: The protein structure's addition chains were eliminated, and only one chain was utilized. Ions, ligands, and water molecules that were present in each protein crystal structure were taken out during dock production. Charges and polar hydrogen bonds were then included. These dock-ready proteins were utilized in other docking processes.[10]

5. Molecular docking process: Pyrex tool was used for analysing the docking studies between 1FLS (MMP 13) and phytochemicals. The dock prepared MMPs and all phytochemicals were reconstructed into PDBQT format. Based on the calculation of free energy interactions, the level of interactions between selected 1FLS (MMP 13) and phytochemicals is determined. Higher potential molecules for interacting with receptors are those whose free energies of binding to the receptor are lower. The optimal docking poses for each 1FLS (MMP 13) was selected for further examination based on the affinity score.

International Journal of Pharmacy and Pharmaceutical Research (IJPPR)
Volume 30, Issue 12, December 2024 ijppr.humanjournals.com ISSN: 2349-7203



Flow diagram of molecular docking study

Result and discussion [4]

Protein and ligand preparation:

four MMPs, MMP2, MMP3, MMP8, and MMP12, MMP13 which are a set of enzymes involved in the healing of wounds, were chosen MMP 13 (1FLS) for the docking investigation. Beta caryophyllene is a natural bicyclic sesquiterpene that is a constituent of many essential oils which is naturally present in *W. chinensis* and *W. prostrata* leaf extracts, was chosen as the ligand for an evaluation of its interactions with specific MMP13(1FLS) involved in the wound healing process. The 3D structure of beta caryophyllene and MMP13(1FLS) are shown below.

Fig no 2.3D structure of 1FLS

Docking interaction and analysis:

Molecular docking analysis has been one of the most basic and important strategy for drug discovery. It allows prediction of molecular interactions that hold together a protein and a ligand in the bound state. The docking studies were done using Pyrex tool. The prepared all phytochemicals was docked with MMP13(1FLS) protein. The best dock conformation between MMP13 and all phytochemicals were predicted using the best binding affinity values and molecular interactions. The selected best poses were analyzed for hydrogen and hydrophobic bond donor residues between the MMP13 active site and phytoconstituents.

Interaction between phytoconstituents and protein (MMP13)

MMP13 belongs to metalloelastase group of enzymes, which are essential for tissue repairing process. Yet, MMP13 overexpression would cause inflammatory cells to infiltrate the body and would slow the healing of wounds.

Table no.2. Active sites of protein

Protein	Plants	Active site
1FLS	*Wedelia chinensis*	80,81,83,116, 119, 141
1FLS	*Wedelia Prostrata*	80,82,116,119, 138,141

Binding energies of ligand-receptor from Pyrex tool given below:

Table no 3. Binding energies of ligand-receptors

Ligand	Binding affinity _(kcal/mol)	rmsd/ub	rmsd/lb
1fls_BETA caropohyllene W.chinensis_uff_E=705.49	-7.1	0	0
1fls D limonene W. trilobata E= 51.89	-6.2	0	0
1fls Thymol *W. chinensis* E=67.46	-6.6	0	0
1fls alpha phellandrene W. trilobata E=65.17	-6.3	0	0
1fls alpha pinene w. chinensis E=444.94	-5.9	0	0
1fls alpha terminene w. chinensis E=91.73	-6.2	0	0
1fls alpha thujene W. prostrata E=1199.98	-5.8	0	0
1fls alpha thujene W. gluca E=1203.35	-5.8	0	0
1fls beta caryophyllene w. prostrata E=705.49	-7.1	0	0

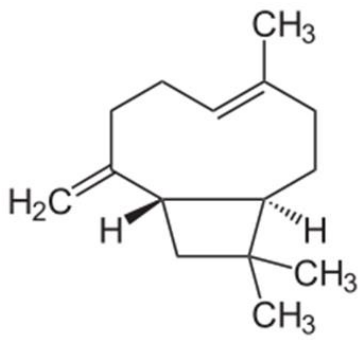
The binding energies of best docked compounds ranged between −8.0 kcal/mol and −11.71 kcal/mol.

From above data we conclude that beta caryophyllene phytoconstituents from *Wedelia chinensis* and *Wedelia Prostrata* shows higher binding affinity with 1FLS protein.

Beta- caryophyllene:

Beta-caryophyllene(trans-(1,9)-methylene-4,11,11-trimethylbicycloundec-4-ene) is a natural bicyclical sesquiterpene found in several plants and essential oils, including *Wedelia chinensis.* Because of its analgesic, antioxidant, antibacterial, and anti-inflammatory properties, beta-caryophyllene is a volatile molecule with a low water solubility.

International Journal of Pharmacy and Pharmaceutical Research (IJPPR)
Volume 30, Issue 12, December 2024 ijppr.humanjournals.com ISSN: 2349-7203



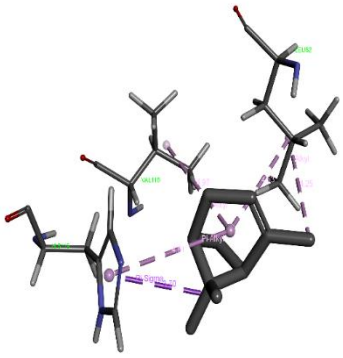
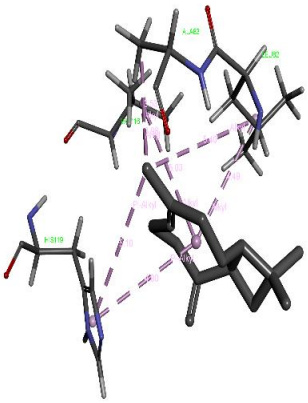


Fig no 3.2D Structures of beta caryophyllene

Fig.no 4. 3D Structure of Beta-caryophyllene (w.



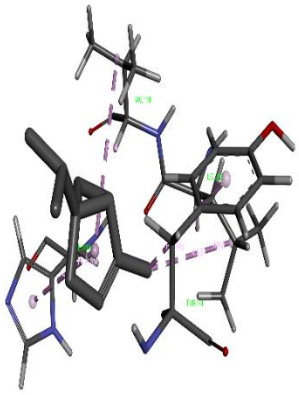
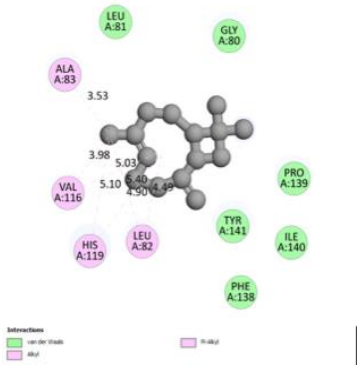


Fig no. 5. Beta caryophyllene (w. prostrata)

Fig no.6. Alpha pinene



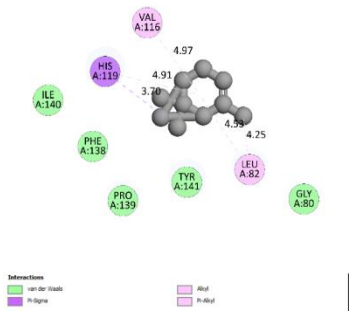


Fig no. 7. Alpha phellandrene

Fig no. 8. Alpha terminene

Conclusion:

For the control and treatment of microbial infections and wounds, phytochemicals hold enormous potential. To treat and manage infections and wounds, phytochemicals must be discovered and developed. Nonetheless, uniformity is required. Before proposing phytochemicals for therapeutic use, safety and scientific evaluation must be completed.[3]

In our above study we looked at the potential of several phytochemicals that can be extracted from *Wedelia chinensis*.[12] Our docking tests demonstrate that phytochemicals tightly attach to a hypothetical protein active site.[10] From above data beta-caryophyllene has been proved to be one of the potent wound healing agent which has been shown to elicit the cutaneous wound healing better than the other phytoconstituents from *Wedelia* species.[11] From this study we investigate that beta-caryophyllene showed binding affinity to 1FLS(MMP13) protein.[4]

References:

1. Anita Kumari, Sunita Bhatnagar, they had research on Phytochemical analysis and biological evaluation of leaf extracts of *Wedelia chinensis* Pharmacy & Pharmacology *International Journal*, **2016,** Volume 4 Issue 7.
2. Akshay Sharma, Suryamani Khanna, Gaganjot Kaur, Medicinal plants and their components for wound healing applications, *Future Journal of Pharmaceutical Sciences*, **2021**.
3. Rex Jeya Rajkumar S, Muthukumar Nadar, they had review on Phytochemicals as a potential source for antimicrobial, anti-oxidant and wound healing, *MOJ Bioorganic & Organic Chemistry*, **2018**, Volume 2 Issue 2.
4. N A Mokhtar et al 2021, Docking study for assessment of wound healing potential of isosakuratenin isolated from *Chromolaena odorata*: An In-silico approach, *IOP Conf. Series: Materials Science and Engineering*, **2021**.
5. Bano Shamama, Mazumder Avijit, they had review on *Wedelia chinensis* (Asteraceae)- An overview of a potent medicinal herb, *World Journal of Pharmaceutical Research*,**2013**, Volume 6, Issue 6, 488-496.
6. Vipin Kumar Garg, Sarvesh Kumar Paliwa, Wound-healing activity of ethanolic and aqueous extracts of *Ficus benghalensisl*, *Journal of Advanced Pharmaceutical Technology & Research*, Apr-Jun **2011**, Vol 2 Issue 2.
7. Irshad Nomani, Avijit Mazumder, and GS Chakraborthy, Evaluation of Wound Healing Potentiality of Methanolic Extract of *Wedelia chinensis* Whole Plant, *Research Journal of Pharmaceutical, Biological and Chemical Sciences*, July-Sept **2013**, Vol 4, Issue 3, Page no 353-359.
8. Rajesh L. Thangapazham, Shashwat Sharad, Phytochemicals in Wound Healing, *Advances in Wound Care*, **2014**, Vol 00.
9. Matthew P. Caley, Vera L.C. Martins, Metalloproteinases and Wound Healing, *Advances in Wound Care*, **2015**, Vol 4, Page no 1-4.
10. H. R. Umesh K, V. Ramesh, Molecular docking studies of phytochemicals against trehalose–6– phosphate phosphatases of pathogenic microbes, *Springer Open*, **2020**.
11. Harish Basavanthappa Gowdru, Sharath Rajashekarappa, Molecular docking and evaluation of wound healing activity of stigmastatone isolated from bark *of Celastrus paniculatus* Willd, *J Biochem Tech*, **2012**, 3(5).
12. Arkaniva Sarkar, Rushali Agarwal, Molecular docking studies of phytochemicals from *Terminalia chebula* for identification of potential multi-target inhibitors of SARS-CoV-2 protein, *Journal of Ayurveda and Integrative Medicine*, **2022**.

How to cite this article:
Shubhangi Mali et al. Ijppr.Human, 2024; Vol. 30 (12): 227-233.

Conflict of Interest Statement: All authors have nothing else to disclose.