

Different Treatment Modalities of Recurrent Aphthous Stomatitis: A Mini Review Article

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Abstract

Recurrent aphthous stomatitis (RAS), commonly known as recurrent oral ulcers or canker sores, is one of the most prevalent oral mucosal disorders affecting approximately 20–25% of the general population. It is characterized by recurrent episodes of painful ulceration affecting non-keratinized oral mucosa. Although the exact etiology remains unclear, multiple factors including genetic predisposition, immunological dysfunction, nutritional deficiencies, hormonal changes, psychological stress, and microbial agents have been implicated. The primary goals of treatment are pain reduction, acceleration of ulcer healing, prolongation of remission periods, and prevention of recurrence. Numerous therapeutic modalities have been investigated, including topical, systemic, laser-based, herbal, and adjunctive approaches. These treatment strategies range from local anti-inflammatory and immunomodulatory agents to systemic therapies, as well as emerging laser applications and natural plant-derived products, in addition to the supportive adjunctive measures aimed at symptom control and enhancement of healing. This review summarizes the current treatment approaches for RAS.

Keywords: Recurrent aphthous stomatitis, oral ulcers, topical therapy, systemic therapy, biologics, laser therapy, herbal medicine.

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Background

Recurrent aphthous stomatitis (RAS) is the most common inflammatory ulcerative disorder of the oral cavity, characterized by recurrent episodes of painful ulceration affecting the oral mucosa. It is considered a diagnosis of exclusion, as other local or systemic causes of oral ulceration must be ruled out before establishing a definitive diagnosis [1]. Epidemiological studies have shown that RAS accounts for approximately 25% of recurrent oral ulcers in adults and up to 40% in children [2]. Clinical severity of conditions varies considerably among individuals, ranging from occasional minor ulcers to severe recurrent lesions that may interfere with eating, speaking, and overall quality of life. RAS is classified into three clinical forms [3] as shown in Table 1.

1. Minor Aphthous Ulcer

Minor aphthous ulceration is the most prevalent clinical subtype of recurrent aphthous stomatitis (RAS), Abosalem et al., 2026

accounting for approximately 70–80% of all cases. Clinically, these lesions present as small, round or oval ulcers measuring less than 10 mm in diameter, covered by a yellowish or gray white pseudomembrane and surrounded by an erythematous halo. They predominantly affect non-keratinized oral mucosal surfaces, including the labial and buccal mucosa and the floor of the mouth. The condition affects males and females equally, with the peak age of onset occurring between 10 and 19 years. Typically, patients develop between one and five ulcers per episode. Minor aphthous ulcers heal spontaneously within 10–14 days without residual scarring. Recurrences are common and generally occur at intervals ranging from 4 to 14 months [4].

2. Major Aphthous Ulcer

Major aphthous ulceration is a less common but more severe form of recurrent aphthous stomatitis, affecting approximately 10% of affected individuals. This subtype, also referred to as *Periadenitis Mucosa Necrotica Recurrens*,

is characterized by deep, painful ulcers exceeding 10 mm in diameter. The lesions commonly involve the lips, buccal mucosa, tongue, palate, and pharynx. Similar to minor aphthous ulceration, there is no significant sex predilection, and the disease frequently manifests between the ages of 10 and 19 years. Patients typically present with one to ten ulcers per episode. These lesions may persist for up to six weeks or longer and often demonstrate a prolonged healing period. Although healing may occur with or without scar formation, scarring is relatively uncommon. Owing to their size, depth, and chronicity, major aphthous ulcers may clinically resemble malignant lesions, thereby posing a diagnostic challenge. The condition usually develops after puberty and may follow a chronic recurrent course lasting several decades, with relapses often occurring at intervals of less than one month [5].

3. Herpetiform Aphthous Ulcer

Herpetiform aphthous ulceration is the least common subtype of recurrent aphthous stomatitis, accounting for approximately 1–10% of cases. It is characterized by the recurrent eruption of numerous small, painful ulcers that may coalesce to form larger irregular ulcerative areas. Lesions may occur throughout the oral cavity, including the lips, buccal mucosa, tongue, palate, gingiva, pharynx, and floor of the mouth. Unlike the minor and major forms, herpetiform aphthous ulceration demonstrates a higher prevalence among females. This predominance has been attributed to potential hormonal and psychosocial influences, as episodes may be precipitated by emotional stress or menstrual cycles in susceptible individuals. The condition is distinguished by its frequent recurrence, multiplicity of lesions, and significant associated pain, which may adversely affect oral function and quality of life [6]. RAS is characterized by a complex and multifactorial etiology, where various systemic and local triggers interact to precipitate mucosal breakdown. A primary cornerstone in RAU pathogenesis involves genetic predisposition coupled with viral and bacterial infections; specific human leukocyte antigen (HLA) types often dictate an altered immune response, which can be abnormally activated by microbial antigens present in the oral cavity. In tandem with these microbiological influences, RAU frequently manifests as a secondary symptom of underlying systemic diseases, including inflammatory bowel diseases (such as Crohn's disease and Celiac disease) and nutritional deficiencies like iron, folate, or vitamin B12 anemias.

Furthermore, acute psychological stress and mechanical injuries act as potent local exacerbating factors; emotional distress alters immune regulation via the hypothalamic-pituitary-adrenal axis, while minor oral trauma—such as accidental cheek biting or dental interventions—directly compromises mucosal integrity, paving the way for ulceration. Lastly, hormonal disturbances, particularly fluctuations in progesterone and estrogen levels during the luteal phase of the menstrual cycle or pregnancy, are well-documented contributors that influence mucosal keratinization and susceptibility to lesions. Consequently, managing RAU effectively necessitates a holistic diagnostic approach that addresses this intricate web of interrelated systemic, genetic, and environmental determinants [7] as shown in Figure 1. Current management of recurrent aphthous ulcers is mainly supportive and focuses primarily on symptomatic relief through the use of topical therapeutic

agents. Treatment should be individualized according to the severity of the condition, considering factors such as the frequency of ulcer recurrence, the intensity of pain, and the patient's response to previous therapies. The primary goals of treatment are to alleviate pain, reduce functional impairment, improve patient comfort, and decrease both the frequency and severity of recurrent episodes [8].

4. Topical therapies

Topical therapies include several pharmacological classes, including corticosteroids, cyclosporine, retinoids, antimicrobials, and local anesthetics [8]. Among these, topical corticosteroids are considered the first-line treatment due to their ability to reduce local inflammatory responses responsible for ulcer formation. Common agents include dexamethasone (0.5 mg/5 mL), triamcinolone (0.1% gel), fluocinonide (0.05% gel), and clobetasol (0.05% gel). Notably, clobetasol, a class I superpotent corticosteroid, has demonstrated superior clinical efficacy in comparison to other agents [9-10-11]. Immunomodulatory therapies include cyclosporine and retinoids. Cyclosporine may be administered systemically or topically and has also been used as an oral rinse with variable but promising outcomes. Retinoids, such as isotretinoin, tretinoin, and retinoic acid in different formulations and concentrations, have been employed in the management of recurrent aphthous conditions [9-10]. Antimicrobial agents, including tetracycline, chlorhexidine gluconate, and diluted hydrogen peroxide, have been shown to reduce both the duration and severity of pain associated with oral ulcers. Local anesthetics such as lidocaine (2% viscous solution, gel, or spray) and benzocaine are commonly used to provide symptomatic pain relief [10-12]. Furthermore, bioadhesive and occlusive agents, including Gelclair, sucralfate, bismuth subsalicylate, and 2-octyl cyanoacrylate, have demonstrated clinical benefit by forming a protective barrier over ulcerated surfaces, thereby shielding exposed nerve endings and promoting symptomatic relief and improved healing outcomes [12].

5. Systemic therapies

They are considered when patients with recurrent aphthous stomatitis (RAS) show inadequate response to topical treatment alone, particularly in cases of frequent or severe outbreaks. A variety of oral systemic agents have been reported in the literature to reduce disease severity and improve clinical outcomes. Oral antimicrobial agents such as penicillin G have been shown to decrease both ulcer size and pain intensity. In addition, combination regimens including clofazimine with rifampin and dapsone have demonstrated efficacy in reducing the development of new lesions [13]. Nutritional supplementation with zinc has also been associated with improved wound re-epithelialization and enhanced healing at a dose of approximately 50 mg/day. Pentoxifylline has shown some benefit in reducing severity of outbreaks; however, its effect on preventing recurrence is limited and its use may be restricted by gastrointestinal side effects. Low-dose tetracyclines may also provide clinical improvement due to their anti-inflammatory and matrix metalloproteinase-inhibiting properties [13]. Systemic corticosteroids, particularly oral prednisone (typically initiated at 25 mg/day with gradual tapering), remain first-line therapy for acute severe episodes of the RAS.

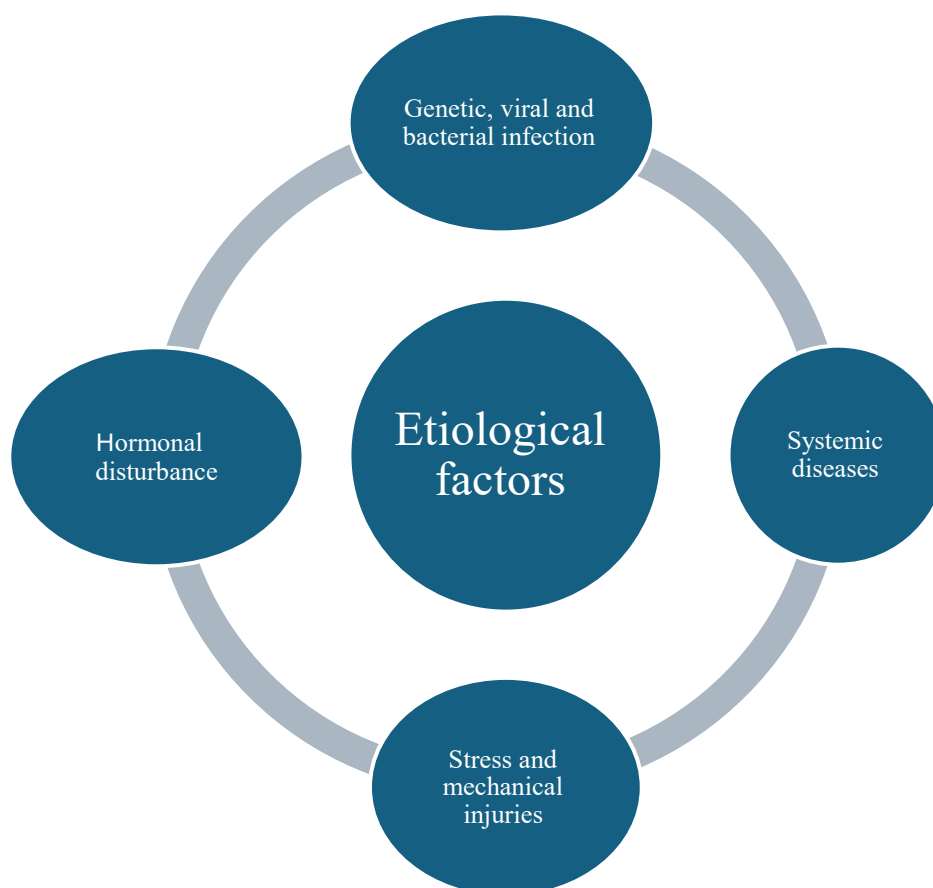


Figure 1: Etiological factors of Recurrent Aphthous ulcers

Table 1: Types of Recurrent Aphthous ulcers

Type	Occurance	Ulcer diameter	Healing time	Tissue Scarring	Anatomical sites	Number
Minor	80%	<10 mm	7-14 days	No	Lips, Cheeks, Floor of mouth	1-5
Major	10-15%	>10 mm	Up to 6 weeks	Yes	Lips, soft palate	1-10
Herpetiform	5-10%	1-3mm	7-30 days	No	Anywhere in mouth	10-100

Table 2: Evidence-Based Preventive Approaches in RAS

Preventive strategy	Intervention
Oral hygiene optimization	Regular brushing, non – SLS toothpaste ³⁵
Antiseptic mouth rinses	Chlorhexidine gluconate ³⁶
Correction of hematinic deficiencies	Iron, vitamin12 folate, zinc supplementation ³⁴
Dietary modification	Avoid spicy\ acidic foods; identify triggers ³⁵
Stress Control	Behavioral therapy, sleep regulation ³⁵
Avoidance of local trauma	Dental smoothing, adjustment of prosthesis ³⁵
Smoking modification	Smoking caseation ³⁷
Barrier protection	Protective gels, adhesive pastes that forms physical shield over mucosa reducing trauma ⁹
Management of systemic causes	Screening for Behcet's disease, Celiac disease, IBD ⁷

However, their use is limited by potential adverse effects and the contraindications in certain patient populations. In such cases, leukotriene receptor antagonists such as montelukast (10 mg/day) have been shown to provide comparable efficacy in pain reduction and lesion healing when compared with systemic corticosteroids [13]. For patients with refractory disease or inadequate response to corticosteroids, immunomodulatory and steroid-sparing agents may be considered. These include colchicine (starting at 0.5 mg/day and titrated up to 1.5 mg/day), dapsone (starting at 25 mg/day and increasing gradually up to 100 mg/day), and thalidomide (50–100 mg/day), the latter being highly effective but significantly limited by its adverse effect profile [13]. More recently, high-dose ascorbic acid supplementation (approximately 2000 mg/m²/day) has been investigated as an adjunctive therapy, showing a reduction in ulcer frequency and pain severity. This effect is thought to be mediated through its antioxidant properties and modulation of neutrophil-driven inflammatory pathways via reactive oxygen species (ROS) [14]. Overall, ascorbic acid may be considered a supportive adjunct to conventional systemic and topical therapies due to its relatively safe profile.

6. Laser therapy

Low-level laser therapy (LLLT), also known as cold laser therapy, is a non-invasive form of energy that acts on the peripheral regions of target tissues. It uses wavelengths ranging from 630 to 1100 nm and power levels between 2 and 200 mW [15-16]. This therapy has a biostimulatory effect, promoting tissue healing, exerting anti-inflammatory actions on cells and tissues, and helping to reduce pain of various origins [16-17]. Different types of lasers, such as Nd:YAG, CO₂, and diode lasers, have been used in the treatment of recurrent aphthous stomatitis (RAS). These lasers have shown superior results in pain reduction and faster healing¹⁷. One of the main advantages of LLLT is its short, localized application, which can be delivered in contact or non-contact modes. This makes it unaffected by salivary washout and free from systemic side effects [17-18].

7. Herbal therapy

Herbal and natural therapies have gained increasing attention as adjunctive or alternative treatments for Recurrent Aphthous Stomatitis. This interest is mainly due to their anti-inflammatory, antimicrobial, antioxidant, and wound-healing properties, along with a generally favorable safety profile compared to long-term corticosteroid use. Evidence from clinical studies suggests that several medicinal plants can reduce ulcer size, pain intensity, and healing time, although the overall quality of evidence remains variable [19].

8. Common Herbal Agents Used in RAS

A variety of herbal and natural agents have been investigated for their potential role in the management of recurrent aphthous stomatitis (RAS), largely due to their anti-inflammatory, antioxidant, antimicrobial, and wound-healing properties. Aloe vera has been widely studied and is reported to reduce pain and accelerate re-epithelialization through its anti-inflammatory and antioxidant effects [20]. Similarly, licorice demonstrates significant clinical efficacy in reducing ulcer size, pain intensity, and healing time, primarily owing to its mucoprotective and anti-inflammatory actions [21]. Thyme honey, rich in bioactive compounds such as EGCG, Abosalem et al., 2026

ferulic acid, and carvacrol, contributes to the suppression of inflammatory cytokines (including IL-6, IL-1 β , TNF- α , and PGE₂), thereby reducing inflammation and promoting epithelial regeneration and faster healing [22]. Curcumin has also been shown to inhibit inflammatory mediators and support tissue repair, and it has been incorporated into mouthwash and gel formulations for RAS management [23]. Chamomile provides flavonoids with soothing and anti-inflammatory effects that help alleviate pain and erythema associated with aphthous ulcers [24].

In addition, pumpkin seed oil contains essential fatty acids, vitamins, and minerals that may support healing and reduce inflammation, although further clinical evidence is required to confirm its efficacy [25]. Sumac (*Rhus coriaria*) and myrtle (*Myrtus communis*) are rich in phenolic compounds and flavonoids, offering strong antioxidant and antibacterial effects that may enhance healing and reduce lesion severity [26-27]. Guava extract and *Punica granatum* (pomegranate) exhibit notable antimicrobial and antioxidant activities, which help combat pathogenic bacteria and neutralize reactive oxygen species involved in ulcer pathogenesis, thereby promoting faster recovery [28-29]. Purslane (*Portulaca oleracea*), green tea (*Camellia sinensis*), and *Kaempferia galanga* Linn. also contain bioactive compounds with anti-inflammatory and antioxidant properties that support oral wound healing, with varying levels of clinical evidence [30-31]. Echinacea has been studied for its immunomodulatory and anti-inflammatory effects, although findings regarding its efficacy in RAS remain inconsistent [32]. Finally, propolis has demonstrated promising results in reducing pain and accelerating healing through its combined anti-inflammatory and tissue-repair properties when applied topically [33].

9. Adjunctive and preventive measures

Adjunctive strategies play an important role in comprehensive management. These include identification and correction of nutritional deficiencies, particularly iron, vitamin B12, and folate, which have been associated with increased susceptibility to RAS [34]. Stress management is also considered beneficial, as psychological stress has been reported as a triggering or exacerbating factor in susceptible individuals [35]. Preventive behavioral measures such as maintaining good oral hygiene, avoiding trauma, eliminating triggering foods (spicy, acidic, and abrasive foods) may reduce the frequency and severity of episodes. Additionally, use of sodium lauryl sulfate (SLS)-free toothpaste has been suggested to decrease recurrence in some patients, possibly due to reduced mucosal irritation [35] as shown in Table 2.

10. Conclusion

In conclusion, the management of RAS should follow a stepwise, individualized approach based on disease severity and patient needs. Topical therapies remain the first-line treatment for most patients due to their effectiveness in reducing pain and inflammation, whereas systemic therapies are reserved for severe, recurrent, or refractory cases. Laser therapy has emerged as a promising modality that provides rapid pain relief and promotes faster healing, while herbal therapies have gained increasing attention because of their anti-inflammatory and wound-healing properties. Despite the availability of multiple treatment options, no single therapy can completely prevent recurrence. Therefore, optimal

disease control requires the integration of appropriate therapeutic modalities with preventive strategies, including the identification and avoidance of triggering factors, maintenance of good oral hygiene, stress management, and correction of nutritional deficiencies, ultimately improving patient outcomes and quality of life.

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