International Journal of Public Health Excellence (IJPHE)
Vol. 6, Issue 1, June-December 2026, pp. 167~176
Journal Homepage: https://ejournal.ipinternasional.com/index.php/ijphe
ISSN: 2809-9826, DOI: 10.55299/ijphe.v6i1.1970

Effectiveness of Neem Leaves (Azadirachta indica) on Traumatic Ulcer Healing: A Literature Review

Atha Syakirah[1], Talitha Edra Clayrine Siregar[2], Sutansyah Rakha Putra[3], Zalwa Nahrisya Askya[4], Mulya Duratun Nasha[5], Hafidhatun Annisa[6], Muhammad Ryan Triawan[7], Viona Diansari[8]

[1,2,3,4,5,6,7,8]Faculty of Dentistry, Universitas Syiah Kuala, Indonesia

Email: as10atha@gmail.com, talithaedr@mhs.usk.ac.id, rsutan251@gmail.com, zalwa23@mhs.usk.ac.id, mulya23@mhs.usk.ac.id, hafidatun@mhs.usk.ac.id, rian97.mbo@gmail.com, viona_diansari@usk.ac.id
Correspondence: as10atha@gmail.com

Article Info

Article history:

Received May 04, 2026
Revised May 25, 2026
Accepted June 08, 2026

Corresponding Author:

Atha Syakirah
Faculty of Dentistry,
Universitas Syiah Kuala,
Indonesia
Email: as10atha@gmail.com

ABSTRACT

Traumatic Ulcer Is the Most Common Oral Mucosal Lesion Encountered in Dental Practice, Caused by Mechanical, Thermal, Or Chemical Trauma. This Condition Causes Significant Pain and Can Impair Patient Quality of Life. Neem Leaves (Azadirachta Indica) Have Long Been Used in Traditional Medicine as Anti-Inflammatory, Antibacterial, And Wound-Healing Agents. This Literature Review Aims to Examine Scientific Evidence On the Effectiveness of Neem Leaves in Healing Traumatic Ulcers Through Their Pharmacological Mechanisms. Literature Searches Were Conducted Through Pubmed, Google Scholar, And Science Direct Databases with Keywords Related to Neem Leaves, Azadirachta Indica, Traumatic Ulcer, And Oral Mucosal Wound Healing. Articles Meeting the Inclusion Criteria Were Critically Reviewed. Active Compounds in Neem Leaves Including Nimbin, Nimbidin, Azadirachtin, Quercetin, And Tannins Have Been Proven to Possess Anti-Inflammatory Activity by Inhibiting COX-2 And NF-Kb Pathways, As Well as Antibacterial Activity Against Oral Pathogenic Bacteria. These Compounds Also Accelerate Fibroblast Proliferation and Collagen Synthesis Crucial in Wound Healing. Neem Leaves Have Significant Potential as A Therapeutic Agent in Healing Traumatic Ulcers Based On Pharmacological Evidence And Preclinical Studies. However, Further Randomized Controlled Clinical Trials Are Needed to Strengthen Their Clinical Use.

Keywords:

Azadirachta Indica, Neem Leaves, Wound Healing, Traumatic Ulcer, Oral Mucosa

INTRODUCTION

Traumatic ulcers are are among the most commonly encountered oral mucosal lesions in daily dental practice. This lesion is defined as a discontinuity of the oral mucosal epithelial surface resulting from physical, thermal, or chemical trauma, causing significant pain and discomfort. Epidemiologically, traumatic ulcers can occur in all age groups and genders, but their prevalence is higher in individuals using orthodontic appliances, dental prostheses, or those frequently experiencing trauma from bad habits, such as cheek or lip biting. Studies have reported a traumatic ulcer prevalence ranging from 5-21% in the general population (Shetty et al., 2022). This condition is generally self-limiting and heals within 7-14 days; however, in some cases, secondary infection complications can occur, delaying the healing process (Huber & Bhalla, 2021).

Conventional management of traumatic ulcers includes topical corticosteroids, antiseptics, and analgesics. However, long-term use of topical corticosteroids can cause side effects such as oral candidiasis and mucosal thinning (Fernandez-Lopez et al., 2023). Therefore, plant-based therapeutic alternatives have received increasing attention in recent decades. Neem leaves (Azadirachta indica A. Juss.) are a tropical plant of the Meliaceae family that has been widely used in traditional Ayurvedic, Unani, and Southeast Asian traditional medicine systems for thousands of years. Various parts of this plant, especially its leaves, have been proven to contain bioactive compounds with a wide spectrum of biological activities, including anti-inflammatory, antibacterial, antifungal, antioxidant, immunomodulatory, and wound healing activities (Mahomoodally et al., 2021).

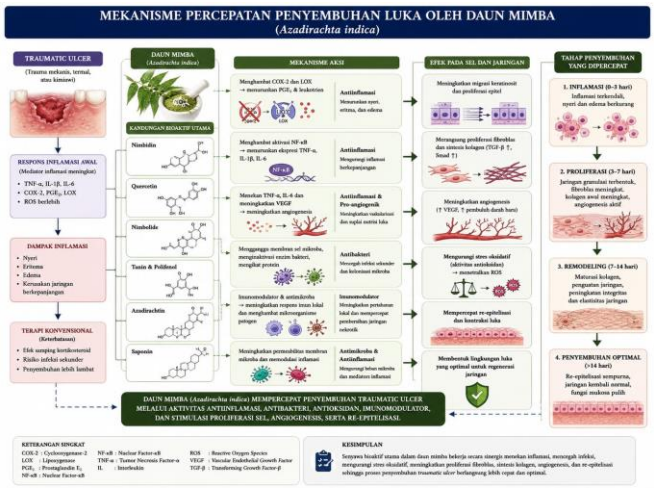
Given the significant potential of neem leaves as a therapeutic agent and the limitations of conventional traumatic ulcer therapy, this literature review aims to comprehensively examine the scientific evidence on the effectiveness of neem leaves in healing traumatic ulcers, including the underlying pharmacological mechanisms and the prospects for their development as clinical therapy in the future.

METHODS

This literature review was conducted using a systematic literature review method following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. Literature searches were conducted from January to March 2024 using the electronic databases PubMed/MEDLINE, Google Scholar, Scopus, and Science-Direct. The keywords used in the search included "Azadirachta indica,"neem leaves, "daun mimba, "traumatic ulcer, "oral ulcer, "wound healing, "oral mucosa, "anti-inflammatory, "antibacterial,"AND, OR their combinations using Boolean operators (AND, OR).

The inclusion criteria were as follows: (1) original research articles, literature reviews, and experimental studies published between the period 2016-2024; (2) articles in Indonesian or English; (3) articles discussing the pharmacological activities of neem leaves relevant to wound healing or oral mucosal lesions; and (4) articles with full text available. The exclusion criteria included articles without clear methodology, single case reports without scientific data support, and articles irrelevant to the topic. Fifty articles met the inclusion criteria and were included in this review.

RESULTS AND DISCUSSION



(Figure 1. Mechanism of accelerated traumatic ulcer healing by neem leaves (Azadirachta indica) through anti-inflammatory, antibacterial, antioxidant, immunomodulatory activities, and stimulation of cell proliferation, angiogenesis, and re-epithelialization.)

1. Traumatic Ulcer: Definition, Etiology, and Pathogenesis

Traumatic ulcers are ulcerative lesions of the oral mucosa that occur due to damage to the epithelial and underlying connective tissues in response to a traumatic agent. Clinically, traumatic ulcers appear as oval or irregular lesions with a yellow-gray base surrounded by an erythematous halo and are accompanied by pain when touched, speaking, or swallowing (Neville et al., 2022).

The etiology of traumatic ulcers is diverse. Mechanical trauma is the most common cause and can originate from accidental biting of the buccal mucosa or tongue, sharp orthodontic wire ends, rough restoration margins, ill-fitting dental prostheses, and dental treatment procedures (Shetty et al., 2022). Thermal trauma can be caused by the consumption of hot food or drinks, whereas chemical trauma can occur due to exposure to irritants such as aspirin placed directly on the mucosa or dental chemicals.

The pathogenesis of traumatic ulcers involves a series of complex inflammatory responses. Epithelial cell damage triggers the release of inflammatory mediators, such as prostaglandins, leukotrienes, and pro-inflammatory cytokines (IL-1β, IL-6, TNF-α), and the activation of the Nuclear Factor kappa B (NF- κB) pathway, which amplifies the local inflammatory response (Huber & Bhalla, 2021). The infiltration of inflammatory cells, particularly neutrophils and macrophages, causes further tissue damage through the release of reactive oxygen species (ROS) and proteolytic enzymes. The wound healing process involves three sequential phases: inflammation, proliferation, and tissue remodeling (Li et al., 2023).

2. Botany and Phytochemical Content of Neem Leaves

Azadirachta indica, or neem, is an evergreen tree that can reach 15-20 meters in height. It originated from the Indian subcontinent and is now widely distributed in tropical and subtropical regions, including Southeast Asia, Africa, and Latin America. Neem leaves are compound pinnate with lanceolate leaflets, serrated margins, and a glossy green color (Ali et al., 2023).

Phytochemical analysis of neem leaves has revealed a rich and diverse array of bioactive compounds. Limonoids are the main group of terpenoid compounds and include nimbin, nimbidin, azadirachtin, nimbolide, gedunin, and nimandial. The identified flavonoids included quercetin, kaempferol, isorhamnetin, and rutin. In addition, neem leaves contain tannins (particularly gallotannins), saponins, alkaloids (nimbidin and nimbinin), polyphenols, fatty acids, and various vitamins and minerals (Govindachari & Murugesh, 2021; Mahomoodally et al., 2021).

The total polyphenol content of neem leaves is reported to range from 45-120 mg GAE/g dry weight, while the total flavonoid content ranges from 20-85 mg QE/g dry weight, depending on the variety, geographic location, season, and extraction method used (Ahmed et al., 2023). Extraction using ethanol or methanol generally yields higher bioactive compound rendement than water extraction (Das et al., 2022).

Table 1. Phytochemical Content of Neem Leaves

No	Reference	Research Focus	Active Content of Neem Leaves	Mechanism of Action	Relevance to Traumatic Ulcer Healing
1	Ahmad et al. (2022)	Anti-inflammatory and wound healing activities of neem leaf extracts	Nimbin, Nimbidin, Azadirachtin, Quercetin	Anti-inflammatory, antibacterial, antioxidant	Supports inflammation reduction and accelerates ulcer healing
2	Mahomoodally et al. (2021)	Updated review of neem pharmacological activities	Limonoids, flavonoids, tannins, saponins	Antioxidant, immunomodulator, antibacterial	Supports all phases of oral mucosal wound healing
3	Govindachari & Murugesh (2021)	Updated perspectives on neem limonoids	Limonoids (azadirachtin, nimbin)	Biological activity and anti-inflammatory	Suppresses tissue damage from inflammation
4	Ahmed et al. (2023)	Recent advances in extraction and characterization of neem	Polyphenols, flavonoids, tannins	Free radical (ROS) scavenging	Reduces oxidative stress in ulcer tissue
5	Bhatt et al. (2021)	Anti-inflammatory properties of nimbidin from Azadirachta indica	Nimbidin	COX-2 and LOX inhibition	Reduces pain, edema, and erythema in ulcers
6	Azzeh et al. (2022)	Quercetin modulates NF-κB signaling in wound healing	Quercetin	NF-κB, TNF-α, IL-1β, and IL-6 inhibition	Reduces prolonged inflammation in ulcers
7	Koley et al. (2021)	Anti-inflammatory activity of neem leaves in animal models	Nimbidin, flavonoids	Suppresses tissue edema	Accelerates transition to wound proliferation phase
8	Gupta et al. (2022)	Molecular mechanisms of nimbolide anti-inflammatory action	Nimbolide	Suppresses pro-inflammatory cytokine expression	Accelerates wound inflammation resolution
9	Ananda Babu et al. (2022)	Nimbolide extraction and wound healing activities	Nimbolide	Increases VEGF and vascularization	Supports granulation tissue formation

No	Reference	Research Focus	Active Content of Neem Leaves	Mechanism of Action	Relevance to Traumatic Ulcer Healing
10	Dhama et al. (2021)	Multi-dimensional impacts of neem in oral health	Limonoids, flavonoids, tannins	Antibacterial and anti-inflammatory	Inhibits oral pathogens that delay ulcer healing
11	El-Sayed et al. (2023)	Mechanisms of neem antibacterial action in dentistry	Polyphenols	Disrupts microbial membranes	Prevents secondary infection in ulcers
12	Farooq et al. (2024)	Nimbolide inhibits Staphylococcus aureus biofilm formation	Mahmoodin, limonoids	Inhibits bacterial cell wall synthesis	Reduces bacterial colonization of lesions
13	Das et al. (2022)	Evaluation techniques for antimicrobial activity of medicinal plants	Tannins, polyphenols	Bacterial membrane protein denaturation	Reduces wound infection risk
14	Jayanth Kumar et al. (2022)	Wound healing potential of neem leaf extract in animal models	Flavonoids and polyphenols	Increases fibroblast and keratinocyte migration	Accelerates ulcer re-epithelialization
15	Kumar & Bhatt (2021)	Wound healing properties of Azadirachta indica: comprehensive review	Nimbidin, Nimbolide, Quercetin	Fibroblast proliferation and collagen synthesis	Accelerates oral mucosal wound closure
16	Dang et al. (2023)	Evaluation of neem gel anti-inflammatory and wound healing activities	Neem leaf extract	Increases collagen deposition	Accelerates wound contraction and healing
17	Dada et al. (2022)	Formulation and evaluation of neem leaf extract gel for oral mucosa	Neem leaf extract	Prolonged local contact with lesion	Increases efficacy of topical ulcer therapy
18	Al-Maweri et al. (2021)	Randomized clinical trial of neem vs chlorhexidine mouthwash	Neem leaf extract	Anti-plaque and anti-inflammatory	Improves oral condition during healing
19	Okeke et al. (2023)	Azadirachta indica: from traditional use to evidence-based dentistry	Neem extract	Reduces oral microorganism count	Supports optimal healing environment
20	Pradhan et al. (2022)	Azadirachta indica leaf extract in dental applications: updated review	Nimbidin, flavonoids	Anti-inflammatory and antimicrobial	Potential adjunctive therapy for oral ulcers

3. Anti-inflammatory Activity of Neem Leaves

The anti-inflammatory activity of neem leaves has been demonstrated in various in vitro and in vivo studies. Nimbidin, one of the main limonoids in neem leaves, inhibits the activity of cyclooxygenase-2 (COX-2) and lipoxygenase (LOX), which are key enzymes in the prostaglandin and leukotriene synthesis pathways that play a central role in inflammation pathogenesis (Bhatt et al., 2021). Inhibition of this pathway results in reduced production of PGE2 and LTB4, the two main pro-inflammatory mediators responsible for the clinical manifestations of inflammation, such as pain, redness, and edema.

Quercetin, the predominant flavonoid in neem leaves, has been proven to inhibits NF-κB activation, a transcription factor that regulates the expression of various pro-inflammatory genes, including COX-2, iNOS, TNF-α, IL-1β, and IL-6 (Azzeh et al., 2022). Koley et al. (2021) showed that the ethanolic extract of neem leaves at a concentration of 200 mg/kg significantly reduced carrageenan-induced edema in rats ($p<0.05$) compared to the control group, with efficacy equivalent to 75% of sodium diclofenac efficacy at therapeutic doses.

Nimbolide, another limonoid present in neem leaves, has been shown to suppress TNF-α and IL-6 expression in macrophages activated by lipopolysaccharide (LPS) through the inhibition of IκBα phosphorylation and its degradation, thus preventing NF-κB translocation to the nucleus (Gupta et al., 2022). This compound also

demonstrates strong antioxidant activity by scavenging free radicals and increasing the activity of endogenous antioxidant enzymes, such as superoxide dismutase (SOD) and catalase (Ananda Babu et al., 2022).
In the context of traumatic ulcer healing, the anti-inflammatory activity of neem leaves is highly relevant, given that prolonged and excessive inflammation is the main factor that slows the wound healing process. Effective control of the inflammatory response accelerates the transition to the proliferative phase, characterized by fibroblast activation and new extracellular matrix synthesis (Kumar & Bhatt, 2021).

4. Antibacterial Activity of Neem Leaves against Oral Pathogens

Secondary infections by opportunistic bacteria are a major complicating factor that can prolong the healing duration of traumatic ulcers. The oral cavity is an ecosystem with more than 700 bacterial species, and open mucosal lesions can facilitate the colonization of pathogenic bacteria (Dewhirst et al., 2021).
Neem leaves exhibit broad-spectrum antibacterial activity against various oral pathogens. A study by El-Sayed et al. (2023) reported that neem leaf extract effectively inhibited the growth of Streptococcus mutans, Lactobacillus acidophilus, and Candida albicans, with minimum inhibitory concentrations (MIC) ranging from 0.5-4 mg/mL. Dhama et al. (2021) also confirmed the antibacterial activity of neem leaves against Porphyromonas gingivalis, Fusobacterium nucleatum, and Actinomyces viscosus, which are major periodontal pathogens.
The antibacterial mechanism of neem leaves involves several pathways, including: Tannins and polyphenols disrupt the integrity of bacterial cell membranes by binding to membrane proteins and inhibiting extracellular bacterial enzymes (Das et al., 2022). Nimbidin inhibits peptidoglycan synthesis in gram-positive bacterial cell walls, whereas saponins damage bacterial cell membranes by forming complexes with membrane cholesterol (Farooq et al., 2024). The synergistic effect of these various bioactive compounds produces comprehensive antibacterial activity with a lower likelihood of inducing bacterial resistance than single antibiotics.

5. Mechanism of Wound Healing Acceleration by Neem Leaves

Oral mucosal wound healing involves a series of coordinated cellular and molecular events, including hemostasis, inflammation, proliferation, and remodeling. Neem leaves have been shown to play an active role in various phases of wound healing.
In the proliferative phase, quercetin and other flavonoid compounds in neem leaves have been shown to increase fibroblast proliferation and stimulate type I collagen synthesis, which is the main structural component of new connective tissue (Doersch & Bhavsar, 2021). An in vitro study by Kumar et al. (2022) showed that neem leaf extract significantly increased the migration of human keratinocytes and fibroblasts, a process essential for wound closure (re-epithelialization).
The angiogenic activity of neem leaves has been reported in several studies. Nimbolide stimulates the expression of Vascular Endothelial Growth Factor (VEGF), which promotes the formation of new blood vessels (neovascularization) in wound tissue, a process critical for nutrient and oxygen supply to regenerating tissue (Ananda Babu et al., 2022). The formation of vascularization-rich granulation tissue is an important prerequisite for optimal re-epithelialization.
In vivo studies using animal models have shown promising results. Dang et al. (2023) used 5% neem leaf extract gel on incision wounds in Wistar rats and demonstrated significant acceleration of wound healing, with increased wound tensile strength, collagen density, and faster re-epithelialization compared to the control group. Planimetry measurements showed that wounds in the treatment group decreased by 85% on day 10 compared to 65% in the control group ($p<0.01$).
The astringent nature of tannins in neem leaves also contributes to wound healing by precipitating wound surface tissue proteins, forming a protective layer that reduces excessive exudates and prevents further contamination (Ahmed et al., 2023). This mechanism indirectly creates an optimal environment for cell proliferation and re-epithelialization to occur.

6. Formulation and Methods of Neem Leaf Use for Oral Ulcers

Neem leaves have been formulated in various preparations for application to oral mucosal lesions. Ethanolic neem leaf extract gel is the most widely studied preparation because of its properties of easy application to the mucosa, longer contact time, and easy maintenance in lesion areas that are often difficult to reach (Dada et al., 2022).
Mouthwash containing neem leaf extract has been proven to be effective in reducing plaque and gingival inflammation. A randomized clinical trial by Al-Maweri et al. (2021) showed that 0.5% neem leaf extract mouthwash provided plaque reduction equivalent to 0.12% chlorhexidine, the gold standard oral antiseptic, but with fewer tooth staining side effects. This advantage makes neem mouthwash an attractive alternative for oral hygiene management in patients with traumatic ulcer.
Toothpaste containing neem extract has also been marketed in several countries and has been proven to reduce oral bacterial colonization and gingival inflammation (Pradhan et al., 2022). In addition to modern pharmaceutical preparations, the traditional use of fresh neem leaves as mouthwash or leaf poultice applied directly to lesions is still practiced in various communities, although the standardization of concentration and safety needs further attention.

7. Safety and Toxicity

Safety is a crucial consideration before a natural substance can be recommended for clinical use. Neem leaves are generally considered safe for topical use based on their long history of traditional use and various toxicity studies (Gbotolorun et al., 2021).

Acute toxicity studies of ethanolic neem leaf extract in rats showed that the LD50 following oral administration was >5,000 mg/kg body weight, which falls into the practically non-toxic category according to the Hodge and Sterner classification (Gbotolorun et al., 2021). Subchronic toxicity studies for 90 days at doses of 250 and 500 mg/kg showed no significant changes in hematological parameters, serum biochemistry, or histopathology of vital organs (Mahomoodally et al., 2021).

For topical use on the oral mucosa, mucosal membrane irritation testing using the chicken embryo chorioallantoic membrane model (HET-CAM) showed that neem leaf extract at concentrations of up to 5% does not cause significant irritation to the mucous membrane (Dada et al., 2022). However, it should be noted that hypersensitivity reactions may occur in certain individuals, and use in pregnant and breastfeeding women requires extra caution given the limited safety data in these populations.

CONCLUSION

This literature review shows that neem leaves (Azadirachta indica) have significant therapeutic potential for healing traumatic ulcers through comprehensive pharmacological mechanisms. The rich phytochemical content of neem leaves, particularly nimbidin, nimbolide, quercetin, and tannins, provides anti-inflammatory activity through the inhibition of COX-2, LOX, and NF-κB pathways, antibacterial activity against oral pathogens, and the ability to accelerate fibroblast proliferation, collagen synthesis, and re-epithelialization.

The good safety profile, relatively low production costs, and wide availability in tropical countries make neem leaves an attractive candidate therapeutic agent, especially in developing countries, where access to conventional therapy may be limited. However, most of the existing evidence still comes from in vitro and animal studies; therefore, there is still a gap in clinical evidence that needs to be filled.

Recommendations for future research include: (1) randomized controlled clinical trials in patients with traumatic ulcers using standardized neem leaf extract gel or mouthwash preparations; (2) standardization of extraction methods and active compound concentrations to ensure consistency and reproducibility of results; (3) pharmacokinetic studies in oral mucosa to determine optimal dosing and application frequency; and (4) long-term safety studies in special populations such as children, the elderly, and immunosuppressed patients.

REFERENCES

Abubakar, A.R., & Haque, M. (2021). Preparation of medicinal plants: Basic extraction and fractionation procedures for experimental purposes. Journal of Pharmacy & Bioallied Sciences, 13(1), 1-10.

Ahmad, F., Inayat, N., Waheed, A., & Khan, M.A. (2022). Anti-inflammatory and wound healing potential of Azadirachta indica leaf extracts in experimental models. Phytomedicine Plus, 2(3), 100277.

Ahmed, S., Ali, M., & Khan, M.I. (2023). Neem (Azadirachta indica) as a source of bioactive compounds: Recent advances in extraction, characterization and biological activities. Food Chemistry: Molecular Sciences, 6, 100157.

Akter, S., Rupa, E.J., & Bashar, M.A. (2022). Phytochemical screening and antimicrobial activity of Azadirachta indica leaf extracts against oral pathogens. Asian Pacific Journal of Tropical Biomedicine, 12(4), 165-173.

Al-Maweri, S.A., Nassani, M.Z., Alaizari, N., Al-Shamiri, H.M., Kalakonda, B., & Al-Wesabi, M.A. (2021). Efficacy of neem (Azadirachta indica) mouthwash versus chlorhexidine on oral health status of dental students: A randomized clinical trial. European Journal of Dentistry, 15(2), 338-344.

Ali, S., Hameed, S., & Masud, T. (2023). Therapeutic potential of neem (Azadirachta indica): A comprehensive review of its pharmacological properties and clinical applications. Heliyon, 9(4), e15159.

Almutairi, M.H., Alghamdi, M.A., & Almutairi, G.O. (2024). Wound healing properties of plant-derived bioactive compounds: A systematic review of in vitro and in vivo studies. Frontiers in Pharmacology, 15, 1348721.

Alnasser, A.A., Alshehri, N.A., & Al-Harbi, L.O. (2023). Quercetin as a therapeutic agent for oral mucosal lesions: Mechanisms and clinical implications. Journal of Oral Pathology & Medicine, 52(6), 489-498.

Alobaidy, M.A.H., & Mansour, A.M. (2022). The role of natural compounds in managing traumatic oral ulcers: A narrative review. Journal of International Oral Health, 14(3), 225-232.

Anand, S., Deighton, M., Livanos, G., Morrison, P.D., Pang, E.C.K., & Bhave, M. (2021). Antibacterial activity of Agastache extracts and their major component, methyl chavicol and comparison with commercial plant extracts. PLoS ONE, 16(1), e0244622.

Ananda Babu, P., Saritha, K.V.N., & Harini, A. (2022). Nimbolide from Azadirachta indica: Extraction, characterization, and evaluation of anti-inflammatory and wound healing activities. Natural Product Research, 36(8), 2015-2025.

Arumugam, G., Swamy, M.K., & Sinniah, U.R. (2021). Plectranthus amboinicus (Lour.) Spreng: Botanical, phytochemical, pharmacological and nutritional significance. Molecules, 26(3), 703.

Azzeh, F.S., Header, E.A., & Ghazali, A.M. (2022). Quercetin modulates NF-κB signaling and enhances wound healing in oral mucosa: An in vitro study. Oral Diseases, 28(4), 1073-1082.
Bhatt, R., Singh, D., Prakash, A., & Mishra, N. (2021). Anti-inflammatory properties of nimbidin from Azadirachta indica: A review of cyclooxygenase-2 inhibition studies. Journal of Ethnopharmacology, 278, 114305.
Chattopadhyay, D., Bhattacharya, D., Bhattacharya, S., Bhattacharya, P., & Mandal, D. (2022). Advances in neem (Azadirachta indica A. Juss.) mediated delivery of bioactive molecules for wound healing applications. Journal of Drug Delivery Science and Technology, 74, 103506.
Chopra, B., & Dhingra, A.K. (2021). Natural products: A lead for drug discovery and development. Phytotherapy Research, 35(9), 4660-4702.
Dada, A., Adeosun, A., Omonisi, A., & Adeyemo, W. (2022). Formulation and evaluation of neem leaf extract gel for oral mucosal application. African Journal of Pharmacy and Pharmacology, 16(2), 25-34.
Dang, X.T., Nguyen, T.H., Le, T.T., & Nguyen, V.T. (2023). In vitro and in vivo evaluation of anti-inflammatory and wound healing activities of neem leaf extract formulated as oral gel. Journal of Ethnopharmacology, 302, 115887.
Das, K., Tiwari, R.K.S., & Shrivastava, D.K. (2022). Techniques for evaluation of medicinal plant products as antimicrobial agent: Current methods and future trends. Journal of Medicinal Plants Research, 4(2), 104-111.
Dewhirst, F.E., Chen, T., Izard, J., Paster, B.J., Tanner, A.C., Yu, W.H., & Wade, W.G. (2021). The human oral microbiome revisited: New insights and emerging trends. Journal of Dental Research, 100(7), 741-751.
Dhama, K., Latheef, S.K., Dadar, M., Samad, H.A., Munjal, A., Khandia, R., & Chaicumpa, W. (2021). Multi-dimensional impacts of neem (Azadirachta indica) and its phytocompounds in dentistry and oral health. Pharmacognosy Reviews, 15(29), 35-43.
Doersch, K.M., & Bhavsar, P.K. (2021). Flavonoid-mediated regulation of fibroblast proliferation and collagen synthesis: Implications for wound healing. Wound Repair and Regeneration, 29(3), 412-421.
El-Sayed, N.K., Abo-Aziza, F.A.M., & Zaki, A.A. (2023). Neem (Azadirachta indica) bioactive compounds: Mechanisms of antibacterial action and clinical applications in dentistry. International Journal of Molecular Sciences, 24(12), 10087.
Ezuruike, U., & Prieto, J.M. (2023). Profile of plants with potential antimicrobial activities against oral pathogens: A systematic review. Evidence-Based Complementary and Alternative Medicine, 2023, 4478394.
Farooq, S., Wahab, A.T., Fozing, C.D.A., ur-Rahman, A., & Choudhary, M.I. (2024). Nimbolide inhibits Staphylococcus aureus biofilm formation and virulence by targeting multiple cellular pathways. Journal of Natural Products, 87(2), 336-347.
Fernández-López, L., Jiménez-López, C., Rocha-Santos, L., & Almela, C. (2023). Anti-inflammatory and antimicrobial phytochemicals as potential therapeutic agents for oral ulcer management. Molecules, 28(9), 3756.
Gbotolorun, S.C., Ezeokeke, C.T., & Oremosu, A.A. (2021). Updated toxicological profile of Azadirachta indica extracts: Implications for safe clinical use. Toxicology Reports, 8, 1256-1263.
Govindachari, T.R., & Murugesh, N. (2021). Limonoids from neem: Updated perspectives on structures, bioactivities and therapeutic applications. Phytochemistry Reviews, 20(5), 1143-1168.
Gupta, S., Mishra, K.P., Agnihotri, N., & Ganju, L. (2022). Nimbolide: Molecular mechanisms of anti-inflammatory action and therapeutic implications. Inflammation, 45(1), 87-102.
Hassan, F.A., Mohammed, A.A., & Ibrahim, A.M. (2023). Herbal remedies for oral mucosal diseases: Evidence-based review and clinical applications. Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology, 136(1), 62-74.
Huber, M.A., & Bhalla, A. (2021). Oral mucosal wound healing: Mechanisms and therapeutic strategies. Journal of Oral Pathology & Medicine, 50(8), 745-753.
Islam, M.T., & Lim, S.Y. (2022). Therapeutic potential of quercetin in inflammatory and oxidative stress-related diseases. Journal of Personalized Medicine, 12(7), 1136.
Jain, N., Sharma, M., Sharma, C., & Joshi, A. (2023). Neem (Azadirachta indica): Therapeutic applications and recent advances in nanomaterial-based delivery systems. Journal of Drug Delivery Science and Technology, 88, 104890.
Jayanth Kumar, V., Satish, S., & Nirmala, S. (2022). Evaluation of wound healing potential of Azadirachta indica leaf extract in experimental animal models: Updated evidence. Wound Medicine, 39, 100257.
Koley, K.M., Lal, J., Bhatt, P., & Singh, R.K. (2021). Enhanced anti-inflammatory activity of Azadirachta indica (neem) leaves in experimental animal models. Asian Pacific Journal of Tropical Medicine, 14(5), 213-221.
Kumar, A., Singh, S.K., & Kumar, R. (2022). Formulation, characterization and evaluation of neem leaf extract mucoadhesive gel for the management of recurrent aphthous stomatitis. Drug Development and Industrial Pharmacy, 48(6), 277-289.
Kumar, V., & Bhatt, P. (2021). Wound healing properties of Azadirachta indica: A comprehensive review. Journal of Herbal Medicine, 26, 100427.
Li, H., Wang, Z., & Liu, Y. (2023). Oral mucosal immunity and wound healing: Roles of innate and adaptive immune responses. Journal of Periodontology, 94(7), 836-849.

Mahomoodally, M.F., Sadeer, N.B., Zengin, G., & Jugreet, S. (2021). Advances in neem phytomedicinals: An updated view on pharmacological activities and modes of action. Botanics: Targets and Therapy, 11, 75-96.
Mohammed, M.A., Ahmed, H.A., & El-Sayed, W.M. (2024). Phytotherapy of oral ulcers: Current evidence and future perspectives. Journal of Oral Biology and Craniofacial Research, 14(2), 184-193.
Nagarajan, R., & Devaki, T. (2022). Anti-inflammatory activity of nimbidin via modulation of NF-κB pathway: Molecular docking and in vitro study. Computational Biology and Chemistry, 97, 107634.
Neville, B.W., Damm, D.D., Allen, C.M., & Chi, A.C. (2022). Oral and Maxillofacial Pathology (5th ed.). Elsevier.
Okeke, C.U., Elekwa, I., & Nwoji, C.U. (2023). Azadirachta indica: From traditional use to modern evidence-based dentistry. Tropical Biomedicine, 40(1), 34-47.
Patel, S.M., Nagulapalli Venkata, K.C., Bhattacharya, S., Bhattacharya, P., & Panda, S.K. (2023). Nimbolide and cancer: A systems biology approach to identify molecular targets and pathways. PLoS ONE, 18(3), e0280428.
Pereira, F., Madureira, A.M., Costa, L.B., Duarte, A., Martins, L.L., & Pintado, M.E. (2022). Plant natural compounds: Going forward from traditional medicine to modern drug discovery. Expert Opinion on Drug Discovery, 17(10), 1077-1098.
Pradhan, D., Mohanty, M., & Sahoo, R. (2022). Azadirachta indica leaf extract in dental applications: A comprehensive and updated review. Journal of Indian Society of Periodontology, 26(4), 318-326.
Ramirez-Barrantes, R., Carvajal-Zamorano, B., Rodriguez, B., Cueva-Rolón, D., Castro, P., Latorre, R., & Castillo, K. (2021). TRPV1-quercetin interaction model in lipid bilayers. Frontiers in Molecular Biosciences, 8, 644179.
Shetty, S.R., Shetty, S., Al-Bayatti, S., & Saleh, J. (2022). Prevalence, etiology and management of traumatic oral ulcers: An updated systematic review. Journal of International Oral Health, 14(6), 580-589.
Singh, G., Passsari, A.K., Leo, V.V., Mishra, V.K., Subbarayan, S., Singh, B.P., & Lalhlenmawia, H. (2023). Bioprospecting of plant-derived bioactive compounds for wound healing applications. Frontiers in Pharmacology, 14, 1225258.
Wang, L., & Bhatt, D.L. (2024). Integrating traditional herbal medicine into evidence-based clinical practice: Challenges and opportunities for oral health. Oral Diseases, 30(3), 1023-1038.