



International Journal of Scientific Research in Dental and Medical Sciences

www.ijrdms.com



Effectiveness of Aloe vera in the Management of Oral Mucosal Diseases: A Systematic Review

A. F. M. Shakilur Rahman^{a,*}, Tamiral Jannat^b, Ismat Ara Haider^c

^a Department of Oral and Maxillofacial Surgery, Rajshahi Medical College, Rajshahi, Bangladesh

^b Department of Pharmacology, Sir Salimullah Medical College, Dhaka, Bangladesh

^c Department of Oral and Maxillofacial Surgery, Dhaka Dental College Hospital, Dhaka, Bangladesh

ARTICLE INFO

Article history:

Received 11 January 2021

Received in revised form 21 February 2021

Accepted 01 March 2021

Available online 07 March 2021

Keywords:

Aloe vera

Oral lichen planus

Oral submucous fibrosis

Recurrent aphthous stomatitis

ABSTRACT

Background and aim: Aloe vera is also called Aloe barbadensis Miller. Aloe vera has been utilized for its numerous salutary properties. It has been utilized for fast wound healing and pain alleviation. There are few clinical studies recorded where Aloe vera is utilized in the treatment of oral mucosal diseases. The rationale for this review is to study clinical trials to assess the adequacy of Aloe vera in the treatment of oral mucosal diseases.

Materials and methods: PubMed (Central), Wiley online library, Elsevier, Google scholar, and Hinary were used from the electronic databases using keywords until December 2020 to perform systematic literature. The quest was based on the terms of Mesh. Randomized or quasi-randomized clinical trials, cross-sectional and case-control studies included in this review. Literatures in English were only considered for this review. Review articles, experimental studies, and in-vitro studies were excluded in this review.

Results: A total of 20 articles met the inclusion criteria. These articles were clinical trials for assessing the efficiency of Aloe vera in oral mucosal diseases that showed the efficacy of Aloe vera in oral submucous fibrosis, oral lichen planus, burning mouth syndrome, recurrent aphthous stomatitis, and chemotherapy-induced stomatitis. It showed fewer beneficial effects on radiation-induced mucositis.

Conclusion: In the future, Aloe vera can play a promising role in various oral diseases. More studies should be performed in the future to determine the appropriate dose and effects on oral mucosal diseases. Evaluating possible side effects and long-term application of Aloe vera is also recommended.

1. Introduction

Aloe vera is a herb that has been used as traditional medicine by many cultures to remedy different diseases. It has a place in the Liliaceae family having roughly 360 species that develop effortlessly in hot and dry climates. Just two plants are cultivated for commercial purposes: Aloe barbadensis Miller and Aloe arborescens (Fig. 1). The parenchymatous cells in the leaf extract of Aloe vera usually contain colorless mucilage gel (Aloe vera gel) that comprises 98-99% water with 1-2% phytochemical components.^[1] Africa, the Arabian Peninsula, Madagascar, and the islands of the Indian Ocean are the homelands of Aloe.^[2] Aloe vera has triangular, plump leaves as well as serrated edges. It has plentiful seeds within its fruits and flowers. The leaf comprises three layers with unique chemical composition and has diverse pharmacological properties (Fig. 2).^[3] Aloe vera not only improves the immune system but moreover has wound healing, anti-inflammatory, antifungal, antiseptic, pain-relieving, and anti-tumor properties.^[4] Aloe vera is related to many well-being benefits include, wound healing, hypoglycemic or antidiabetic, anti-inflammatory, immunomodulatory, hepatoprotective, and gastro-protective effects.^[5-7] Antimicrobial, antiviral, and antifungal anticancer properties have also been reported in previous studies.^[8] Aloe vera, in some cases referred to as a "miraculous" plant, has been used by mankind for centuries. The oral mucosa is the oral cavity lining having several functions, for example, defense, sensation, secretion, and is histologically suited to the particular oral condition. Oral well-being is essential to the

quality of life of people of all ages.^[11] Any alteration in the oral mucosal surface that may appear as red, white, ulcerative, and pigmented lesions, any swelling, or as varieties of developmental defects, may be categorized as oral mucosal lesions.^[9] Oral mucosal lesions may lead to irritation or pain that can impair the routine activities of individuals, such as chewing, drinking, and talking, which can later cause symptoms including bad breath, dry mouth, or abnormal sensation of the oral cavity.^[10] Infections from bacteria, fungi, viruses, parasites, and several other pathogens are some of the wide spectra of causes contributing to alterations in the oral mucosa. The physical and thermal factors, alterations in the immune response, systemic diseases, neoplasia, injuries, and other triggers cause the oral mucosal lesion. Aging problems are one of the factors among these etiologies.^[11] In dentistry, Aloe vera gel was also used and yielded positive outcomes. It was also used to manage post-extraction dry socket, endodontic, and periodontal diseases. Studies utilizing toothpaste from Aloe vera have demonstrated efficacy against the most cariogenic bacteria. Research findings have shown that Aloe vera has significant therapeutic applications in the treatment of oral diseases, including oral lichen planus (OLP), oral submucous fibrosis (OSF), oral mucositis induced by radiation (RIOM), chemotherapy-induced oral mucositis (CIOM), burning mouth syndrome (BMS), xerostomia or dry mouth, and recurrent aphthous stomatitis (RAS).^[1, 5, 12] The purpose of this review study was to collect evidence-based research on Aloe vera's

* Corresponding author. A. F. M. Shakilur Rahman

E-mail address: raselblackpearl@gmail.com

Department of Oral and Maxillofacial Surgery, Rajshahi Medical College, Rajshahi, Bangladesh

<http://doi.org/10.30485/ijrdms.2021.269101.1105>



application and determine its clinical efficacy in the treatment of different oral mucosal diseases.

2. Materials and methods

Search Strategy

A review of research journals on the efficacy of Aloe vera in oral mucosal diseases was done in this article. Using the following electronic databases, a systematic electronic search was carried out: PubMed(Central), Wiley online library, Elsevier, Google scholar, and Hinary using keywords till December 2020. The quest was based on the terms of Mesh. Keywords like Aloe vera, oral lichen planus, oral mucosa, oral submucous fibrosis, and recurrent aphthous stomatitis were scanned for a database of indexed articles. This review article aimed to assess the effectiveness of Aloe vera in the treatment of oral mucosal diseases. The following inclusion and exclusion criteria were formulated to choose the right clinical trials. This literature review was performed based on the main consideration of the PRISMA guidelines (Fig. 3).

Inclusion Criteria

Randomized or quasi-randomized clinical trials cross-sectional and case-control studies where Aloe vera was applied to treat oral mucosal diseases included in this review. Studies were only considered if they were issued as complete articles in English.

Exclusion Criteria

Review articles, experimental studies, and in-vitro studies were excluded in this review.

Study Selection

We searched for studies that fulfilled the eligibility requirements listed above. Then, we reviewed the complete title and abstract of the papers. Articles that did not meet the eligibility requirements and similar articles were excluded from the review. We had attempted to seek complete papers for all possible competent trials. Studies that satisfied the inclusion criteria were included in this review report.

3. Results

The primary computer search strategy and accompanying manual search produced 193 titles (Fig. 3). In the first example, the author chose the articles by reading the titles and abstracts of the retrieved papers, and 127 were omitted because those papers did not fulfill the eligibility requirements. Of those 66 papers, 37 were disqualified as animal studies, in vitro studies, or review articles. The remaining 29 publications that matched the eligibility requirements were thoroughly studied. Of these 29 papers, only 20 clinical trials satisfied our inclusion requirements for our review study. Out of 20 articles, four were on oral lichen planus (OLP) patients, five on oral submucous fibrosis (OSF), and four on recurrent aphthous stomatitis (RAS). Other studies were conducted on patients with burning mouth syndrome (BMS), radiation-induced oral mucositis (RIOM), chemotherapy-induced oral mucositis (CIOM), and xerostomia. Most studies have shown statistically valid evidence of the effectiveness of Aloe vera in the treatment of oral lesions. Data such as author details, study year, study design, study sample, treated oral mucosal condition, Aloe vera formulation, outcomes, complications, and any comments for this study were extracted. The abstract of these clinical trials is tabulated in Table 1.



Fig. 1. External morphology of Aloe vera.

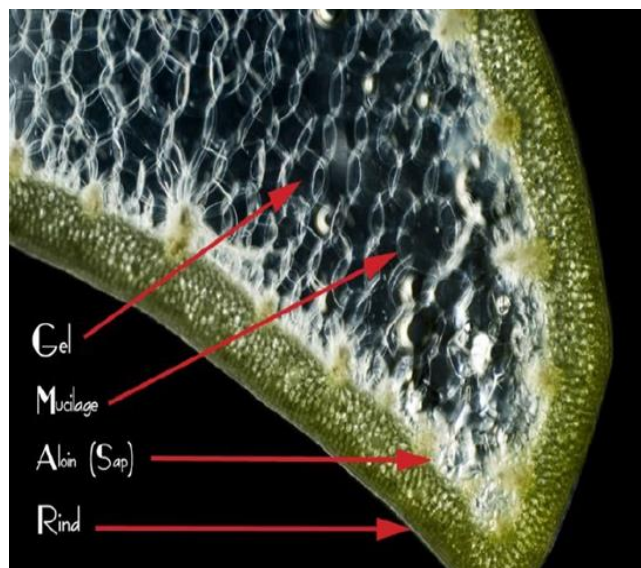


Fig. 2. Three layers of Aloe vera leaf.

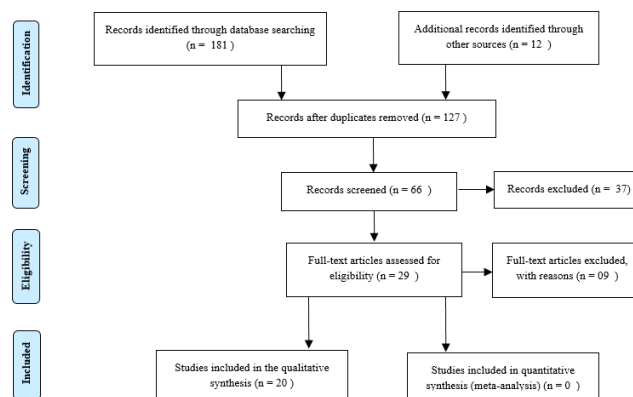


Fig 3. PRISMA Flow Diagram.

Table 1. Clinical trials of Aloe vera in treating oral mucosal lesions.

Authors with study design	Oral diseases	Aloe vera formulation	Patients	Direction of application	Results	Adverse effects	Remarks
Giroh et al., (2019) ^[13] A randomized, single-blind clinical study.	RAS	Topical Aloe vera gel.	Thirty-four individuals with clinical manifestations of minor aphthous stomatitis, divided into two groups with 17 patients each. Group A: Topical Aloe vera gel. Group B: Topical triamcinolone acetonide (0.1%) oral paste.	Used three times daily for seven days or before the ulcer disappears completely.	Triamcinolone acetonide oral paste was reported to be beneficial in wound healing than Aloe vera. On the other hand, Aloe vera gel had a better impact in reducing pain and burning sensation.	Nothing reported.	Aloe vera may be used in people who are allergic to steroid drugs and as an alternative option.
Mansour et al., (2013) ^[14] A randomized, double-blind, vehicle-controlled study.	RAS	Aloe vera gel (0.5%)	In total three groups, each consisting of 30 patients: Group I: Mucoadhesive gel with Aloe Vera. Group II: Mucoadhesive gel with myrrh Extract. Group III: Placebo (Plain mucoadhesive gel).	Application of gel four times daily for five days.	Absolute ulcer healing was reported in 76.6% of patients using Aloe vera gel. Erythema & exudation was subsided in 86.7% & 80% patients respectively.	No side effects were reported	Topical use of Aloe vera may be a safe alternative in patients with RAS.
Babae et al., (2012) ^[15] A randomized double-blind study.	RAS	Aloe vera gel (2%).	Aloe vera gel: 20 patients. Placebo gel (Control): 20 patients.	Aloe vera gel & placebo applied thrice daily for ten days. Drinking and eating were avoided at least for half an hour.	In the Aloe vera treated group, the duration of complete wound healing, pain score, wound size, and inflammation zone diameter was significantly lower at specific time points following treatment than in the control group.	Nothing reported	2% Aloe vera gel effectively reduces aphthous stomatitis pain, ulcer size, and wound healing period.

Authors with study design	Oral diseases	Aloe vera formulation	Patients	Direction of application	Results	Adverse effects	Remarks
Shi et al., (2020) ^[16] A randomized double-blind study.	RAS	Aloe vera fermentation gel.	46 patients Aloe vera fermentation gel (AA group). Chitosan gel (AC group).	Apply a layer of gel on the ulcer three times a day until the ulcer disappeared.	AA group had Better effects on healing time than the AC group. AA group decreases the harmful oral bacteria.	No serious adverse effect was reported.	The capability of Aloe vera fermentation gel to treat RAS patients has optimistic prospects for clinical applications.
Alam et al., (2013) ^[17] A randomized clinical trial.	OSF	Gel	Sixty subjects with OSF receiving medicinal (30) & surgical (30) treatment of OSF. Each group was divided randomly into group A (15 patients with Aloe vera) and group B (15 patients without Aloe vera).	Aloe vera is used as an adjuvant treatment and medicinal treatment (hyaluronidase +dexamethasone, n = 30) and surgical treatment (n = 30). Topical Aloe vera gel applied twice daily for up to 6 months.	The Aloe vera group had considerable progress in most symptoms of OSF (P< .01) compared with the other group treated without Aloe vera in both the medicinal and surgical categories.	Nothing reported	Aloe vera gel, as an adjuvant, was effective in the treatment of OSF.
Anuradha et al., (2017) ^[18] A randomized clinical trial.	OSF	Juice (Systemic) and gel (Topical).	Group A: 37 patient (AV juice & gel) Group B: 37 patients (hydrocortisone and hyaluronidase).	Group A: For three months. Group B: Intralesional injection was given for six weeks along with antioxidant.	Study parameters (burning sensation, mouth opening, the flexibility of the cheek, and protrusion of the tongue) Both of the groups showed statistically significant results of improvements in all the study parameters.	Nothing reported	An alternative, safe and effective treatment option for the management of oral submucous fibrosis could be Aloe vera.

Authors with study design	Oral diseases	Aloe vera formulation	Patients	Direction of use	Results	Adverse effects	Remarks
Sudarshan et al., (2012) ^[19] A randomized controlled trial.	OSF	Aloe vera gel (5 mg).	Twenty subjects enrolled in the study. Group A: 10 patients received Aloe vera gel. Group B: 10 patients received	Group A: Apply 5mg thrice daily topically for three months. Group B: Antioxidant capsules twice daily for three months.	Study variables were burning sensation, mouth opening, cheek flexibility. In contrast to the antioxidant group, Aloe vera revealed a significant decrease in burning sensation, increased in mouth	Nothing reported.	The Aloe vera group exhibited a significant response to treatment compared to the group of

			antioxidant capsules.		opening, and flexibility of the cheek.		Antioxidants. It is found to be relatively safe, topically applicable, readily accessible, inexpensive, non-invasive, and effective in the treating OSF.
Patil et al., (2015) ^[20] A randomized controlled trial.	OSF	Aloe vera gel (5 mg).	42 subjects diagnosed with OSF were included in the study and divided equally into two groups. Group A: spirulina group Group B: aloe vera group.	Group A: 500 mg of spirulina was prescribed in two divided doses for three months. Group B: Topical application 5 mg Aloe vera gel was given three times a day for three months. It was recommended that patients not eat or drink for 15 minutes after applying Aloe vera gel.	Important clinical progress in mouth opening was observed in Group A patients. No substantial improvement was observed between the 2 groups in burning sensation ($p = 0.06$) and lesion-associated pain ($p = 0.04$).	Nothing reported.	In OSF patients, both the medications demonstrated improvement in the clinical condition. Spirulina, however, may bring substantial clinical changes in complaints such as mouth opening.
Patil et al., (2014) ^[21] A randomized single-blind study.	OSF	Aloe vera gel (5 mg).	The research included 120 subjects with OSF. Patients were diagnosed clinically and pathologically and were evenly split into two groups. Group A: Oxitard group. Group B: Aloe vera group.	Group A: Two oxitard capsules were administered two times a day for three months. Group B: Topical application of 5 mg Aloe vera gel three times a day for three months.	The improvement in burning sensations between both the groups was not statistically meaningful ($p=0.002$).	Nothing reported.	Oxitard capsules have been shown to bring about major clinical advances in OSF treatment compared to Aloe vera gel regarding the evaluation of symptoms such as opening the mouth, protrusion of the tongue, difficulty in swallowing, and speech, and lesion-related pain.

Authors with study design	Oral diseases	Aloe vera formulation	Patients	Direction of use	Results	Adverse effects	Remarks
Leiva-Cala et al., (2019) ^[22] A randomized controlled trial.	Traumatic oral ulcer (TOU).	Aloe vera gel (80%).	A total of 140 patients were divided into two groups. Group A: Aloe vera (AV). Group B: 0.12% Chlorhexidine (CHX) gel.	The use of either Aloe vera gel or CHX gel after the cementation procedure for fixed orthodontic treatment was randomly assigned to patients over 12 years having permanent dentition.	The average TOU incidence was 43.6%. Overall, 5.7% of patients treated with Aloe vera gel did not experience from TOUs, while a sum of 57 (81.4%) of patients treated with CHX gel had experienced with TOUs. These results showed a meaningful statistical outcome ($p < 0.001$).	No adverse effects were reported.	The findings showed that the application of Aloe vera gel in patients with fixed orthodontic appliances might be essential for successful TOU prevention.
Choonhakarn et al., (2008) ^[23] A randomized double-blind study.	OLP	Gel	Aloe vera : 27 Placebo: 27	Applied topically for eight weeks.	Aloe vera had a good response in 22 (81%), one (4%) had a similar response in the placebo group ($P < 0.001$). 2 (7%) had cured completely in the AV group. Symptom (Burning pain) improve in 63% of Aloe vera group, 7% of the Placebo group ($P < 0.001$).	No serious adverse effect was reported.	AV gel can be a safe option in the treatment of OLP.
Salazar et al., (2010) ^[24] A randomized double-blind study.	OLP	Gel	Aloe vera: 32 Placebo: 32	0.4 ml (70% concentration) thrice daily.	Aloe vera group had pain remission on the sixth week (31.2%) & 12 th week (61%). Placebo group: Pain remission on 6 th week (17.2%) & 12 th week (41.6%). Not statistically significant in both of the groups.	No side effects reported.	In patients with OLP, topical AV improves the total quality of life score.

Authors with study design	Oral diseases	Aloe vera formulation	Patients	Direction of use	Results	Adverse effects	Remarks
Mansouri et al., (2011) [25] A randomized double-blinded clinical Trial.	OLP	Aloe vera mouth wash (Barij Essence Company, Tehran, Iran).	A total of 46 patients, divided into two groups. Group A: Aloe vera (AV) Group B: Triamcinolone acetonide 0.1% paste (TA)	Aloe vera mouthwash- Two tablespoons four times daily. Triamcinolone acetonide paste- Applies on the oral lesion four times daily. The treatment period was four weeks for both groups.	74% of group A patients showed some healing effect on the last follow-up (2 months), whereas group B showed in 78% cases.	Nothing stated.	Aloe vera mouth wash can be a safe alternative to TA in the treatment of oral lichen planus.
El-Soudany et al., (2013) [26] Self-controlled single-blinded clinical trial.	OLP	Aloe vera (AV) high molecular weight fractions (0.1% Ointment).	Twenty patients with the bilateral oral lesion. Both sides were treated with Aloe vera & placebo simultaneously.	Applied on the oral mucosal lesion thrice daily.	75% had complete remission with Aloe vera treated sites, whereas 10% showed partial remission in placebo treated sites.	No side effects reported.	Aloe vera ointment proved its efficacy in the treatment OLP compared to placebo.
Lopez et al., (2013) [27] A randomized clinical trial.	BMS	0.5 ml Aloe vera gel at 70% conc.	75 patients: 3 groups Group I (Tongue protector) Group II (Tongue protector + Aloe vera) Group III (Tongue protector + Placebo)	Applied 3 times daily.	No statistically significant differences between the groups (P = 0.210) Clinical improvement was found in group II.	Nothing reported.	The tongue protector and Aloe vera are effective for managing patients with BMS.
Sahebjaamee et al., (2015) [28] Triple blind, randomized, controlled clinical trial.	Radiation-induced mucositis.	Aloe vera gel	In total, 26 patients, 13 patients consist in each group. Group I: Aloe vera mouth wash. Group II: Benzydamine mouth wash.	Mucositis severity was evaluated during the radiotherapy course.	No statistical difference between the two groups was reported regarding mucositis grade change during the study period (P= 0.09).	Nothing reported.	Aloe vera mouth wash had shown the same efficacy as benzydamine regarding alleviation of radiation-induced mucositis symptoms.

Authors with study design	Oral diseases	Aloe vera formulation	Patients	Direction of use	Results	Adverse effects	Remarks
Su et al., (2004) ^[29] A randomized double-blind study.	RIOM	Aloe vera gel (94.5%)	A total of 58 head neck cancer patient receiving treatment with radiotherapy, divided into two groups (Aloe vera & placebo).	Not stated.	Statically same results in both groups regarding all study parameter (Quality-of-life scores, weight loss percentage, pain medication use, hydration requirement, oral infections).	Nothing reported.	Oral Aloe vera gel did not improve RIOM-related symptoms. In the Aloe vera group, the mean quality-of-life scores were greater.
Mansouri et al., (2016) ^[30] A randomized controlled clinical trial.	Chemotherapy-induced stomatitis.	Aloe vera mouth wash	The study sample comprises 32 patients in each group. Group A: Aloe vera. Group B: control group (Regular mouthwashes, comprising normal saline, chlorhexidine, and nystatin).	5 ml of Aloe vera solution for 2 minutes thrice daily and keep away from taking foods for half an hour after chemotherapy for 2 weeks.	Aloe vera mouthwash considerably decreased the intensity of stomatitis and its pain contrasted to the control group.	Nothing reported.	Aloe vera can develop the patients' dietary condition, reduce stomatitis and its pain intensity, and amplify the patients' pleasure.
Alkhouli et al., (2020) ^[31] A randomized controlled clinical trial.	Chemotherapy-induced stomatitis (CIS).	Aloe vera solution.	CIS in 26 children with acute lymphoblastic leukemia (ALL). They were ranged between 3 and 6 years and were randomly allocated to two categories, Aloe- vera (AV) and 5 percent sodium bicarbonate, according to the protocol (13 each).	Sponge sticks were used to spread the materials to the various site of the oral mucosa.	In the Aloe-vera group, CIS conditions were less significant than in the sodium bicarbonate group. In the 2nd, 3rd, 4th, and 7th weeks of follow-up, a statistically significant difference was found in the frequency of different CIS degrees between groups.	Nothing reported.	These results indicate that the therapeutic potential of the Aloe-vera solution in ALL children helps prevent CIS.
Morales-Bozo et al., (2012) ^[32] A randomized control trial.	Xerostomia	Aloe vera as an ingredient in mouth wash.	Seventy-seven patients were divided into two groups. Group 1: (xylitol, sodium fluoride, cetylpyridinium chloride, sodium chloride, and spearmint flavoring). Group 2: (same components as	Two different types of aqueous solutions for rinsing.	The research variables were the burning feeling of the tongue, the need to drink liquids to swallow, and the difficulty of swallowing sensation. Group 1: relieves dry mouth symptoms, the need	Nothing reported.	In patients taking three or more drugs concurrently, both groups were more successful in

		group 1, with the addition of propylene glycol, Aloe vera, glycerine, and citric acid).		to drink water, and difficulty swallowing.		alleviating xerostomia-related symptoms.
				Group 2 , by comparison, alleviates only the latter two symptoms.		

4. Discussion

Aloe vera has different types of active ingredients such as saponins, lignin, salicylic acid, anthraquinones, and amino acids.^[26] The active components show their therapeutic efficacy in different diseases such as a cutaneous wound, bacterial, viral, fungal, cancer, diabetes, gastrointestinal, and hepatic diseases.^[17] The remedial efficiency of Aloe vera has been published in the literature for more than 50 years. A range of controlled clinical trials on Aloe vera has been carried out the previous year to assess the efficiency in the treatment of different diseases as well as in oral mucosal diseases for example recurrent aphthous stomatitis (RAS), oral submucous fibrosis (OSF), oral lichen planus (OLP), burning mouth syndrome (BMS), and radiation-induced oral mucositis (RIOM), and chemotherapy-induced oral mucositis (CIOM). A clinical trial of Aloe vera on oral diseases was first published by Poor et al. in 2002.^[33] The author placed Aloe gel (Saliccept patch freeze-dried pledget) over a tooth socket immediately after extraction to assess efficacy on alveolar osteitis.^[33]

Oral lichen planus (OLP) with various clinical manifestations is a chronic, immunogenic disease. The treatment of OLP includes topical and systemic steroid therapy, retinoids, phototherapy, immunosuppressive drugs. The corticosteroid remains still the first-line choice for the treatment of OLP. No therapy is proved to resolve OLP completely. Aloe vera may be a safe alternative for the treatment of OLP as reported in different studies.^[23-26] Jornet et al.^[27] proposed that the management of oral parafunctional behaviors, along with the application of topical Aloe vera, may defend the oral mucosa from repeated trauma and lessen the symptoms caused by the oral burning syndrome.

Oral submucous fibrosis (OSF) is a premalignant condition usually caused by the chewing of areca nuts that affects oral submucosa. It is more common in the Indian subcontinent as well as in the South Asian Countries. It is manifested clinically by a wide range of signs & symptoms such as burning sensation and restricted mouth opening. A variety of treatment options, including steroid therapy, have been used in OSF's remedy for several years.^[18] It has been concluded in recent studies that Aloe vera can be a convenient alternative in the management of OSF without any consequences.^[17-19] Patil et al.^[20] reported that Aloe vera was efficient in treating OSF, but the outcomes of Aloe vera were lower than the spirulina used in the comparison.

One of the most frequent oral mucosal problems, with a variable frequency of 5-25% worldwide, is recurrent aphthous stomatitis (RAS). According to their size, number, and duration of ulcers, the classification of RAS falls into three categories: major, minor, and herpetiform.^[34] The remedies of RAS include symptomatic relief by applying topical medicines such as anesthetics, analgesics, steroids, tetracycline mouth wash, antacids, and herbal medicines.^[35] Topical Aloe vera may be applied on RAS ulcers to reduce their size effectively and give symptomatic relief, as concluded by different authors.^[13-16] A further research was conducted to determine the effectiveness of Aloe vera gel (80%) in traumatic oral ulcer patients with fixed orthodontic appliances and concluded that it might be necessary to prevent ulcers effectively.^[22]

Chemotherapy is one of the treatment options for treating cancer patients consisting of different types of cytotoxic drugs. There are several side effects relating to chemotherapeutic drugs. Oral mucositis is one of the most common among these side effects. It is reported that 40% and 70% of patients suffered from stomatitis in chemotherapy and bone marrow transplantation, respectively. Almost all of the patients with radiotherapy are affected by stomatitis.^[36] Aloe vera showed the least beneficial effect on radiation-induced stomatitis.^[29] In another study, Aloe vera mouth wash had shown the same efficacy of benzydamine regarding alleviation of radiation-induced mucositis symptoms without any side effects.^[28] Aloe vera can significantly diminish the intensity of stomatitis and its pain in chemotherapy-induced patients.^[30, 31]

Aloe vera and other ingredients (such as salivary supplements and anti-cariogenic agents) help relieve xerostomia symptoms.^[37] Two rinses were developed to alleviate xerostomia by Morales-Bozo et al.^[32] The aqueous solution containing xylitol, sodium fluoride, cetylpyridinium chloride, sodium chloride, and spearmint flavoring was constituted of Rinse 1. With propylene glycol, Aloe vera, glycerine, and citric acid, Rinse 2 was made up with the same ingredients as Rinse 1. In relieving xerostomia-related symptoms, both rinses were efficient. Aloe vera may cause a flush, burning, and tingling sensation or allergic reaction when used topically.^[38] Allergic reactions are mostly occurred due to the presence of anthraquinones.^[39] Three case reports of Aloe vera-induced toxic hepatitis have also been received.^[40]

5. Conclusion

Aloe vera has a wide spectrum of therapeutic efficiency ranging from simple wound healing to complex immunomodulation. Aloe vera may play a promising role in various oral mucosal diseases in the future. More studies should be aimed in the future to determine the optimal concentration, time of application, and its impact on oral mucosal diseases. It is also mandatory to evaluate potential side effects and long-term use of Aloe vera.

Conflict of Interest

The authors declared that there is no conflict of interest.

Acknowledgements

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

References

- [1] Nair GR, Naidu GS, Jain S, Nagi R, Makkad RS, Jha A. Clinical effectiveness of aloe vera in the management of oral mucosal diseases-a systematic review. *Journal of clinical and diagnostic research: JCDR*. 2016;10(8):ZE01-07. doi: 10.7860/JCDR/2016/18142.8222.
- [2] Akev N, Can A, Sütülpınar N, Çandöken E, Özsoy N, Özden TY, et al. Twenty years of research on Aloe vera. *İstanbul Üniversitesi Eczacılık Fakültesi Dergisi*. 2015;45(2):191-215.
- [3] Shrestha A, Acharya A, Nagalakshmi NC. Aloe vera as traditional medicinal plant: A review on its active constituents, biological and therapeutic effects. *World Journal of Pharm. Research*. 2015;4:2146-61.

- [4] Lavanya R, Tatapudi R, Swapna LA, Vijayalaxmi N, Mamatha B. Aloe Barbadensis Miller (Aloe Vera) in Oral Diseases. *International Journal of Contemporary Surgery*. 2013;1(1):19.
- [5] Zagórska-Dziok M, Furman-Toczek D, Dudra-Jastrzębska M, Zygo K, Stanisławek A, Kapka-Skrzypczak L. Evaluation of clinical effectiveness of Aloe vera—a review. *Journal of Pre-Clinical and Clinical Research*. 2017;11(1):86-93. doi: 10.26444/jpcrcr/74577.
- [6] Madhav NV, Bairy K. Hepatoprotective activity of Aloe vera gel against paracetamol induced hepatotoxicity in albino rats. *carbon*. 2011;2(3).
- [7] Kwon KH, Hong MK, Hwang SY, Moon BY, Shin S, Baek JH, et al. Antimicrobial and immunomodulatory effects of Aloe vera peel extract. *Journal of Medicinal Plants Research*. 2011;5(22):5384-92. doi.org/10.5897/JMPR.9000173.
- [8] Sahu PK, Giri DD, Singh R, Pandey P, Gupta S, Shrivastava AK, et al. Therapeutic and medicinal uses of Aloe vera: a review. *Pharmacology & Pharmacy*. 2013;4(08):599. <http://dx.doi.org/10.4236/pp.2013.48086>.
- [9] Espinoza I, Rojas R, Aranda W, Gamonal J. Prevalence of oral mucosal lesions in elderly people in Santiago, Chile. *Journal of oral pathology & medicine*. 2003;32(10):571-5. <https://doi.org/10.1034/j.1600-0714.2003.00031.x>.
- [10] Patil S, Kaswan S, Rahman F, Doni B. Prevalence of tongue lesions in the Indian population. *Journal of clinical and experimental dentistry*. 2013;5(3):e128-e132. doi: 10.4317/jced.51102.
- [11] Cebeci AR, Gulsahi A, Kamburoglu K, Orhan BK, Oztas B. Prevalence and distribution of oral mucosal lesions in an adult Turkish population. *Med Oral Patol Oral Cir Bucal*. 2009;14(6):E272-7.
- [12] Subhash AV, Suneela S, Anuradha C, Bhavani SN, Babu MS. The role of Aloe vera in various fields of medicine and dentistry. *Journal of Orofacial Sciences*. 2014;6(1):5. DOI: 10.4103/0975-8844.132564.
- [13] Giroh VR, Hebbale M, Mhapuskar A, Hiremutt D, Agarwal P. Efficacy of aloe vera and triamcinolone acetonide 0.1% in recurrent aphthous stomatitis: A preliminary comparative study. *Journal of Indian Academy of Oral Medicine and Radiology*. 2019;31(1):45-50. DOI: 10.4103/jiaomr.jiaomr_203_18.
- [14] Mansour G, Ouda S, Shaker A, Abdallah HM. 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. *Journal of Oral Pathology & Medicine*. 2014;43(6):405-9. <https://doi.org/10.1111/jop.12130>.
- [15] Babaee N, Zabihi E, Mohseni S, Moghadamnia AA. Evaluation of the therapeutic effects of Aloe vera gel on minor recurrent aphthous stomatitis. *Dental research journal*. 2012;9(4):381-385.
- [16] 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. *Canadian Journal of Infectious Diseases and Medical Microbiology*. 2020. <https://doi.org/10.1155/2020/8867548>.
- [17] Alam S, Ali I, Giri KY, Gokkulakrishnan S, Natu SS, Faisal M, et al. Efficacy of aloe vera gel as an adjuvant treatment of oral submucous fibrosis. *Oral surgery, oral medicine, oral pathology and oral radiology*. 2013;116(6):717-24. <https://doi.org/10.1016/j.oooo.2013.08.003>.
- [18] Anuradha A, Patil B, Asha VR. Evaluation of efficacy of Aloe vera in the treatment of oral submucous fibrosis—a clinical study. *Journal of Oral Pathology & Medicine*. 2017;46(1):50-5. <https://doi.org/10.1111/jop.12463>.
- [19] Sudarshan R, Annigeri RG, Sree Vijayabala G. Aloe vera in the treatment for oral submucous fibrosis—a preliminary study. *Journal of oral pathology & medicine*. 2012;41(10):755-61. <https://doi.org/10.1111/j.1600-0714.2012.01168.x>.
- [20] Patil S, Al-Zarea BK, Maheshwari S, Sahu R. Comparative evaluation of natural antioxidants spirulina and aloe vera for the treatment of oral submucous fibrosis. *Journal of oral biology and craniofacial research*. 2015;5(1):11-5. <https://doi.org/10.1016/j.jobcr.2014.12.005>.
- [21] Patil S, Halgatti V, Maheshwari S, Santosh BS. Comparative study of the efficacy of herbal antioxidants oxitard and aloe vera in the treatment of oral submucous fibrosis. *Journal of clinical and experimental dentistry*. 2014;6(3):e265. doi: 10.4317/jced.51424.
- [22] Leiva-Cala C, Lorenzo-Pouso AI, Centenera-Centenera B, López-Palafox J, Gándara-Vila P, García-García A, et al. Clinical efficacy of an Aloe Vera gel versus a 0.12% chlorhexidine gel in preventing traumatic ulcers in patients with fixed orthodontic appliances: a double-blind randomized clinical trial. *Odontology*. 2020;108(3):470-8. <https://doi.org/10.1007/s10266-019-00468-w>.
- [23] Choonhakam C, Busaracome P, Sripanidkulchai B, Sarakarn P. The efficacy of aloe vera gel in the treatment of oral lichen planus: a randomized controlled trial. *British journal of dermatology*. 2008;158(3):573-7. <https://doi.org/10.1111/j.1365-2133.2007.08370.x>.
- [24] Salazar-Sánchez N, López-Jornet P, Camacho-Alonso F, Sánchez-Siles M. Efficacy of topical Aloe vera in patients with oral lichen planus: a randomized double-blind study. *Journal of oral pathology & medicine*. 2010;39(10):735-40. <https://doi.org/10.1111/j.1600-0714.2010.00947.x>.
- [25] Mansourian A, Saheb-Jamee M, Momen-Beitollahi J, Momen-Heravi F, Esfehiani M, Khalilzadeh O. Comparison of aloe vera mouthwash with triamcinolone acetonide 0.1% on oral lichen planus: a randomized double-blinded clinical trial. *The American Journal of the Medical Sciences*. 2011;342(6):447-51. <https://doi.org/10.1097/MAJ.0b013e3182171164>.
- [26] El-Soudany K, Yagi A, Kabbash A. A self-controlled single blinded clinical trial to evaluate oral lichen planus after topical treatment with Aloe vera. *Journal of Gastroenterology and Hepatology Research*. 2013;2(4):503-7.
- [27] López-Jornet P, Camacho-Alonso F, Molino-Pagan D. Prospective, randomized, double-blind, clinical evaluation of Aloe vera B barbadensis, applied in combination with a tongue protector to treat burning mouth syndrome. *Journal of Oral Pathology & Medicine*. 2013;42(4):295-301. <https://doi.org/10.1111/jop.12002>.
- [28] Saheb-Jamee M, Mansourian A, Hajimirzamohammad M, Zadeh MT, Bekhradi R, Kazemian A, et al. Comparative efficacy of aloe vera and benzydamine mouthwashes on radiation-induced oral mucositis: a triple-blind, randomised, controlled clinical trial. *Oral Health Prev Dent*. 2015;13(4):309-15. doi: 10.3290/j.ohpd.a33091.
- [29] Su CK, Mehta V, Ravikumar L, Shah R, Pinto H, Halpern J, et al. Phase II double-blind randomized study comparing oral aloe vera versus placebo to prevent radiation-related mucositis in patients with head-and-neck neoplasms. *International Journal of Radiation Oncology* Biology* Physics*. 2004;60(1):171-7. <https://doi.org/10.1016/j.ijrobp.2004.02.012>.
- [30] Mansouri P, Haghighi M, Beheshtipour N, Ramzi M. The effect of aloe vera solution on chemotherapy-induced stomatitis in clients with lymphoma and leukemia: a randomized controlled clinical trial. *International journal of community based nursing and midwifery*. 2016;4(2):119-126.
- [31] Alkhouli M, Laflouf M, Alhaddad M. Efficacy of aloe-vera use for prevention of chemotherapy-induced oral mucositis in children with acute lymphoblastic leukemia: a randomized controlled clinical trial.

- Comprehensive child and adolescent nursing. 2020;44(1):49-62. <https://doi.org/10.1080/24694193.2020.1727065>.
- [32] Morales-Bozo I, Rojas G, Ortega-Pinto A, Espinoza I, Soto L, Plaza A, et al. Evaluation of the efficacy of two mouthrinses formulated for the relief of xerostomia of diverse origin in adult subjects. *Gerodontology*. 2012;29(2):e1103-12. <https://doi.org/10.1111/j.1741-2358.2012.00626.x>.
- [33] Poor MR, Hall JE, Poor AS. Reduction in the incidence of alveolar osteitis in patients treated with the SaliCept patch, containing Acemannan hydrogel. *Journal of oral and maxillofacial surgery*. 2002;60(4):374-9. <https://doi.org/10.1053/joms.2002.31222>.
- [34] Chavan M, Jain H, Diwan N, Khedkar S, Shete A, Durkar S. Recurrent aphthous stomatitis: a review. *Journal of oral pathology & medicine*. 2012;41(8):577-83. doi: 10.1111/j.1600-0714.2012.01134.x.
- [35] Altenburg A, Abdel-Naser MB, Seeber H, Abdallah M, Zouboulis CC. Practical aspects of management of recurrent aphthous stomatitis. *Journal of the European Academy of Dermatology and Venereology*. 2007;21(8):1019-26. <https://doi.org/10.1111/j.1468-3083.2007.02393.x>.
- [36] Shabanlouei R, Ahmadi F, Vaez-Gharamaleki J, Haji-Zadeh E, Javad-Zadeh Y. Effect of chamomile mouthwash in the prevention of chemotherapy-induced stomatitis. *Archives of Rehabilitation*. 2006;7(2):70-5.
- [37] Beyari M, Dar-Odeh N. Natural remedies for the dry mouth associated with non-functioning salivary glands. *Journal of Herbal Medicine*. 2015;5(2):113-7. <https://doi.org/10.1016/j.hermed.2015.04.005>.
- [38] Ferreira M, Teixeira M, Silva E, Selores M. Allergic contact dermatitis to Aloe vera. *Contact dermatitis*. 2007;57(4):278-9. <https://doi.org/10.1111/j.1600-0536.2007.01118.x>.
- [39] Surjushe A, Vasani R, Saple DG. Aloe vera: a short review. *Indian journal of dermatology*. 2008;53(4):163. doi: 10.4103/0019-5154.44785.
- [40] Bottenberg MM, Wall GC, Harvey RL, Habib S. Oral aloe vera-induced hepatitis. *Annals of Pharmacotherapy*. 2007;41(10):1740-3. <https://doi.org/10.1345/aph.1K132>.

How to Cite this Article: Shakilur Rahman AFM, Jannat T, Haider IA. Effectiveness of Aloe vera in the Management of Oral Mucosal Diseases: A Systematic Review. *International Journal of Scientific Research in Dental and Medical Sciences*, 2021;3(1):35-45. [10.30485/ijdsrdsms.2021.269101.1105](https://doi.org/10.30485/ijdsrdsms.2021.269101.1105).