Journal of Pioneering Medical Sciences
Received October 2, 2023 Accept December 04, 2023 Publish December 23, 2023.
Volume 12, Issue 3, Pages 20-24

DOI https://doi.org/10.61091/jpms20231235

Exploration of Wound Healing Activity of Phytocompounds from Tridax Procumbens Using Computation Approach

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Abstract Tridax procumbens is a well-known medicinal herb that has traditionally been used to treat wounds and bronchial catarrh. In the current work, target proteins (EGF, PDGF, TGF, VEGF) implicated in wound healing were analyzed using in silico computational analysis of chosen active phytoconstituents of Tridax procumbens. Studies have shown that these targets are essential in wound healing and injury repair. This study aims to see if Caffeic acid, Epicatechin, Kaempferol, and Tannic acid can bind to and enhance the activity of specific proteins. The current research relies heavily on a computer-based molecular docking tool that simulates the in vivo situation and uses a unique algorithm to evaluate a ligand molecule's binding affinity and pose to a receptor. According to the findings, tannic acid had a great affinity with all of the target proteins studied in this investigation. Thus, this chemical should be investigated further as a potential therapeutic candidate.

Key Words Disease, Health, Innovative, Gingival, Molecular docking, Periodontal, Tridax procumbens, Wound healing

1. Introduction

Wound healing is a process in which injured tissues are repaired, and their function is restored. In order to restore tissue integrity, various cell types are involved in wound healing. Though all biological systems have built-in repair mechanisms, supplying external support/stimuli can speed up the process by promoting tissue healing. Antiseptics, sulfa-antibiotics, skin barrier emollients, collagen-specific enzymes, corticosteroids, and plant compounds could all be stimulants [1].

Furthermore, the FDA has yet to approve a direct medication candidate for wound healing that targets complete wound closure. As a result, developing medication candidates specifically for wound closure is critical for improving cutaneous wound management [2]. Natural compounds are evolving as potential drug candidates. However, various plant sources/plant derivatives have long been known to have pharmacological value, such as antimicrobial/anti-inflammatory activity, better tissue remodeling ability, and activation of immune and migrating cells [3]. Furthermore, various plant extract compositions and combinations have been trademarked for their antibacterial, anti-inflammatory, and wound-healing properties [4]. This demonstrates that isolating and identifying phytochemicals with specialized healing properties and their combinatorial ability is a reasonable approach for future treatments, such as its application as a wound dressing material for periodontal flap surgery or gingival surgical procedures. As a result of their wound-healing properties, plant-derived chemicals are garnering much attention as Complementary and Alternative Medicines (CAMs) [5].

Tridax procumbens is a species of tridax. Linn is a common weed and a flowering plant with various therapeutic properties. Wound healing, diarrhea, epilepsy, hypertension, hepatotoxicity, bleeding, and metabolic syndrome have all been treated with the herb [6]. Tridax procumbens has historically been used in India as an anticoagulant, antifungal, and insect repellant. In folk medicine, leaf extracts were used to cure infectious skin problems. Apart from gastritis and heartburn, it is a well-known ayurvedic treatment for liver problems or hepatoprotective properties [7]. Due to a lack of knowledge, the current work used an insulin strategy to explore the wound-healing impact of phytochemicals from Tridax procumbens Linn.

Computer-based receptor-ligand binding is a good strategy for structure-based drug screening, and specific phytocom-

pounds or combinations of a few phytochemicals can be predicted in a few hours utilizing molecular docking and interaction [8]. On the other hand, the molecular docking tool is used to estimate the interaction between a small molecule (ligand) and a macromolecule (protein), which explains the behavior of small molecules at the binding site of a target receptor [9], [10].

2. Materials and Methods

Protein Retrieval and Preparation

Four Target proteins; EGF -(Pdb id:1JL9), PDGF- (Pdb id:3MJG), TGF-(Pdb id:1PY5), VEGF -(Pdb id:2VPF) were selected for the current study. The structures were obtained from the https://www.rcsb.org/ website in PDB format. Further, the 3D PDB file of these proteins as processed using 'A' chain and eliminating allied ligands along with crystallographic water molecules, and adding polar hydrogen atoms.

Ligand Structure Preparation

In four phyto-constituents of T. procumbens were selected as dynamic inhibitory ligands for the existent study. All selected ligand structures except were attained in SDF format from the https://pubchem.ncbi.nlm.nih.gov/website and changed to PDB format using Online SMILES translator and structure file generator tool [11].

Docking using Autodock version 4.0 of pyrx Software

The procedure for docking receptor ligands was carried out using Autodock version 4.0 pyrx software [12]. Docking is the virtual screening of a compound database and estimation on the basis of different scoring features of the effectively binding ligand(s). Molecular docking study was conducted using AutoDock vina in The Python Prescription (PyRx) 0.8 virtual screening tool. The grid points for the X, Y and Z axes have been set. The grid core was put in the pocket core of the binding site. Protein and ligands have been encoded into pdbqt formats. Default docking algorithms have been set up in compliance with the required docking protocol. For each ligand protein complex, individual docking procedures have been performed. The results were ranked in the order of increasing docking energies.

3. Results and Discussion

Computer-aided drug design (CADD) has emerged as a thriving program in modern drug development, as it not only reduces the cost and labor associated in the drug development process, but also speeds it up by helping scientists to focus their efforts during biological and synthetic testing [13].

For this investigation, the phytoconstituents of T. procumbens were chosen. T. procumbens drink is traditionally used to cure bronchial catarrh and asthma. Antiviral, immunomodulatory, anti-inflammatory, and analgesic activities are also reported. Results of the present study, highlighted that selected phytoconstituents, showed good binding affinity with the target proteins involved in the wound healing pathway. Selected four compounds (Caffeic acid, Epicatechin, Kaempferol and Tannic acid) exhibited overall high binding affinity towards all targets selected. The docking results of all compounds with selected target proteins are shown in Table 1 to Table 4 and their hydrogen bond interactions are shown in Figure 1 to Figure 4.

Compound Name	EGF Docking Score Kcal/mol	Hydrogen bond interaction
Caffeic acid	-5	ARG-45
		CYS-14
Epicatechin	-6	ARG-45
		CYS-14
Kaempferol	-5.6	ARG-45
		ASP-17
Tannic acid	-7.4	GLN-594
		ARG-577
		PRO-578
		PRO-578
		ASN-659
		GLY-660
		SER-669
		GLU-715
		LYS-721
		ASN-724
		TYR-730
		GLU-765

Table 1: Molecular interaction of EGF with phytocompounds

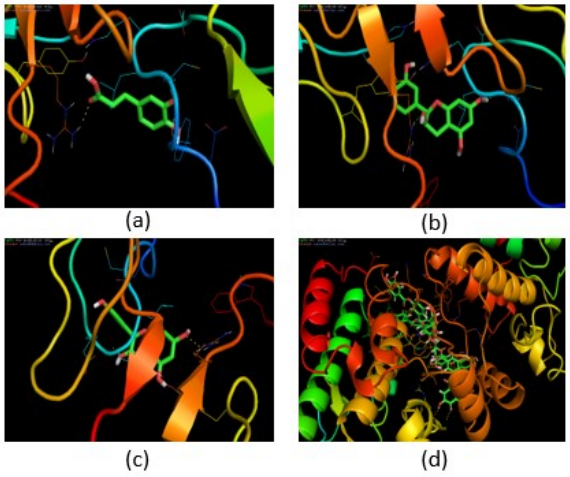

Figure 1: Molecular interaction of EGF with a) Caffeic acid b) Epicatechin c) Kaempferol d) Tannic acid

EGF promotes epidermal cell regeneration and plays an important role in cutaneous wound healing by stimulating keratinocyte proliferation and migration. It also encourages granulation tissue development and fibroblast motility. The molecular docking results of this EGF with selected four compounds are shown in Table 1 and Figure 1.

Results of this study showed that Tannic acid showed the highest binding affinity with a docking score of -7.4kcal/mol, and it also formed the twelve hydrogen bonds with EGF. Followed by Tannic acid, the compound Epicatechin showed a strong binding affinity with a score of -6 kcal/mol, and it also formed the two hydrogen bond interactions with the

Compound Name	TGF Docking Score Kcal/mol	Hydrogen bond interaction
Caffeic acid	.-7.2	LYS-232
		TYR-249
		HIS-283
		ASP-351
Epicatechin	-9.7	LYS-232
		LYS-237
		LEU-278
		SER-280
Kaempferol	-9.6	LYS-232
		TYR-249
		LEU-278
		SER-280
		ASP-351
Tannic acid	-8.5	GLU-209
		ARG-215
		ASP-290
		ASN-293
		ASN-338

Table 2: Molecular interaction of TGF with phytocompounds

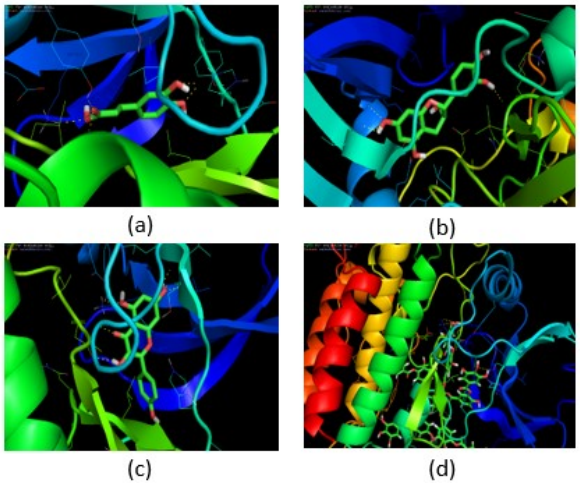

Figure 2: Molecular interaction of TGF with a) Caffeic acid b) Epicatechin c) Kaempferol d) Tannic acid

Compound Name	PDGF Docking Score Kcal/mol	Hydrogen bond interaction
Caffeic acid	-5.5	VAL-22
		SER-50
Epicatechin	-7.4	VAL-22
		GLY-51
Kaempferol	-6.4	THR-20
		VAL-22
Tannic acid	-6.8	THR-20
		GLU-21
		VAL-22
		ARG-48
		CYS-49
		SER-50
		ARG-56
		GLY-51

Table 3: Molecular interaction of PDGF with phytocompounds

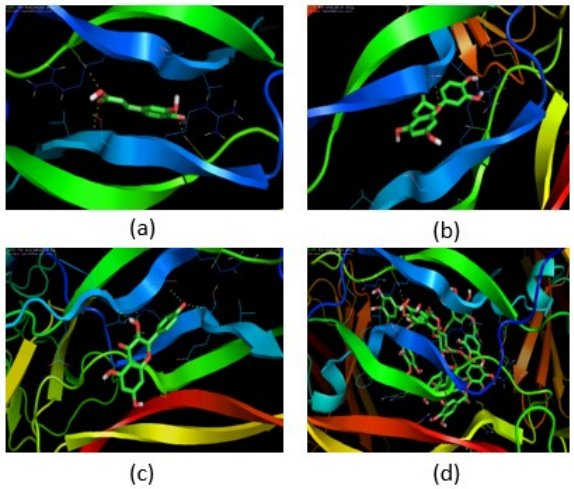

Figure 3: Molecular interaction of PDGF with a) Caffeic acid b) Epicatechin c) Kaempferol d) Tannic acid

Compound Name	VEGF Docking Score Kcal/mol	Hydrogen bond interaction
Caffeic acid	-5.7	TYR-21
		CYS-61
		ASN-62
Epicatechin	-7.5	TYR-21
		CYS-61
		ASP-63
Kaempferol	-7.5	TYR-21
Tannic acid	-7.8	TYR-21
		TYR-25
		ASP-41
		GLN-79
		GLU-93
		ARG-82

Table 4: Molecular interaction of VEGF with phytocompounds

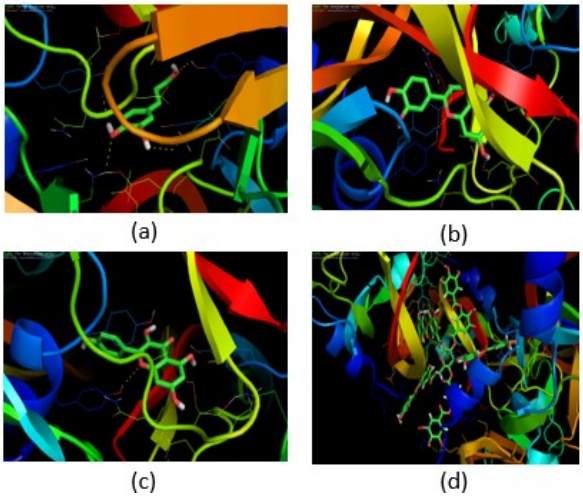

Figure 4: Molecular interaction of VEGF with a) Caffeic acid b) Epicatechin c) Kaempferol d) Tannic acid

amino acid residues ARG-45 and CYS-14. Kaempferol and Caffeic acid also form strong binding with two hydrogen bond interactions, ARG-45 and CYS-14, with a binding score of -5.6 and -5 kcal/mol, respectively. The overall analysis of this docking showed that all the compounds interacted with ARG-45 and CYS-14 residues. So, these residues may be responsible for the function of this EGF protein.

TGF-1 is a growth factor family that is associated with a variety of critical cellular processes. TGF- is involved in various wound healing processes, including inflammation, angiogenesis stimulation, fibroblast proliferation, collagen synthesis and deposition, and remodeling of the new extracellular matrix. TGF-1 signaling is frequently lost in chronic, nonhealing wounds. In the present study, molecular docking was carried out between the TGF and phytocompounds from T. procumbens.

Analysis of docking results showed that Epicatechin showed a strong binding affinity with a docking score of -9.7 kcal/mol. The involvement of many hydrogen bond interactions also confirmed the good of Epicatechin with TGF. It formed the four hydrogen bond interactions through the amino acids LYS-232, LYS-237, LEU-278, and SER-280. Tannin acid formed a powerful interaction with TGF-β Compared to all other compounds because it formed so many hydrogen bonds with the target protein and showed an excellent docking score of -8.5 kcal/mol. Kaempferol also exhibited perfect binding in terms of scoring parameters. It showed a docking score of -9.6 kcal with five hydrogen bond interactions through the amino acids LYS-232, TYR-249, LEU-278, SER-280, and ASP-351. Caffeic acid also showed the lowest binding affinity of -7.2 kcal/mol and formed the four hydrogen bond interactions through LYS-232,TYR-249, HIS-283, and ASP-351.

From these results, it is observed that LYS-232 formed the hydrogen bond interaction with all the compounds. So, this may act as a critical residue for TGF.

In vitro, PDGF increases chemotaxis, proliferation, and the production of novel genes in monocytes-macrophages and fibroblasts, which are important for tissue healing. As a result, PDGF and other wound-produced polypeptide growth factors may be important regulators of extracellular matrix deposition in healing wounds. As a result, PDGF has the capacity to guide or impact the key actions required for a normal wound-healing response. In the present study, PDGF was also selected as one of the target proteins.

Results of docking studies showed that Tannic acid showed strong binding with a binding score of -6.8kcal/mol and formed the eight hydrogen bond interaction through the THR-20, GLU-21, VAL-22, ARG-48, CYS-49, SER-50, ARG-56 and GLY-51. Followed by Tannic acid, the Epicatechin, Kaempferol, and Caffeic acid also showed good binding with a binding score of -7.4, -6.4, and -5.5 kcal/mol, respectively. All three compounds formed two hydrogen bond interactions with PDGF.

VEGF promotes wound healing through various methods, including collagen deposition, angiogenesis, and epithelialization. The mitogenic, chemotactic, and permeability properties of VEGF in the clinical setting may potentially aid in promoting the repair of nonhealing wounds in arterial occlusive disease and diabetes. In this study, selected compounds Caffeic acid, Epicatechin, Kaempferol, and Tannic acid showed strong binding with binding scores of -5.7, -7.5,-7.5, and-7.8 kcal/mol, respectively. Except for Kaempferol, all the compounds formed more than two hydrogen bonds with VEGF. So, these compounds showed the very results with VEGF, which may play a role in wound healing. Future scope of the study lies in exploring this herb's application in managing oral mucosal and periodontal diseases [14]–[17].

An analysis of these interaction studies indicated that tannic acid showed excellent binding with all target proteins selected for this study compared to other compounds.

4. Conclusion

The phytoconstituents of Tridax procumbens were tested in the hunt for a new natural medicine utilized for wound healing using the molecular docking methodology. The findings of this study suggested that these four molecules, namely Caffeic acid, Epicatechin, Kaempferol, and Tannic acid, could be employed as possible therapeutic candidates for wound healing since all these compounds interacted well with target proteins involved in wound healing. As a result, this study argues that the selected phytoconstituents of T. procumbens can successfully regulate wounds and may function as a wound dressing for skin and mucosal wounds following experimental validation.

Acknowledgements

The authors would like to thank all data collectors and study participants involved in the study.

Conflict of Interest

The authors declare no conflict of interests. All authors read and approved final version of the paper.

Authors Contribution

All authors contributed equally in this paper.

References

[1] Bayat, A., McGrouther, D. A., & Ferguson, M. W. J. (2003). Skin scarring. BMJ, 326, 88-92.

[2] Eaglstein, W. H., Kirsner, R. S., & Robson, M. C. (2012). Food and Drug Administration (FDA) drug approval end points for chronic cutaneous ulcer studies. Wound Repair Regen, 20(6), 793-796.

[3] Upadhyay, B., Parveen, Dhaker, A. K., & Kumar, A. (2010). Ethnomedicinal and ethnopharmaco-statistical studies of Eastern Rajasthan, India. J Ethnopharmacol, 129, 64-86.

[4] Wangchuk, P. (2018). Therapeutic applications of natural products in herbal medicines, biodiscovery programs, and biomedicine. Journal of Biologically Active Products from Nature, 8(1), 1-20.

[5] Ambika, A. P., & Nair, S. N. (2019). Wound Healing Activity of Plants from the Convolvulaceae Family. Adv Wound Care (New Rochelle), 8(1), 28-37.

[6] Suseela, L., Sarasvathy, A., & Brindha, P. (2002). Pharmacognostic studies on Tridax procumbens L. (Asteraceae). Journal of Phytological Research, 5(2), 141-147.

[7] Wani, D. S., Sogi, A. A., Wani, B. S., Gill, U. S., & Shivhare. (2010). Physico-chemical properties of starches from Indian kidney bean (Phaseolus vulgaris) cultivar. Int. J. Food Sci. Technol., 45, 2176-2185.
[8] Morris, G. M., & Lim-Wilby, M. (2008). Molecular docking. Methods Mol Biol, 443, 365-382.
[9] Yadav, D., Talapatra, S. N., Gupta, K., & Swarnakar, S. (2017). Alteration of morphology and constituents of Azadirachta indica leaf due to air pollution and exploiting the phenomenon for medicinal usage on gastric ulcer through molecular docking. International Journal of Pharmaceutical Sciences Review and Research, 44(2), 103-111.
[10] Meng, X.-Y., Zhang, H.-X., Mezei, M., & Cui, M. (2011). Molecular docking: A powerful approach for structure-based drug discovery. Current Computer-Aided Drug Design, 7(2), 146-157.
[11] Oellien, F., & Nicklaus, M. C. (2004). Online SMILES translator and structure file generator. National Cancer Institute, 29, 97-101.
[12] Morris, G. M., Huey, R., Lindstrom, W., Sanner, M. F., Belew, R. K., Goodsell, D. S., & Olson, A. J. (2009). AutoDock4 and AutoDockTools4: Automated docking with selective receptor flexibility. Journal of Computational Chemistry, 30, 2785-2791.
[13] Yu, W., & MacKerell, A. D., Jr. (2017). Computer-aided drug design methods. Methods in Molecular Biology, 1520, 85-106.
[14] Sivaharini, S., Jeevitha, M., & Narayan, V. (2021). Assessment of periodontal status in patients with oral leukoplakia. International Journal of Dentistry and Oral Science, 8(8), 3866-3870.
[15] Deepak, A., Prabakar, J., & Jeevitha, M. (2020). Prevalence and severity of periodontal and oral hygiene status among 30-40 years old adult population attending a private dental college-a hospital based cross sectional study. International Journal of Dentistry and Oral Science, 7(12), 1242-1246.
[16] Johnson, J., Shanmugam, R., & Lakshmi, T. (2022). A review on plant-mediated selenium nanoparticles and its applications. J Popul Ther Clin Pharmacol, 28(2), e29-e40.
[17] Ushanthika, T., Smiline Girija, A. S., Paramasivam, A., & Priyadharsini, J. V. (2021). An in silico approach towards identification of virulence factors in red complex pathogens targeted by reserpine. Natural product research, 35(11), 1893-1898.