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# USE OF ALOE VERA IN THE TREATMENT OF ORAL LICHEN PLANUS-A SYSTEMATIC REVIEW

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## ABSTRACT

Oral lichen planus is a common, chronic mucosal disease associated with a cell-mediated immunological dysfunction. Symptomatic OLP is painful and complete healing is rare. Aloe vera has anti-inflammatory properties, its use as an herbal remedy in oral lichen planus is increasing. This systematic review aims in evaluating the use of Aloe Vera in the treatment of oral lichen planus. To determine the use of aloe vera in the treatment of oral lichen planus. The following electronic databases were searched namely PubMed(Mesh), Wiley online library, Cochrane Library using key words aloe vera and oral lichen planus. The total number of articles obtained are 27 (Wiley online library -5, Pub Med -17, Cochrane Library- 1, Hand search – 4) with preset inclusion and exclusion criteria to select the appropriate clinical trial. The search strategy included 5 potentially relevant articles for literature review. These randomized controlled trials reported that aloe vera is a well-tolerated, safe, effective alternative to corticosteroids with less side-effect in treating oral lichen planus. However there is weak evidence to support aloe vera in reducing pain and improving clinical signs of OLP compared to placebo. Even though the results in some of the studies were positive and promising, there was insufficient evidence to support the superior effectiveness of aloe vera in treating oral lichen planus.

**KEYWORDS:** **Aloe vera, Oral lichen planus (OLP), Gel**

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## INTRODUCTION

Oral lichen planus (OLP) is a chronic inflammatory condition that is probably of multifactorial origin, often idiopathic with an immunopathogenesis involving T-cells [1,2] OLP can be clinically classified into three types of lesions: white reticular, atrophic or erosive and ulcerative. The most common site of involvement is the posterior buccal mucosa, followed by the anterior two third of tongue, labial mucosa, attached and vermilion of the lower lip. [3, 4] an array of treatments have been proposed for OLP: topical or systemic corticosteroids, cyclosporine, retinoid, azathioprine, tacrolimus, pimecrolimus, photo chemotherapy and surgery.[6, 7] various treatment modalities have resulted in partial deterioration of symptoms but not a complete cure. Topical corticosteroids are the mainstay of OLP treatment. Shortly after discontinuation of the therapy, there is recurrence of lesions, and the patient should use medicines for a long time.[8] The main problem of these treatments is represented by the side effects. Candidiasis was commonly found and in addition bad taste, dry mouth,sore throat and swollen mouth may occur as minor side effects from some topical steroids.[9,10] The Egyptians called Aloe Vera plant as “the plant of immortality”.[11] Some aesthetic and medicinal products are made from the mucilaginous tissue in the center of the AV leaf, which they called as the AV gel. The AV gel contains anthraquinones, which are accountable for the strong laxative effects of aloes.[12, 13, 14] the pharmacological actions of Aloe Vera include anti inflammatory, antibacterial, hypoglycemic effects and antifungal properties. [15] Aloe Vera has been used for skin conditions including radio dermatitis, genital herpes infection and psoriasis, with good results[16] .This systematic review aims in evaluating the use of Aloe vera in the treatment of oral lichen planus.

## MATERIALS AND METHODS

### *SEARCH STRATEGY*

The following electronic databases were searched namely Pub Med (Mesh), Wiley online library, Cochrane Library using key words aloe vera and oral lichen planus. The total number of articles obtained are 27 (Wiley online library -5, Pub Med -17, Cochrane Library- 1, Hand search – 4).[Figure 1]The current review article aims in evaluating the use of Aloe vera only in lichen planus hence the following inclusion and exclusion criteria was devised to select the appropriate clinical trial.The articles were screened on the basis of title and abstract. Full text was then procured for the relevant articles which fulfilled the inclusion criteria. Only articles published in the English language were considered for this review.

### *ELIGIBILITY CRITERIA* [TABLE 1]

***Inclusion criteria***: Randomized blinded study on human clinical trials where Aloe Vera is used in Treatment of oral lichen planus alone.

***Exclusion criteria****:* In-vitro studies, Animal studies, Non-randomized and experimental studies, case reports, case series, literature reviews. All irrelevant studies were excluded and the reasons for their exclusion were noted.

### *OUTCOME MEASURES*

Pain reduction and Clinical improvement of OLP after 4-8weeks of treatment was measured as the primary outcome of the study. Secondary outcomes comprised of complete resolution of OLP after 4-8weeks of therapy

### *METHODOLOGICAL QUALITY ASSESSMENT*

The following criteria were used to assess the methodological quality of the RCTs: randomization, explanation of sequence generation for randomization, explanation of allocation concealment, blindness methods, sample size calculation, evaluating for comparability of baseline data, intention to treat analysis, and patient follow-up after the final treatment. Risk of bias- These were categorized according to the following- Low risk of bias (bias less likely to seriously alter the results) if all criteria were met. Moderate risk of bias (bias that raises some ambiguity about the results) if one or more criteria were partly met. High risk of bias (bias that seriously weakens acceptance of the results) if one or more criteria were not met [TABLE 4, 5]

## RESULTS

This systematic review includes 5 trials in which Aloe Vera is used in the treatment of oral lichen planus. The total number of patients included in all the five studies was 224. The major outcomes measured in these studies were pain reduction, clinical improvement, potential and effective adverse effects. Visual analogue scale was used for evaluating pain and burning sensation and thongprasom index for clinical improvement and healing. [24, 25, 26] in most of the trials. The results of these trials are tabulated as follows in Table 2. Soudany et al in his trial has evaluated the treatment response based on the criteria of Carrozzo and Gandolfo[18]. Complete remission (few or no symptoms), Partial remission (the symptoms have decreased with erythematous areas) and No response (the symptoms persist). Fifteen patients (75%) had complete remission at treated side and two patients (10%) had partial remission while one patient showed no response to treatment (5%). Only one patient dropped out of the study. While placebo sides showed partial remission reproduced in two cases only (10%) and no response in others sides. There was a rapid subjective and objective improvement with topical AHM treatment. C. Choonhakarn et al in his trial had shown that Twenty-two of 27 patients treated with AV (81%) had a good response after 8 weeks of treatment, while one of 27 placebo-treated patients (4%) had a similar response. Furthermore, two patients treated with AV (7%) had a complete clinical remission. Burning pain completely disappeared in nine patients treated with AV (33%) and in one treated with placebo (4%). Symptomatology improved by at least 50% (good response) in 17 patients treated with AV (63%) and in two treated with placebo

(7%). No serious side-effects were found in both groups. Mansourian et al, had shown that Aloe Vera and Triamcinolone Acetonide significantly reduced visual analogue scale score, Thongprasom score and the size of the lesions after treatment and after 2 months of discontinuation of the treatment. In the AV group, 74% of patients and in the TA group 78% of patients showed some degrees of healing in the last follow-up. Reddy et al, had shown that clinical signs and symptoms were observed after 8 weeks of therapy, it was determined that aloe vera gel was more effective than triamcinolone acetonide in the treatment of oral lichen planus. Salazar-Sánchez et al in his randomized double blinded study had shown that, there are no statistically significant differences recorded between both groups in relation to pain after 6 and 12 weeks. In the AV group, complete pain remission was achieved in 31.2% of the cases after 6 weeks, and in 61% after 12 weeks. In the placebo group, these percentages were 17.2% and 41.6%, respectively. There were no adverse effects in any of the groups. Table 3 summarizes the level of evidence for the included treatment modalities. According to all the trials reported, Aloe Vera was a well-tolerated, Safe and effective alternative therapy for oral lichen planus. However there is weak evidence to support aloe vera in reducing the pain and improving clinical signs of OLP compared to placebo. The studies available in literature are short-term studies, hence Long-term studies are required with larger sample size to emphasize the use of aloe vera in treatment of oral lichen planus.

**Figure 1**
***Flowchart Showing Search Strategy***

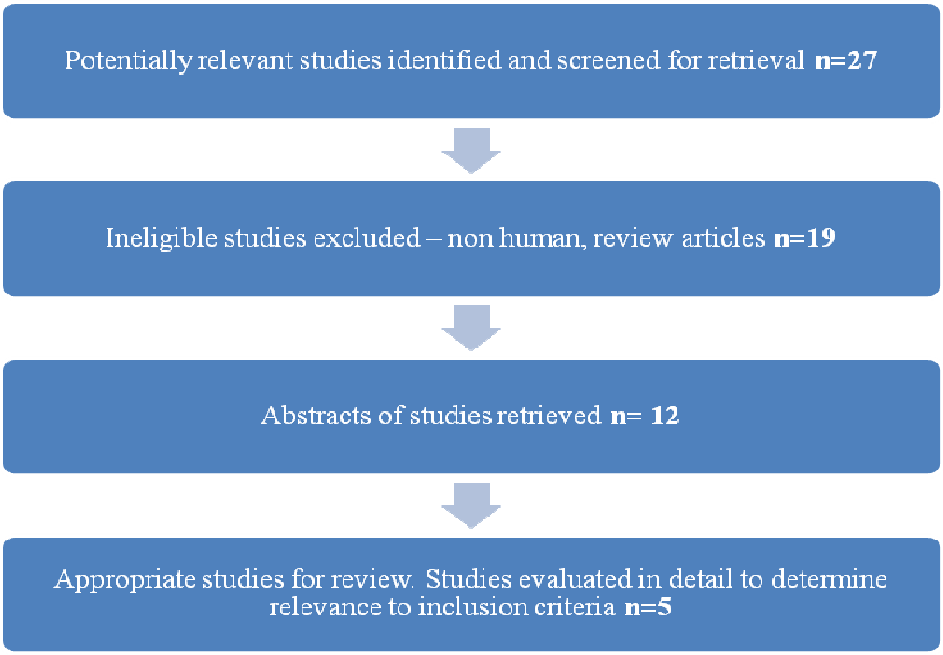


**Table 1**
***Articles selected for the systematic review***

| S.NO | ARTICLE | AUTHOR/ YEAR OF PUBLICATION | JOURNAL |
|---|---|---|---|
| 1 | Randomized trial of aloe vera gel vs triamcinolone acetonide ointment in the treatment of oral lichen planus | Reddy RL et al-2012[23] | QUINTESSENCE INTERNATIONAL 2012 |
| 2 | The efficacy of aloe vera gel in the treatment of oral lichen planus: a randomized controlled trial | C. Choonhakarn et al-2007[24] | British Journal of Dermatology 2008 |
| 3 | Efficacy of topical Aloe vera in patients with oral lichen planus: a randomized double-blind study | N. Salazar-Sánchez et al-2010[25] | Journal of oral pathology and medicine 2010 |
| 4 | Comparison of Aloe Vera Mouthwash With TriamcinoloneAcetonide 0.1% on Oral Lichen Planus: A Randomized Double-Blinded Clinical Trial | Mansourian et al-2011[26] | The American Journal of the Medical Sciences 2011 |
| 5 | A Self-controlled Single Blinded Clinical Trial to Evaluate Oral Lichen Planus after Topical Treatment with Aloe Vera | K El-Soudany et al-2013[22] | Journal of Gastroenterology and Hepatology Research 2013 |

**Table 2**
***Characteristics of the included studies***

| YEAR OF STUDY AND STUDY DESIGN | FORM OF ALOE VERA USED | DOSAGE AND DIRECTIONS | NUMBER OF PATIENTS | ORAL DISEASE | RESULTS-CLINICAL IMPROVEMENT & PAIN SCORE | THERAPY DURATION | ADVERSE EFFECTS | OUTCOME MEASURES |
|---|---|---|---|---|---|---|---|---|
| 1.KEl-Soudany et al-2013<br>Self- controlled single blinded clinical trail [22] | *Aloe Vera* (AV) high molecular weight fractions ointment | Ointment was asked to be applied 3 times daily at affected site for 4-8 weeks, placebo gel to left | 20pts<br>15 Females+ 5males | Oral lichen planus | AV ointment<br>75%- complete remission<br>10%- partial remission<br>5%- no response<br>5%-dropped out.<br>Placebo<br>10%-Partial Remission<br>Decrease in Pain scores. | 8 weeks | No side effects | Decrease both in clinical signs and in pain scores.<br>AHM ointment showed well tolerated, safe and effective treatment to OLP |
| 2. Reddy RL et al-2012 randomized double blinded study trail [23] | Aloe Vera Gel vs. Triamcinolone acetonide Ointment | Gel and ointment was asked to be applied 3 times daily and pt. was recalled every 2,4,6,8 weeks | 40pts<br>23males+ 17femlaes | Oral lichen planus(erosive and ulcerative lesions)<br>Erosive n==18<br>Atrophic n=14 | **Gel-**<br>45%-complete remission<br>30%-partial remission<br>15%-less response<br>10%-very less response<br>0%-no response<br>**Ointment-**<br>15%-complete remission<br>30%-partial remission<br>40%-less response<br>5%-very less response<br>10%-no response | 8 weeks | No side effects | Aloe vera gel is a Safe alternative treatment for oral lichen planus |
| 3.Mansouri an et al-2011 randomized double blinded clinical trail [26] | Aloe vera Mouth wash vs. Triamcinolone Acetonide | Mouth wash or Triamcinolone Acetonide was asked to be applied 4 times daily for 6 months | 46pts were randomly divided into 2 groups | Oral lichen planus(erosive and ulcerative lesions0 | **Mouthwash-**<br>74%-some degree of healing in last follow up.<br>**Triamcinolone acetonide-**<br>78%- some degree of healing in last follow up. | 4 weeks Follow up 2 months<br>Evaluated on 8,16 day | No side effects | Aloe vera mouthwash is an effective substitute for TA in the treatment of OLP |
| 4.N. Salazar-Sánchez et al-2010 randomized double blinded clinical trail [25] | Gel vs. Placebo | 0.4ml of gel or placebo was asked to be applied 3 times daily and pt. was recalled every 0,6,12 weeks | 64pts | Oral lichen planus(erosive and ulcerative lesions) | **Gel-**<br>31.2%-pain remission after 6 weeks<br>61%- pain remission after 12 weeks.<br>**Placebo-**<br>17.2%-complete remission<br>41.6%-good remission<br>Improves the total quality of life score. | Evaluated at 6&12weeks | No side effects | The topical application of AV improves the total quality of life score in patients with OLP. |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| 5.C.Choonhakarn et al-2007 Randomized double blinded control trail [24] | Aloe Vera Gel vs. Placebo | Gel and placebo was asked to be applied twice daily and pt. was recalled every 2,4,6,8 weeks | 54pts 34 females+ 20males | Oral lichen planus(erosive and ulcerative lesions) | **Gel-** 7%-complete remission 81%-good response 7%-poor response 4%-no response **Placebo-** 0-complete remission 4%-good response Burning pain reduced In AV-33% In Placebo-4% Symptomatology- 50%Good response In 63%- AV In 7%- Placebo | 8 weeks | No side effects. | AV gel is statistically significantly more effective than placebo in inducing clinical and symptomatological improvement of OLP.AV gel can be considered a safe alternative treatment for patients with OLP |

**Table 3**
***Level of evidence***

| STUDY | TYPE OF STUDY | LEVEL OF EVIDENCE |
|---|---|---|
| K El-Soudany et al-2013[22] | Self-controlled single blinded clinical trail | LEVEL II |
| N. Salazar-Sánchez et al-2010[25] | Randomized double blinded clinical trail | LEVEL II |
| Reddy RL et al-2012[23] | Randomized double blinded control trail | LEVEL II |
| C. Choonhakarn et al-2007[24] | Randomized double blinded control trail | LEVEL II |
| Mansourian et al-2011[26] | Randomized double blinded control trail | LEVEL II |

**Table 4**
***Risk of bias- major criteria***

| STUDY | SAMPLE JUSTIFIED | BASELINE COMPARISON | I/E CRITERIA | METHOD ERROR |
|---|---|---|---|---|
| Reddy RL et al-2012[23] | Yes | Yes | No | No |
| C. Choonhakarn et al-2007[24] | Yes | Yes | Yes | No |
| N. Salazar-Sánchez et al-2010[25] | Yes | Yes | Yes | No |
| Mansourian et al-2011[26] | Yes | Yes | Yes | No |
| *K El-Soudany* et al-2013[22] | Yes | Yes | Yes | No |

**Table 5**
***Risk of bias- minor criteria***

| STUDY | RANDOMISATION | ALLOCATION CONCEALMENT | ASSESSOR BLINDED | DROPOUTS | WITHDRAWLS |
|---|---|---|---|---|---|
| Reddy RL et al-2012[23] | Yes | No | Yes | No | Low |
| C. Choonhakarn et al-2007[24] | Yes | Yes | Yes | No | Low |
| N. Salazar-Sánchez et al-2010[25] | Yes | Yes | Yes | Yes | Moderate |
| Mansourian et al-2011[26] | Yes | Yes | Yes | No | Low |
| *K El-Soudany* et al-2013[22] | No | Yes | Yes | Yes | Low |

## DISCUSSION

The main aim of the current therapies for OLP is to reduce pain and eliminate the lesions. Although it is believed that there is no definitive cure for OLP, the basic treatment in mild to moderate cases is corticosteroid therapy. Treatment is primarily aimed at reducing the severity and duration of lesions because there is no convinced cure for the disease, the therapy that has its use at the least side effects is most favorable. Up-regulation of intercellular adhesion molecules and cytokines, IL-2, IL-4 and IL-10,secreted by activated lymphocytes and keratinocytes, and tumor necrosis factor (TNF-α) can play a role in the pathogenesis of OLP[17,18] Recent data suggest that AV also has anti-inflammatory effects by inhibiting the cyclooxygenase pathway and reduces prostaglandin E2 production from arachidonic acid.[19,20] Thus, if proven the use of aloe vera as a medicinal treatment in the use of oral lichen planus it would benefit majority of the population in India who believes in natural type of treatment modalities. In the trail conducted by Choonhakarn[24] the effect of 70% AV gel on OLP was considerably better than that of placebo. The outcomes showed decreases both in clinical signs and in pain scores. Mild adverse effects were reversible and AV was generally well tolerated. Hayes[27] was the first to do a research on aloe vera where he described a 52-year-old woman who developed LP in the oral cavity and on her hands. The treatment commenced with drinking 2 oz. of stabilized AV juice daily and applying 75% AV cream on the lip and hands. After 4 weeks, the OLP had disappeared and the hand lesions showed slight improvement. In the study conducted by Salazar-Sanchez et al[20] AV solution consisting of 70% aloe juice among the 32 cases in the AV group, complete pain remission was achieved in 31.2% of the cases after 6 weeks and in 61% after 12 weeks, suggesting that the topical application of AV improves the total quality of life score in patients with OLP. Studies conducted by K El-Soudany et al[22] also stated that there was a decrease both in clinical signs and in pain scores while using *Aloe vera* (AV) high molecular weight fractional ointments.AHM ointment was shown to penetrate tissue, relief pain, reduce inflammation and increase blood supply to the damaged area. The basic treatment in mild to moderate cases is corticosteroid therapy. Treatment is primarily aimed at reducing the severity and duration of lesions. Mansourian et al[26] used Triamcinolone acetonide in comparison with aloe vera mouth wash to treat patients with OLP, the study revealed that Aloe vera mouthwash is an effective substitute for Triamcinolone acetonide in the treatment of OLP. These data collected further enhances the need to focus on more researches towards the properties and uses of aloe vera gel as a treatment option in cure for OLP and also further studies are needed to compare the efficacy of different orotransmucosal drug delivery methods concerning AV, depends strongly on its bio adhesive properties, bioavailability, and solubility[21] .There is no doubt that aloe Vera has multiple and few unique properties with least side-effects, well-tolerated, safe, effective alternative to corticosteroids and are more economical. However there is weak evidence to support aloe vera in reducing pain and improving clinical signs of OLP compared to placebo.

## CONCLUSION

This systematic review has proven the demand for future clinical trials to assess the use of aloe vera in treating oral lichen planus, Hence it can be concluded that from analyzing the above 5 articles that aloe Vera in various forms can be beneficial to the patients who are suffering with OLP without any side effects, furthermore positive studies with a larger sample size should be emphasized and conducted so that the properties of the plant is well understood and better made use of. Even though the results in some of the studies were positive and promising, there was not sufficient evidence to support the superior effectiveness of using aloe vera in treating oral lichen planus.

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