



Plant-Based Therapeutics for Oral Ulcers: Current Evidence and Future Perspectives

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ABSTRACT

Oral ulcers, encompassing recurrent aphthous stomatitis (RAS) and chemotherapy- or radiotherapy-induced oral mucositis (OM), remain among the most common and distressing conditions affecting the oral mucosa. Conventional management relies heavily on topical corticosteroids, antiseptics, and analgesics, which provide symptomatic relief but carry risks of local and systemic adverse effects with long-term use. Over the past decade, a substantial body of preclinical and clinical research has examined plant-derived agents — including curcumin, aloe vera, liquorice, chamomile, Myrtus communis, honey, and propolis — as alternative or adjunctive therapies for oral ulcerative disease. This review synthesises evidence published largely within the last ten years, drawing on randomised controlled trials, systematic reviews, and network meta-analyses, to evaluate the efficacy, proposed mechanisms of action, and safety profile of plant-based therapeutics for oral ulcers. Across multiple trials, these agents have consistently reduced ulcer size, shortened healing time, and relieved pain, with efficacy in several studies approaching or matching that of triamcinolone acetonide and other standard agents, alongside a favourable tolerability profile. Emerging nanotechnology-based and mucoadhesive delivery platforms are discussed as strategies to overcome the poor bioavailability and short residence time that have historically limited the clinical translation of phytochemicals in the oral cavity. Despite encouraging findings, small sample sizes, heterogeneous formulations, and inconsistent outcome measures across studies limit definitive conclusions, underscoring the need for standardised, adequately powered trials.

Keywords: *recurrent aphthous stomatitis; oral mucositis; medicinal plants; phytotherapy; curcumin; aloe vera; liquorice; honey; propolis; nanotechnology*

1. Introduction

The oral mucosa is a frequent site of ulcerative lesions that, despite their generally benign and self-limiting nature, cause considerable pain, difficulty with eating and speech, and reduced quality of life. Among these, recurrent aphthous stomatitis (RAS), commonly known as canker sores, is the most prevalent ulcerative disorder of the oral cavity, affecting an estimated 5–25% of the general population, with some surveys reporting even higher figures depending on the population studied and diagnostic criteria used [1–3]. A second major category, oral mucositis (OM), arises as a dose-limiting toxicity of cancer chemotherapy and head-and-neck radiotherapy and is characterised by erythema, erosion, and ulceration of the mucosa, often severe enough to necessitate treatment interruption [27,32].

The precise aetiology of RAS remains incompletely understood, though it is now regarded as a T-cell-mediated immunological reaction, with tumour necrosis factor-alpha (TNF- α) implicated as a key inflammatory mediator, and contributing factors including local trauma, stress, haematologic deficiencies, gastrointestinal disease, and genetic predisposition [4,5]. Conventional first-line management of RAS and OM centres on topical corticosteroids (for example, triamcinolone acetonide), antiseptic mouth rinses such as chlorhexidine, and topical or systemic analgesics [2]. While effective for symptom control, prolonged corticosteroid use is associated with candidiasis, mucosal atrophy, and delayed healing, prompting sustained interest in alternative, better-tolerated interventions [14].

Medicinal plants have a long history of traditional use for oral ulcerative conditions across diverse healing systems, including Ayurveda, traditional Persian and Iranian medicine, and traditional Chinese medicine [6,9,36]. Over the last decade, this traditional use has been increasingly subjected to rigorous clinical evaluation, with numerous randomised controlled trials assessing botanicals such as curcumin, aloe vera, licorice, chamomile, Myrtus communis, honey, and propolis for both RAS and cancer therapy-induced OM. This review synthesises this recent evidence base, discusses the proposed

mechanisms underlying the therapeutic effects of these agents, considers their safety and current limitations, and outlines emerging nanotechnology-based delivery strategies that may enhance their future clinical utility.

2. Epidemiology and Classification of Oral Ulcerative Conditions

2.1 Recurrent Aphthous Stomatitis

RAS typically presents as recurrent, round-to-oval, shallow ulcers with an erythematous halo and a yellow-grey pseudomembranous centre, affecting the non-keratinised oral mucosa such as the labial and buccal mucosa, ventral tongue, and soft palate [2,4]. Three clinical subtypes are recognised: minor RAS (the most common, accounting for roughly 80% of cases, with lesions 3–10 mm in diameter that heal within 10–14 days without scarring), major RAS (larger, deeper ulcers that may take weeks to heal and can scar), and herpetiform RAS (multiple small clustered ulcers) [2,3]. The condition most commonly affects individuals between 10 and 40 years of age, and population surveys have reported prevalence estimates ranging from around 5% to over 25%, with point prevalence and lifetime prevalence differing substantially across study populations [1].

2.2 Oral Mucositis

OM is an inflammatory and ulcerative complication of cytotoxic chemotherapy and head-and-neck radiotherapy, resulting from a complex multi-phase biological cascade involving reactive oxygen species generation, pro-inflammatory cytokine release, epithelial apoptosis, and secondary microbial colonisation of ulcerated mucosa [32]. Its severity is commonly graded using the World Health Organization (WHO) 0–4 scale or the Radiation Therapy Oncology Group (RTOG) scale, and severe OM (grade ≥ 3) is associated with treatment breaks, reduced nutritional intake, and compromised oncological outcomes, making effective and well-tolerated preventive and therapeutic strategies clinically important [27,31].

3. Rationale for Plant-Based Therapeutics in Oral Ulcer Management

Plant-derived agents are attractive candidates for oral ulcer management because many possess a combination of anti-inflammatory, antioxidant, antimicrobial, analgesic, and wound-healing properties attributable to bioactive constituents such as curcuminoids, flavonoids, saponins, tannins, and polysaccharides [8,9]. Compared with corticosteroids, herbal agents are frequently reported to have a more favourable adverse-effect profile, with systematic reviews of herbal interventions in adolescent and adult populations describing limited adverse effects and good overall tolerability [6]. Furthermore, several plant extracts appear to act on multiple pathogenic mechanisms simultaneously — for example, suppressing pro-inflammatory cytokine pathways while also exerting direct antimicrobial activity against oral pathogens — which may explain their comparable efficacy to single-mechanism pharmaceutical agents in several head-to-head trials [8,25].

4. Current Evidence: Plant-Based Agents in Recurrent Aphthous Stomatitis

4.1 Curcumin (*Curcuma longa*)

Curcumin, the principal curcuminoid of turmeric, has been the most extensively studied phytochemical for RAS over the past decade. Multiple randomised controlled trials have compared topical curcumin gel (typically 1–5%) against triamcinolone acetonide, the conventional gold-standard topical steroid. Early trials found comparable reductions in ulcer size, pain, and healing time between curcumin gel and triamcinolone, with curcumin showing fewer adverse effects [12,13]. A 2020 trial evaluating a higher 5% curcumin orabase concentration reported no statistically significant difference from 0.1% triamcinolone acetonide in lesion size, pain severity, or overall efficacy index, supporting curcumin as a non-steroidal alternative of comparable effectiveness [14]. A more recent randomised trial similarly found that 2% curcumin gel produced faster healing, greater patient satisfaction, and fewer side effects than triamcinolone acetonide over a seven-day treatment course [11]. Because native curcumin suffers from poor aqueous solubility and bioavailability, nanomicelle-based curcumin formulations have also been trialled; a double-blind randomised comparison of 1% curcumin nanomicelle gel versus conventional 2% curcumin gel found the nanomicelle formulation more effective at enhancing RAS healing despite its lower nominal concentration, illustrating the value of delivery-system optimisation [15]. Combination approaches, such as curcumin with honey, have also been evaluated in controlled trials with favourable results relative to standard care [16].

4.2 Aloe vera

Aloe vera gel and its polysaccharide constituent acemannan have shown consistent benefit for RAS in randomised trials. A three-arm placebo-controlled trial comparing Aloe vera gel, 5% amlexanox paste, and placebo in patients with minor RAS found that Aloe vera produced a significantly greater reduction in ulcer size and pain by day five than both amlexanox and placebo [17]. A probiotic-fermented Aloe vera gel was shown in another randomised trial to accelerate RAS healing while also normalising the relative abundance of oral bacterial genera associated with ulceration, suggesting a microbiome-modulating mechanism in addition to direct mucosal effects [18]. Acemannan, the principal immunomodulatory polysaccharide of Aloe vera, has independently been shown in a randomised trial to reduce aphthous ulcer size and pain relative to placebo [19]. Aloe vera has also been formulated together with myrrh in mucoadhesive gels, with both single-agent gels outperforming a plain vehicle placebo for ulcer size, pain, erythema, and exudation over a five-day treatment period [20].

4.3 Licorice (*Glycyrrhiza glabra*)

Licorice root extract, delivered as dissolving oral patches, bioadhesive patches, mouth rinses, and gargle solutions, has one of the more extensive randomised trial bases among botanicals used for RAS. An early controlled trial of a dissolving glycyrrhiza patch found significantly reduced ulcer size and pain by day four to eight compared with a placebo patch and a no-treatment control [21]. Subsequent trials of licorice bioadhesive hydrogel patches similarly reported reduced pain and shortened healing time across repeated ulcer episodes [22]. A double-blind randomised trial of licorice-containing diphenhydramine solution and a separate trial of licorice gargle juice both demonstrated rapid, statistically significant reductions in pain scores within one to two days of treatment relative to placebo [23,24]. A 2023 systematic review consolidating these trials concluded that topical licorice consistently reduces RAS pain, ulcer size, and healing time in a dose-dependent manner, with proposed mechanisms including inhibition of the cyclooxygenase pathway, antioxidant activity, antibacterial effects against *Streptococcus mutans* and *Porphyromonas gingivalis*, and elevation of epidermal growth factor levels that support mucosal re-epithelialisation; no significant adverse effects were reported across the pooled trials [25,26].

4.4 Chamomile (*Matricaria recutita*)

Chamomile extract, administered as a mouth rinse or incorporated into an orabase vehicle, has also been evaluated against triamcinolone acetonide and placebo. A randomised, triple-blind, placebo-controlled trial of chamomilla mouth rinse reported significant reductions in ulcer number, pain, and burning sensation compared with placebo, without adverse effects [33]. In a three-arm trial comparing chamomile orabase, triamcinolone orabase, and placebo, both active treatments reduced ulcer size and pain by day three relative to placebo, although triamcinolone showed superiority over chamomile for complete ulcer resolution time by day six; chamomile nonetheless produced high patient satisfaction scores [34].

4.5 Myrtus communis (Myrtle)

Myrtus communis, used historically in Iranian traditional medicine for aphthous conditions termed “Gholaa,” has been evaluated in several randomised controlled trials over the past decade. A double-blind, controlled before-after trial of a myrtle oral paste found statistically significant reductions in ulcer size, pain, erythema, and exudation relative to placebo, along with improved oral-health-related quality of life scores [35]. A subsequent trial comparing 2.5% and 5% concentrations of myrtle essential oil extract found both concentrations effective in reducing pain and lesion size, informing optimal dosing for future formulations [37]. A narrative review bridging traditional and modern evidence concluded that *M. communis* is effective for minor RAS, while calling for larger comparative trials of its various topical formulations [36].

4.6 Other Botanicals

Beyond the agents discussed above, a range of other plants have shown activity against oral ulcers in clinical or preclinical studies, including guava, papaya, *Capsicum annuum*, noni fruit, coconut oil, myrrh, *Rosa damascena*, and combination herbal mouthwashes containing *Punica granatum* (pomegranate), *Portulaca oleracea* (purslane), and *Boswellia serrata* [6,9]. A systematic review of animal experimental studies further catalogued extracts of *Musa acuminata* (banana), *Jasminum grandiflorum*, *Ficus deltoidea*, *Bleilla striata*, *Bixa orellana*, *Piper sarmentosum*, and *Salvadora persica* as producing measurable reductions in experimentally induced oral ulcer size and inflammatory cell infiltration, providing mechanistic and preclinical support that complements the clinical trial literature on the more extensively studied agents above [10].

5. Plant-Based Agents in Chemotherapy- and Radiotherapy-Induced Oral Mucositis

5.1 Honey

Honey has accumulated the strongest and most consistent trial evidence among natural agents used for cancer therapy-related OM. In a randomised controlled trial of head-and-neck cancer patients undergoing radiotherapy, honey significantly reduced OM severity on the WHO scale, lowered the cumulative incidence of severe (grade ≥ 3) mucositis compared with usual care, improved quality-of-life scores, and was associated with better maintenance of body weight during treatment [27]. A separate single-blinded randomised trial found that topical honey reduced radiation-induced OM and treatment interruptions compared with povidone-iodine, without adversely affecting tumour response to radiotherapy [31]. In the chemotherapy setting, a randomised trial comparing honey, a honey-and-coffee mixture, and topical steroid syrup for established OM found that both honey-based regimens performed comparably to or better than the steroid regimen for symptom resolution [30]. A paediatric randomised pilot trial similarly found that honey and a honey-beeswax-propolis mixture reduced the severity and healing time of chemotherapy-induced OM [29].

5.2 Propolis

Propolis, a resinous bee product rich in flavonoids and phenolic acids, has also been evaluated in several placebo-controlled trials for OM prevention and treatment during head-and-neck cancer therapy. A randomised, double-blind, placebo-controlled trial of propolis in patients receiving chemotherapy for head-and-neck cancer reported reduced OM severity in the propolis arm [28]. A head-to-head randomised trial comparing honey and Taiwanese green propolis during radiotherapy found that, while both agents reduced OM severity relative to usual care, honey was more effective than propolis at the point of peak mucositis severity [27].

5.3 Synthesis from Network Meta-Analysis

A 2024 network meta-analysis pooling randomised controlled trials of natural products for the prevention of cancer-therapy-induced OM identified honey, propolis, chamomile, and *Plantago major* as agents with moderate-certainty evidence supporting reduced incidence, severity, and pain associated with OM, with honey demonstrating particularly strong effects on both overall incidence and moderate-to-severe cases [32]. This quantitative synthesis lends further support to the individual trial findings summarised above and highlights honey as currently the best-supported plant- or bee-derived agent for OM prophylaxis.

6. Mechanisms of Action

Across the botanicals reviewed, several converging mechanisms appear to underlie their clinical effects on oral ulcers. Anti-inflammatory activity is the most consistently reported mechanism, mediated through suppression of pro-inflammatory cytokines and inhibition of the cyclooxygenase and nuclear factor-kappa B pathways, as described for curcumin, licorice, and *Myrtus communis* [8,25]. Antioxidant activity, through free-radical scavenging, is proposed to limit oxidative tissue injury during both spontaneous RAS flares and the reactive-oxygen-species-driven early phase of chemoradiotherapy-induced OM [7,8]. Direct antimicrobial activity against oral pathogens such as *Streptococcus mutans* and *Porphyromonas gingivalis* has been demonstrated for licorice and several other botanicals, potentially reducing secondary infection and biofilm-related delay of healing [25]. Wound-healing and re-epithelialisation-promoting effects, including elevation of epidermal growth factor and modulation of the local oral microbiome, have been reported for licorice and fermented Aloe vera gel respectively [18,25]. Finally, immunomodulatory activity, exemplified by the acemannan polysaccharide of Aloe vera, may help correct the aberrant T-cell-mediated inflammatory response thought to underlie RAS pathogenesis [4,19].

7. Safety, Tolerability, and Current Limitations of the Evidence

A consistent finding across the reviewed trials is the favourable safety profile of plant-based topical therapies, with the large majority of studies reporting no significant adverse effects and, in several head-to-head comparisons, fewer side effects than triamcinolone acetonide [6,11,25]. This tolerability supports their consideration as first-line or adjunctive options, particularly for patients requiring frequent or prolonged treatment for recurrent disease.

Nonetheless, important limitations temper the strength of current conclusions. Most trials enrol relatively small numbers of participants (commonly 30–90 patients), limiting statistical power and generalisability [17,33,35]. Formulations, concentrations, and vehicles vary considerably between studies of the same plant — for example, curcumin concentrations ranging from 1% to 5% and myrtle extracts prepared as pastes, essential oils, or decoctions — which complicates direct comparison and meta-analytic pooling [14,15,37]. Outcome measures and follow-up durations are similarly heterogeneous across trials, and few studies have assessed recurrence rates or long-term disease control beyond a single ulcer episode [36]. Systematic reviewers have also cautioned that although herbal remedies are often perceived as inherently safer than pharmaceutical agents, this assumption requires continued verification through rigorously designed and adequately powered trials rather than being taken for granted [6,9].

8. Future Perspectives: Nanotechnology and Novel Delivery Systems

A recurring translational barrier for plant-based oral ulcer therapeutics is the poor aqueous solubility, chemical instability, and short mucosal residence time of many phytochemicals, which limits their bioavailability and clinical effect despite promising in vitro and animal data [39]. Nanotechnology-enabled delivery systems are increasingly being explored to address these constraints. Curcumin-loaded polymeric nanoparticles, for instance, have been engineered with favourable particle size, low polydispersity, and high encapsulation efficiency, and the clinical trial comparing curcumin nanomicelle gel with conventional curcumin gel for RAS already provides early evidence that such formulations can enhance therapeutic performance at lower nominal drug concentrations [15,39].

Mucoadhesive drug delivery systems represent a second major area of innovation, designed to prolong contact time between phytochemical-based formulations and the oral mucosa despite continuous salivary flushing [38]. Chitosan-based nanoparticles are a particularly well-studied mucoadhesive platform: their positive surface charge promotes interaction with the negatively charged mucous membrane and transient opening of epithelial tight junctions, improving penetration and residence time of encapsulated phytochemicals, while chitosan's biocompatibility and biodegradability support its suitability for repeated oral use [40]. Emerging work on nanostructure-based curcumin carriers and on functionalised metal nanoparticles combined with antioxidant or polysaccharide components has shown anti-inflammatory and tissue-protective effects with slower, more sustained release compared with free drug in models of oral mucosal injury, although this evidence currently derives mainly from in vitro and animal studies rather than clinical trials [38,39]. Three-dimensional printing of mucoadhesive dosage forms and stimuli-responsive polymer systems have also been proposed as next-generation manufacturing approaches for personalised, site-specific delivery of plant-derived actives to oral ulcers [38].

Collectively, these developments suggest that the next decade of research in this field is likely to shift from establishing basic clinical efficacy of crude plant extracts toward optimising their pharmaceutical delivery, standardising formulations and dosing, and generating the larger, adequately powered, and methodologically consistent randomised trials — including head-to-head and dose-ranging designs — needed to support formal integration of plant-based agents into evidence-based oral ulcer management guidelines [38,40].

9. Conclusion

A substantial and growing body of clinical trial evidence published over the last decade supports the efficacy of several plant-derived agents — most notably curcumin, aloe vera, licorice, chamomile, *Myrtus communis*, honey, and propolis — in reducing ulcer size, pain, and healing time in both recurrent aphthous stomatitis and cancer therapy-induced oral mucositis, frequently with efficacy comparable to standard topical corticosteroids and a favourable safety profile. Honey currently holds the strongest evidence base for oral mucositis prevention, while curcumin and licorice are the most extensively trialled agents for recurrent aphthous stomatitis. However, heterogeneity in formulations, concentrations, and outcome measures, together with generally small trial sizes, means the evidence, while encouraging, is not yet sufficient to replace standard care outright. Continued methodological rigour, standardisation of botanical formulations, and the application of nanotechnology-enabled and mucoadhesive delivery systems represent the most promising avenues for translating this evidence into reliable, guideline-level therapeutic options for oral ulcer management.

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Mathimugaselvan. k had principal responsibility for the conception, design of the study and drafting of manuscript. Santhosh Kumar.G was responsible for the revision of the manuscript for important intellectual content, Dr.G. Mariyappan, Dr. J. Karthi, Dr. S. Swarnalatha contributed towards reviewing of the literature. All authors agreed on the final version of manuscript.

References

- Reddy SM, Vadivel JK, Ramalingam K. Prevalence of aphthous stomatitis: a cross-sectional epidemiological study. *Cureus*. 2023;15(11):e49288.
- Chavan M, Jain H, Diwan N, Khedkar S, Shete A, Durkar S. Recurrent aphthous stomatitis: a review. *J Oral Pathol Med*. 2012;41(8):577–583.
- Preeti L, Magesh K, Rajkumar K, Karthik R. Recurrent aphthous stomatitis. *J Oral Maxillofac Pathol*. 2011;15(3):252–256.
- Slebiada Z, Szponar E, Kowalska A. Etiopathogenesis of recurrent aphthous stomatitis and the role of immunologic aspects: literature review. *Arch Immunol Ther Exp (Warsz)*. 2014;62(3):205–215.
- StatPearls Contributors. Recurrent Aphthous Stomatitis. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023.
- A systematic review of medicinal plants and herbal products' effectiveness in oral health and dental cure with health promotion approach. *J Educ Health Promot*. 2023;12:302.
- Cherrada N, Chems A, Gheraissa N, Laib I, Gueboudji Z, El-Shazly M, et al. Gastroprotective efficacy of North African medicinal plants: a review on their therapeutic potential for peptic ulcers. *Food Sci Nutr*. 2024. doi:10.1002/fsn3.4536.
- Plants with anti-ulcer activity and mechanism: a review of preclinical and clinical studies. *Drug Des Devel Ther*. 2024. doi:10.2147/DDDT.S446949.
- Oral ulcerative disease: a systematic review of herbal medicine treatments. *J Ayurveda Integr Med*. 2023.
- Effects of natural extracts in the treatment of oral ulcers: a systematic review of evidence from experimental studies in animals. 2021.
- Kilor V, et al. Curcumin versus triamcinolone acetonide gel in treating minor recurrent aphthous stomatitis: a randomized trial. 2025.
- Manifar S, Obwaller A, Gharehgozloo A, Boorboor Shirazi Kordi HR, Akhondzadeh S. Curcumin gel in the treatment of minor aphthous ulcer: a randomized, placebo-controlled trial. 2012.
- Deshmukh RA, Bagewadi AS. Comparison of effectiveness of curcumin with triamcinolone acetonide in the gel form in treatment of minor recurrent aphthous stomatitis: a randomized clinical trial. *Int J Pharm Investig*. 2014;4(3):138–141.
- Kia SJ, Mansourian A, Basirat M, Akhavan M, Mohtasham-Amiri Z, Moosavi MS. New concentration of curcumin orabase in recurrent aphthous stomatitis: a randomized, controlled clinical trial. *J Herb Med*. 2020;22:100336.
- Comparative efficacy of 1% curcumin nanomicelle gel and 2% curcumin gel for treatment of recurrent aphthous stomatitis: a double-blind randomized clinical trial. 2022.
- Pandharipande R, Chandak R, Sathawane R, Lanjekar A, Gaikwad R, Khandelwal V, Kurawar K. To evaluate efficiency of curcumin and honey in patients with recurrent aphthous stomatitis: a randomized clinical controlled trial. *Int J Res Rev*. 2019;6(12):449–455.
- Yousef NJ, Aljoujou AA, Mashlah AM, Hajeer MY. Assessment of the effectiveness of Aloe vera versus amlexanox in the treatment of recurrent aphthous ulcers: a three-arm placebo-controlled randomized clinical trial. *Cureus*. 2022;14(10):e30693.

18. Shi Y, Wei K, Lu J, Wei J, Hu X, Chen T. A clinic trial evaluating the effects of aloe vera fermentation gel on recurrent aphthous stomatitis. *Biomed Res Int.* 2020;2020:8867548.
19. Bhalang K, Thunyakitpisal P, Rungsirisatean N. Acemannan, a polysaccharide extracted from Aloe vera, is effective in the treatment of oral aphthous ulceration. *J Altern Complement Med.* 2013;19(5):429–434.
20. Clinical efficacy of new aloe vera- and myrrh-based oral mucoadhesive gels in the management of minor recurrent aphthous stomatitis: a randomized, double-blind, vehicle-controlled study. 2013.
21. Martin MD, Sherman J, van der Ven P, Burgess J. A controlled trial of a dissolving oral patch concerning glycyrrhiza (licorice) herbal extract for the treatment of aphthous ulcers. *Gen Dent.* 2008;56(3):206–210.
22. Moghadamnia AA, Motalebnejad M, Khanian M. The efficacy of the bioadhesive patches containing licorice extract in the management of recurrent aphthous stomatitis. *Phytother Res.* 2009;23(2):246–250.
23. Akbari N, Asadimehr N, Kiani Z. The effects of licorice containing diphenhydramine solution on recurrent aphthous stomatitis: a double-blind, randomized clinical trial. *Complement Ther Med.* 2020;50:102401.
24. Liu HL, Hsu PY, Chung YC, Lin CH, Lin KY. Effective licorice gargle juice for aphthous ulcer pain relief: a randomized double-blind placebo-controlled trial. *Pak J Pharm Sci.* 2022;35(5):1321–1326.
25. Dorsareh F, Vahid-Dastjerdi G, Bouyahya A, Zarshenas MM, Rezaie M, Yang WM, Amiri-Ardekani E. Topical licorice for aphthous: a systematic review of clinical trials. *Iran J Med Sci.* 2023;48(5):437–447.
26. Messier C, Epifano F, Genovese S, Grenier D. Licorice and its potential beneficial effects in common oro-dental diseases. *Oral Dis.* 2012;18(1):32–39.
27. Effects of honey and Taiwanese green propolis on oral mucositis and quality of life in head and neck cancer patients undergoing radiotherapy: a randomized controlled trial. *Food Funct.* 2025.
28. AkhavanKarbassi MH, Yazdi MF, Ahadian H, SadrAbad MJ. Randomized double-blind placebo-controlled trial of propolis for oral mucositis in patients receiving chemotherapy for head and neck cancer. *Asian Pac J Cancer Prev.* 2016;17(7):3611–3614.
29. Abdulrhman M, Elbarbary NS, Amin DA, Ebrahim RS. Honey and a mixture of honey, beeswax, and olive oil–propolis extract in treatment of chemotherapy-induced oral mucositis: a randomized controlled pilot study. *Pediatr Hematol Oncol.* 2012;29(3):285–292.
30. Raecessi MA, Raecessi N, Panahi Y, Gharaie H, Davoudi SM, Saadat A, et al. “Coffee plus honey” versus “topical steroid” in the treatment of chemotherapy-induced oral mucositis: a randomised controlled trial. *BMC Complement Altern Med.* 2014;14:293.
31. Honey mitigates radiation-induced oral mucositis in head and neck cancer patients without affecting the tumor response. 2017.
32. Efficacy of natural products in preventing oral mucositis resulting from cancer therapies: a network meta-analysis of randomized controlled trials. 2024.
33. Seyyedi SA, Sanatkhan M, Pakfetrat A, Olyae P. The therapeutic effects of chamomilla tincture mouthwash on oral aphthae: a randomized clinical trial. *J Clin Exp Dent.* 2014;6(5):e535–538.
34. The effect of *Matricaria chamomilla* (chamomile) extract in Orabase on minor aphthous stomatitis: a randomized clinical trial. *J Herb Med.* 2015.
35. Babaee N, Mansourian A, Momen-Heravi F, Moghadamnia A, Momen-Beitollahi J. The efficacy of a paste containing *Myrtus communis* (Myrtle) in the management of recurrent aphthous stomatitis: a randomized controlled trial. *Clin Oral Investig.* 2010;14(1):65–70.
36. Mahboubi M. *Myrtus communis* L. and its application in treatment of Recurrent Aphthous Stomatitis. *J Ethnopharmacol.* 2016;193:481–489.
37. Roustaeizade Z, Akhavan Karbassi MH, Kheirollahi K, Babaei Zarch E. Therapeutic efficacy of different concentrations of *Myrtus communis* (essential oil of common myrtle) in the treatment of recurrent aphthous stomatitis: a randomized controlled clinical trial. *Jorjani Biomed J.* 2018;6(3):63–72.
38. Advancing plant-derived therapeutics through mucoadhesive drug delivery systems: mechanisms, formulation approaches, clinical translation, and future directions. 2026.
39. Nanotechnology-enabled delivery of phytochemicals: from formulation strategies to therapeutic translation. 2026. doi:10.3390/jphytomed1010004.
40. Recent advancement in chitosan-based nanoparticles for improved oral bioavailability and bioactivity of phytochemicals: challenges and perspectives. *Polymers (Basel).* 2021;13(22):4036.