



The Effectiveness of Alum in Treatment of Oral Ulceration: Histological Study

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Abstract

Objectives: Oral ulceration is a widespread and painful condition that affects many individuals globally. Numerous therapeutic options have been explored for its management. Alum, a traditional remedy, has shown potential in promoting wound healing.

Methods: This study aimed to evaluate the impact of topical alum on oral ulcer healing in albino rats. Thirty rats were anesthetized, and standardized ulcers were induced on the left buccal mucosa. The animals were divided into two groups; the control group did not receive any treatment, and the topical alum treated group, in which alum/vaseline paste was applied three times daily. Rats were euthanized at 2, 4, and 8 days post-ulcer induction. Buccal mucosa samples were collected, stained with hematoxylin and eosin (H&E), and examined under a light microscope at ×400 magnification for histopathological evaluation.

Results: No significant histopathological changes were observed in the control group or in the alum-treated ulcers at two days post-induction, with both showing deep ulcerative lesions characterized by complete epithelial loss and inflammatory infiltrates. In the alum-treated group, after four days, partial re-epithelialization was noted, along with mild basal cell hyperplasia, partial keratinization, and remodeling of fibrous connective tissue. By eight days, complete re-epithelialization was achieved. The underlying connective tissue demonstrated organized collagen fibers, indicating advanced scar maturation and tissue remodeling.

Conclusions: Histological examination of topical alum/vaseline application on experimentally induced oral ulceration revealed its potential as a natural topical remedy for enhancing mucosal healing. Alum promoted re-epithelialization, reduced inflammatory cell infiltration, and supported tissue remodeling and scar maturation. Result highlights alum's promising therapeutic role in oral wound management.

Keywords: Recurrent Aphthous Stomatitis (RAS); Oral Ulceration; Alum

Introduction

Oral ulceration, particularly recurrent aphthous stomatitis (RAS), is a common and painful condition affecting millions worldwide. Various treatments have been explored; the available treatment modalities are numerous [1-3]. However, clinicians must consider the side effects of these medications, and they have to prescribe them with caution [4-6].

Natural products have been utilized for decades in the management of various types of oral ulcerations. In many cultures, their therapeutic potential continues to be valued due to their wide availability, low cost, and the common perception that they pose fewer health risks compared to chemically synthesized pharmaceuticals [7-9]. Researchers reported different types of natural products in treating oral ulceration, including alum. FDA recognized an alum as a safe (GRAS) substance [10]. There is no evidence indicating any potential risk to consumers when alum is used within currently approved concentration limits [11,12]. The safety of aluminum compounds, such as alum (potassium aluminum sulfate), has been extensively evaluated in various applications, including cosmetics and food products. Regulatory bodies have assessed their safety profiles and established permissible exposure levels to ensure consumer safety [13,14].

Alum (common synonyms: potassium alum, potash alum, aluminum potassium sulfate, potassium aluminum sulfate, aluminum sulfate, aluminum potassium sulfate dodecahydrate, tawas, Shibble-Yamani) is odorless, white lustrous crystals. It comes in pieces, granules, or powder [15,16]. The molecular formula of alum is $KAl(SO_4)_2 \cdot 12H_2O$. It has an astringent taste and the PH is 3-4 (1 g/1 ml water) [17].

There are various uses of alum in medicine due to its wide spectrum antibacterial and antifungal actions [18-20]. It has incorporated in vaccine formulations to enhance the immune response in treatment of candidal vaginitis, and gastrointestinal spastic disorders [21-23]. In dentistry, many studies demonstrated the effect of alum mouthwash on salivary *S. mutans* counts and reduction in caries formation [24,25]. Also, in the treatment of periodontal diseases against *P. gingivalis* [26]. Furthermore, alum showed significant reduction of the size of oral aphthous ulcers, severity of pain, and healing period with no reported side effect [27].

Unfortunately, there is a lack of studies illustrated the effect of alum on oral ulceration, and almost there is no research has examined the histological effect of alum on oral ulceration. With alum emerging as a traditional remedy, this study evaluates its effectiveness by assessing the histological changes in induced ulcers in rats.

Materials and Methods

- **Ethical Clearance:** This experimental study was approved by the Ethical Committee, Institutional Review Board (IRB), Princess Nourah bint Abdulrahman University, Riyadh, KSA (IRB Registration Number with KACST, KSA: H-01-R-059, IRB Log Number: 21-0098).
- **Alum paste preparation:** Alum and petrolatum were sourced from a local market, Al-Dawaa Pharmacy, Riyadh, Saudi Arabia. Petrolatum is submitted as a form of vaseline (petroleum jelly), which is the commercial form of petrolatum. Paste was formed by mixing alum powder with vaseline to form a fine paste consistency. The ratio of alum powder to vaseline was $\frac{3}{4}$ alum to $\frac{1}{4}$ vaseline. The prepared paste was reserved in sealed containers to be ready for use. The mixed alum paste was applied over the induced ulcer three times daily throughout the study period.
- **Study subjects:** After sample size calculation, based on previous studies performed to examine the efficacy of different topical applications to treat oral ulceration [28-30]. The estimated sample was 30 adult male Albino rats weighing 200-250 g. Animals were kept in a room with a temperature of about 22-24°C, and the animals were exposed to 12:12 hours light-dark cycles. Furthermore, rats were provided with unrestrained access to regular food and water. The experimental procedures complied with the rules and regulations specified in the Guide for the Care and Use of Laboratory Animals [31].

Ulcer induction

Thirty albino rats were anesthetized with an intraperitoneal injection of ketamine and xylazine (90 and 15 mg/kg, respectively). After the anesthetic stage was reached, each animal was put on a surgical table in dorsal decubitus and immobilized with adhesive tape. The mucosa was sterilized by using a swab covered in 0.12%

chlorhexidine gluconate. Ulceration of the left cheek mucosa was provoked by abrasion using a n° 15 scalpel blade [28,32]. To standardize the lesion area, an 8-mm-diameter demarcator was used. The operation technique was standardized for all samples and was performed by the same examiner.

Preparation of sample

After ulcer induction, the rats divided in into two groups

- **Group I:** Control group (15 rats): with oral ulcer and not receiving any treatment.
- **Group II:** Alum group (15 rats): with oral ulcer and receiving topical application of alum/vaseline paste three times daily.

Five rats from each group were sacrificed at day 2, 4 and 8 by an overdose intra-peritoneal injection of 100 mg/kg Phenobarbital sodium (West Ward Pharm., USA). Each wound was excised, maintaining approximately 3 mm of mucosa around the incision.

Sections were cut from buccal mucosa at a thickness of 5 µm and stained with hematoxylin and eosin (H&E) for histopathological evaluation under the light microscope with ×400 magnification by a pathologist [32].

Results

- **Day 2 (control and alum-treated):** Sections from the buccal mucosa demonstrated a deep ulcerative defect with complete loss of the epithelial lining and extension into the underlying

lamina propria (Figure 1 A, B). The ulcer base was covered by a fibrinopurulent membrane with a dense mixed inflammatory infiltrate. In the mucosa adjacent to the ulcer, there was epithelial hyperplasia with acanthosis and parakeratosis at the margins. The underlying lamina propria and submucosa showed prominent granulation tissue formation. No epithelial dysplasia or neoplastic change was identified in the surrounding mucosa.

- **Day 4 (alum-treated):** Sections obtained after 4 days of topical alum application showed partial re-epithelialization of the ulcer surface (Figure 2 A). The newly forming epithelium exhibited mild basal cell hyperplasia with incipient surface keratinization. The lamina propria displayed early fibrous remodeling characterized by increased collagen deposition and a reduced inflammatory infiltrate. Residual granulation tissue persisted; however, capillary density and fibroblast cellularity were lower than at the active ulcer stage, indicating progression toward repair.
- **Day 8 (alum-treated):** All sections from treated sites demonstrated complete re-epithelialization composed of newly formed keratinized stratified squamous epithelium measuring approximately 3–4 cell layers (Figure 2 B). The surface showed mild, physiologic keratinization consistent with normal buccal mucosa. The underlying lamina propria consisted of dense, well-organized collagen bundles with minimal residual inflammation, consistent with scar maturation and advanced tissue remodeling. No dysplastic changes were observed.

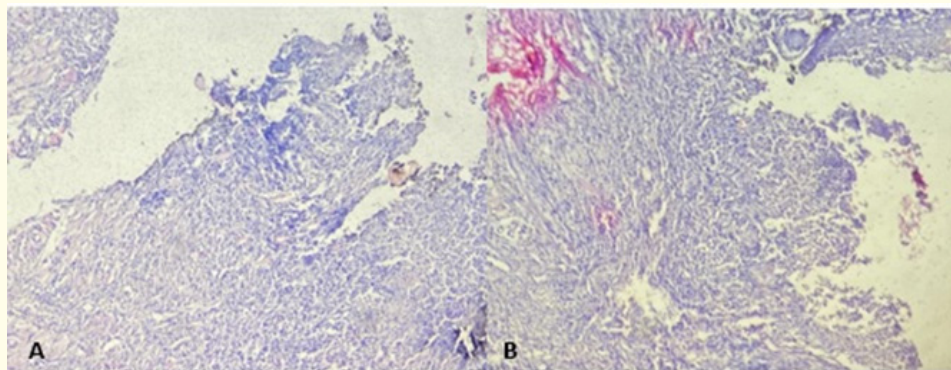


Figure 1: (A) Control Group/Day2: Deep ulceration, complete loss of superficial epithelium and severe inflammatory cell infiltrates deep to the underlying lamina propria. (B) Alum Treated Group/ Days 2: No specific changes noted in ulcer healing.

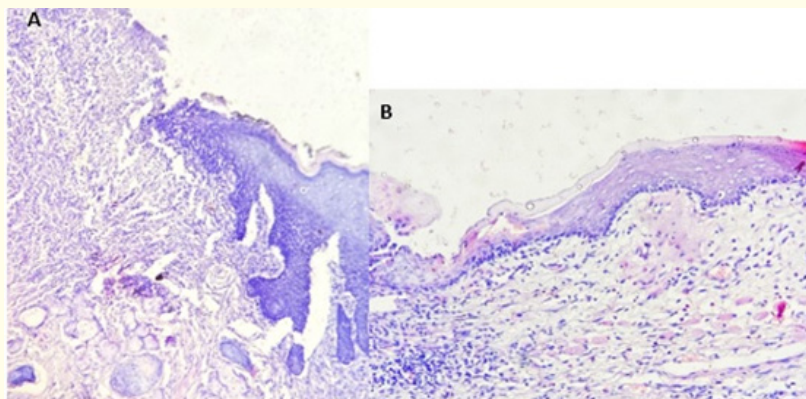


Figure 2: Alum Treated Group: (A) Day 4: Partial re-epithelization, multiple layers of epithelium, and reduction of inflammatory infiltrate. (B) Day 8: Epithelization and focal inflammatory cells represent a return to normal immune surveillance.

Discussion

Within the framework of herbal medicine, alum is recognized for its multifaceted therapeutic properties, including astringent, antimicrobial, anti-inflammatory, antioxidant, analgesic, and anti-pyretic effects. Alum can be applied as a solid or solution to achieve haemostasis in wounds and abrasions, and is also recommended as a mouthwash or gargle in cases of pharyngitis and stomatitis. It has been used in managing oral ulcerations, mucositis, gingivitis, and periodontitis, and evidence suggests it accelerates the healing of recurrent aphthous stomatitis [6,22,30,31,33-35]. Rafieian, *et al.* [36] reported that alum-containing mucoadhesive patches significantly accelerated healing of RAS, with a mean healing time of 7.52 days in the alum group versus 12.2 days in controls, and also reduced ulcer size and pain severity. Similarly, Altaei, *et al.* [37] found that alum application expedited healing and alleviated discomfort associated with RAS. These findings align with the current study, which observed a marked reduction in inflammation eight days after alum patch application.

To the best of our knowledge, no previous studies have specifically examined the histologic effects of alum on oral ulceration. While a limited number of experimental studies, such as that of Motalebnejad, *et al.* [38] have assessed alum's impact on general

oral wound healing in rats, they did not focus on ulcer models nor include detailed histopathological evaluation of tissue response. Therefore, the present study fills a critical gap in the literature by providing histologic evidence on the effect of alum paste in a standardized oral ulcer model, offering new insight into its potential therapeutic mechanisms.

One of the key mechanisms through which alum enhances ulcer healing is its antibacterial activity, which plays a vital role in reducing microbial load and associated inflammation at the ulcer site. Antibacterial activity is fundamental in accelerating ulcer healing, as bacterial colonization prolongs the inflammatory phase and impedes tissue regeneration. Alum demonstrates antimicrobial activity against a range of common oral and wound pathogens, including *Streptococcus mutans* and *Staphylococcus aureus* [39,40]. By reducing bacterial load, alum creates a more favorable environment for collagen synthesis, epithelialization, and angiogenesis, which are critical for tissue regeneration. Among these studies, Wagh, *et al.* [33] evaluated the antimicrobial efficacy of potash alum on oral ulcers and reported significant inhibition of common oral pathogens. Their findings reinforce the alum's role in maintaining a clean wound environment conducive to healing. This aligns with our histologic observations, which demonstrated reduced inflammatory

infiltration and enhanced re-epithelialization in the alum-treated group, suggesting that alum's antimicrobial activity may contribute to its overall wound-healing potential. Furthermore, the antiseptic and the antimicrobial properties of alum help in maintaining a clean wound environment, promoting epithelial closure, and improving histologic outcomes. In parallel, alum's antiseptic activity plays an additional role by reducing microbial colonization at the ulcer site, thereby establishing a more favorable microenvironment for regeneration and epithelial closure. Complementing our findings, Refat, *et al.* [41] showed that a 10% oil-in-water potash alum cream inhibited *S. aureus*, *S. pyogenes*, *E. coli*, and *P. aeruginosa* *in vitro*, implying that alum may curb secondary bacterial colonization and thereby aid in ulcer healing. Importantly, activity was pH-dependent, declining above a pH of 3.5, which underscores the need for mucoadhesive, buffering intraoral formulations to preserve local acidity and prolong contact time. These findings justify adding petrolatum to our alum preparation to provide occlusion and retention, limiting salivary washout, and supporting sustained micro-acidity at the ulcer surface.

In addition to its antimicrobial properties, alum may exert therapeutic benefits through antioxidant and modest anti-inflammatory mechanisms. *In vitro* comparisons of alum and "burnt alum" demonstrated that alum possesses notable radical-scavenging activity in HaCaT keratinocytes, as evidenced by DPPH assays. However, its ability to suppress nitric oxide production in RAW macrophages was limited, with more pronounced **inhibition observed for burnt alum**. These findings suggest that alum's primary mode of action is antioxidant.⁴² These effects are relevant because **excess reactive oxygen species (ROS)** sustain inflammation, impair epithelial regeneration, and hinder matrix remodeling in mucosal wounds. Conversely, **titrating ROS toward physiologic levels** supports the transition to proliferation, **fibroblast activity**, and **collagen deposition** [43,44]. Taken together, alum's **ROS-modulating capacity** provides a biologically plausible pathway by which alum could **attenuate tissue injury** and **facilitate re-epithelialization and collagen organization** in oral ulcers [45].

Alum's astringent and hemostatic actions contract superficial tissues and precipitate proteins, promoting rapid capillary hemostasis and the formation of a clean wound bed. This reduces local edema and exudate and can dampen nociceptor stimulation, thereby helping with pain control during early healing [11,46]. Alum has shown promising clinical applications in dentistry. In pediatric populations, alum-based mouth rinses significantly reduce dental plaque and salivary *Streptococcus* counts, demonstrating good oral tolerability over several weeks of supervised use [47]. Topically, alum has also been effective in managing RAS. Randomized controlled trials have reported that alum-containing adhesive patches and topical formulations provide significant pain relief, reduce ulcer size, and shorten healing time compared with placebo, without notable adverse effects [48].

Clinical studies have demonstrated that alum-containing mucosal patches significantly reduce pain in patients with oral ulcers. For instance, a clinical study by Rafieian, *et al.* [36] using 7% alum-containing mucosal adhesive patches reported a statistically significant reduction in pain severity within just a few days of application compared to placebo-treated controls. Similarly, Bangi, *et al.* [49] reported that alum significantly reduces the severity of pain and duration of healing of RAS without any side effects. Collectively, these findings highlight alum's dual therapeutic benefit: it provides effective symptomatic relief while potentially accelerating healing, supporting its role as both a palliative and curative agent in oral ulcer management. In contrast to our findings, Motalebnejad, *et al.* [38] reported that alum solutions at concentrations ranging from 7% to 14% did not significantly enhance wound healing on the dorsal surface of the rat tongue. Their results suggested that increasing alum concentration in solution form did not provide additional therapeutic benefit. The authors proposed that future investigations should examine alternative concentrations, repeated dosing schedules, and the potential application of alum in other oral wound conditions.

This discrepancy may be attributed to differences in formulation, as our study employed an alum paste rather than a solution, which may allow for greater local retention and more sustained therapeutic action. Although the findings are promising, several limitations should be acknowledged. This study relied on an experimental animal model which, although valuable for obtaining detailed histological insights, may not fully replicate the multifactorial clinical conditions encountered in humans. Variations in ulcer pathogenesis, recurrence patterns, and host immune responses could influence treatment outcomes in real patients. Furthermore, the long-term effects of repeated alum application remain uncertain and warrant additional investigation. Well-designed clinical trials with larger sample sizes and standardized alum-based formulations are necessary to validate its therapeutic efficacy and safety across diverse populations. Additionally, future research could explore the potential benefits of combining alum with other natural or synthetic agents to achieve more enhanced and consistent healing outcomes.

Ethical Clearance

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Competing of Interest

The authors declare that they have no competing interests related to this work.

Data Availability

All data supporting the findings of this study are included within the article and its supplementary materials.

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