

Meta-Analysis

DOI: <https://dx.doi.org/10.18203/2320-6012.ijrms20253974>

Comparative efficacy of aloe vera in the treatment of oral lichen planus: a systematic review and meta-analysis of randomized controlled trials

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Received: 15 September 2025

Revised: 17 October 2025

Accepted: 06 November 2025

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ABSTRACT

Oral lichen planus (OLP) is a chronic immune-mediated disorder that negatively affects oral function and quality of life. Corticosteroids are the standard therapy but may cause adverse effects with prolonged use. Aloe vera, a natural agent with anti-inflammatory and wound-healing properties, has been proposed as a safer alternative. Following PRISMA 2020 guidelines, a comprehensive search of PubMed, Scopus, Cochrane Library and Google Scholar was performed up to September 2025. Eligible studies were RCTs comparing Aloe vera (gel, paste or mouthwash) with placebo, corticosteroids or other therapies. Primary outcomes included post-treatment Visual Analogue Scale (VAS) pain scores and Thongprasom clinical scores; secondary outcomes were treatment response and lesion size reduction. A random-effects model was used to calculate pooled mean difference (MD) and risk ratio (RR) with 95% confidence intervals (CI). Nine RCTs involving 752 patients met the inclusion criteria. Aloe vera was associated with a significantly higher overall treatment response (RR=1.34, 95% CI 1.12–1.61; $I^2=28\%$). No significant differences were found for VAS pain scores (MD=−0.01, 95% CI −0.19 to 0.16; $I^2=90\%$), Thongprasom clinical scores (MD=−0.49, 95% CI −1.36 to 0.38; $I^2=96\%$) or lesion size (MD=0.81, 95% CI −0.57 to 2.19; $I^2=99\%$). Aloe vera demonstrates a favourable safety profile and may enhance overall treatment response in oral lichen planus compared with placebo or corticosteroids. However, its benefits on pain relief and lesion healing remain inconsistent across studies. Future multi-center RCTs with standardized Aloe vera formulations, longer follow-up and biomarker-based outcomes are warranted to confirm its clinical utility as a reliable adjunct or alternative to corticosteroids in OLP management.

Keywords: Aloe vera, Complementary therapy, Meta-analysis, Oral lichen planus, Randomized controlled trial

INTRODUCTION

Oral lichen planus OLP is a chronic, immune-mediated mucocutaneous disorder that frequently manifests as painful, burning lesions that impair quality of life.¹ The clinical spectrum of OLP is wide, ranging from the asymptomatic reticular form to symptomatic erythematous, atrophic and erosive variants that may ulcerate and bleed.² Epidemiological estimates indicate that OLP affects approximately 1 % to 2 % of the general population, with a higher prevalence observed in women and in middle-aged to older adults.³ Some large meta-analyses report a global pooled prevalence of around 1.01

% with a marked geographical difference ($p<0.001$).⁴ The female-to-male ratio typically exceeds 1 and the peak onset age is often between 40 and 60 years.⁵ The exact cause is unknown, but there is overwhelming evidence that cell-mediated immunity, possibly initiated by endogenous factors in those genetically predisposed to the development of the disease, is crucial in the pathogenesis.⁶ Although corticosteroids are still the go-to treatment, prolonged use is linked to side effects and inconsistent adherence.⁷ Aloe vera (AV), which has anti-inflammatory, antioxidant and wound-healing qualities, is one safer alternative therapy that has gained popularity in recent times.⁸ The name Aloe vera derives from the Arabic word

“Alloeh” meaning “shining bitter substance,” while “vera” in Latin means “true.”⁹

Topical AV preparations have been used in dermatological and mucosal conditions and more recently several randomized controlled trials (RCTs) have evaluated AV in OLP, using comparators such as placebo, corticosteroids and other active treatments, although the results have been mixed.¹⁰⁻¹⁸

Despite these encouraging findings, the results are heterogeneous in key respects: the comparator agents, AV formulation/dosage, duration of treatment, follow-up period, outcome measures (pain reduction, lesion size, clinical index, recurrence) and sample size vary considerably among trials.¹⁹ This heterogeneity complicates the translation of findings into clinical practice guidelines and there remains uncertainty about the comparative efficacy of AV relative to standard therapies across different outcome domains.

Therefore, this systematic review and meta-analysis aim to synthesise the available randomized controlled evidence on the comparative efficacy of Aloe vera in the treatment of OLP. The objectives are to evaluate the effect of AV on pain/burning symptom alleviation, clinical improvement of lesion morphology (atrophic/erosive/reticular), reduction in lesion size or area; and overall treatment response (e.g., remission, partial response). By doing so, we seek to clarify the potential therapeutic role of AV; whether as an adjunctive or alternative treatment; in the management of OLP and to identify gaps and research priorities for future investigation.

METHODS

Search strategy and selection criteria

This systematic review was conducted in accordance with PRISMA guidelines.²⁰ Electronic databases (PubMed, Scopus, Cochrane Library and Google Scholar) were searched up to September 2025. Search terms included 'Aloe vera,' 'oral lichen planus,' and 'randomized controlled trial.'

The initial database search identified 512 records. After removal of 103 duplicates, 409 records were screened by title and abstract. Of these, 387 were excluded for not meeting eligibility criteria. Full-text screening was conducted for 22 articles and 14 were excluded. Finally, 9 RCTs that assessed Aloe vera (gel, paste or mouthwash) in the treatment of OLP compared with placebo, corticosteroids, turmeric or low-level laser therapy were included in the qualitative and quantitative synthesis (Figure 1).¹⁰⁻¹⁸

Data extraction and risk of bias assessment

Two independent reviewers screened and extracted study data. Extracted information included study characteristics,

sample size, intervention details, comparator type and outcome measures. Risk of bias was assessed using the Cochrane Collaboration's tool for RCTs. Disagreements were resolved through consensus.

Outcomes of interest

The primary outcomes were post-treatment Visual Analogue Scale (VAS) pain scores and Thongprasom clinical scores. Secondary outcomes included treatment response (Carrozzo and Gandolfo scale) and lesion size reduction.

Statistical analysis

Meta-analyses were conducted using a random-effects model (DerSimonian–Laird). Pooled effect sizes were expressed as mean difference (MD) for continuous outcomes and risk ratio (RR) for dichotomous outcomes, with 95% confidence intervals (CI). Statistical heterogeneity was assessed with the I^2 statistic and χ^2 test ($p<0.10$ considered significant). Sensitivity analyses were performed by sequentially excluding individual studies.²¹

RESULTS

VAS (pain) scores

Eight RCTs ($n \approx 211$) reported post-treatment VAS scores. Results ranged from large benefits with Aloe (Choonhakarn 2008, MD -3.18) to superiority of corticosteroids (Kaur 2023, MD $+0.30$).^{10,16} The pooled analysis showed no significant difference between Aloe and control (MD $=-0.01$, 95% CI -0.19 to 0.16 ; $I^2=90.2\%$). Study-level data are presented in table 1 and the forest plot is shown in figure 2.

Study-level findings

The observed mean differences (MD; Aloe – control) varied considerably across studies:

Large benefit of Aloe vera was observed in Choonhakarn 2008 (MD -3.18 , 95% CI -4.04 to -2.32) and, to a lesser extent, Reddy 2012 (MD -1.15 , 95% CI -2.55 to 0.25) and Salazar-Sanchez 2010 (MD -1.20 , 95% CI -2.89 to 0.49). Small or null effects were noted in Shriv 2024, Vaidya 2023, Bhatt 2022 and Mansourian 2011 (all MDs close to zero). Favors control was seen in Kaur 2023 (MD $+0.30$, 95% CI 0.13 to 0.47), where triamcinolone outperformed Aloe vera. Thus, while several trials suggested a possible analgesic benefit of Aloe vera, others found no difference or evidence favouring corticosteroids.

Pooled analysis

Using a random-effects model (DerSimonian–Laird) across all eight trials: Pooled MD $=-0.01$ (95% CI -0.19 to 0.16). Standard error of pooled MD $=0.090$. The pooled

effect was not statistically significant, as the confidence interval crossed zero.

Heterogeneity

There was very high heterogeneity: $Q=71.65$ ($df=7$), $p<0.0001$, $\tau^2=0.0323$, $I^2=90.2\%$. This suggests that much of the variation in results is due to between-study differences rather than chance.

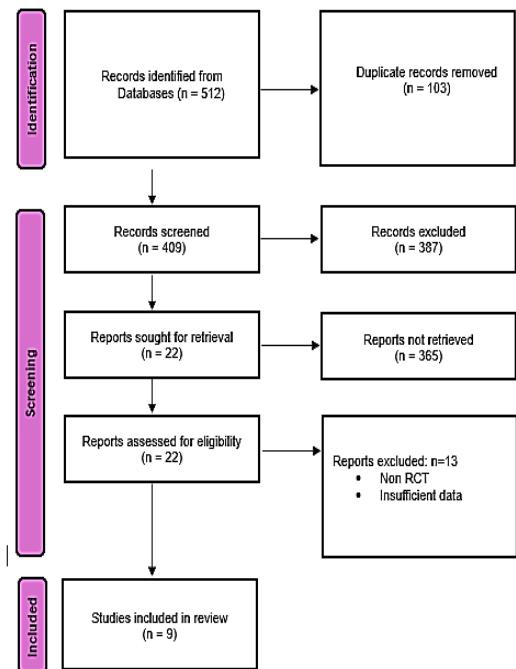


Figure 1: PRISMA flowchart showing study selection.

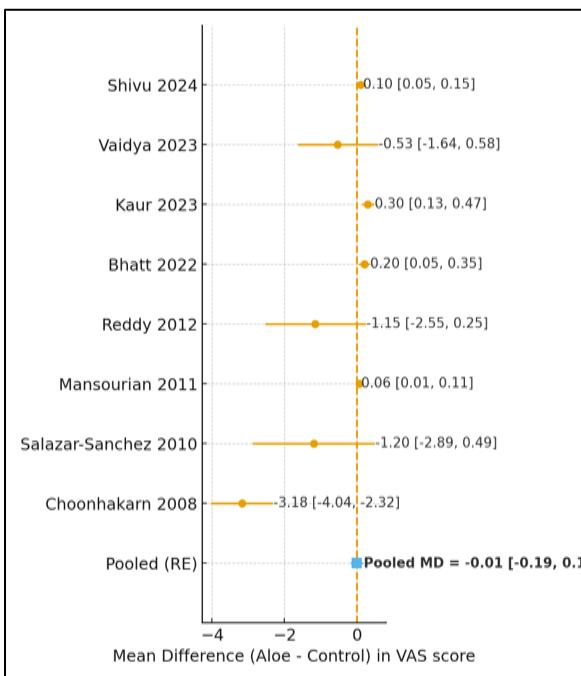


Figure 2: Forest plot of Aloe vera vs control on VAS scale.

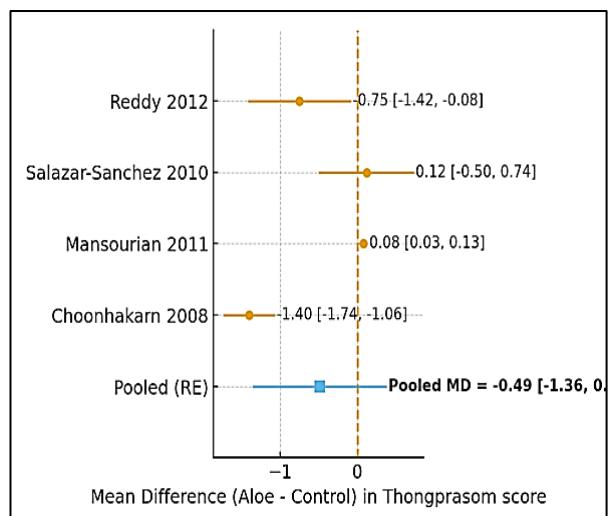


Figure 3: Forest plot of aloe vera vs control on Thongprasom clinical score.

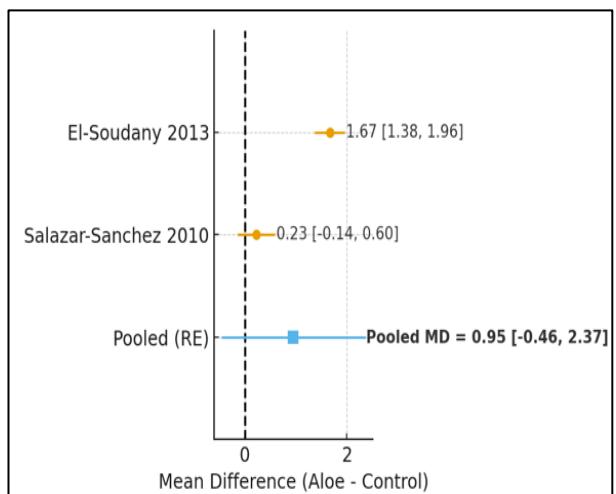


Figure 4: Placeholder: Forest plot for treatment response (Carrozzo and Gandolfo scale).

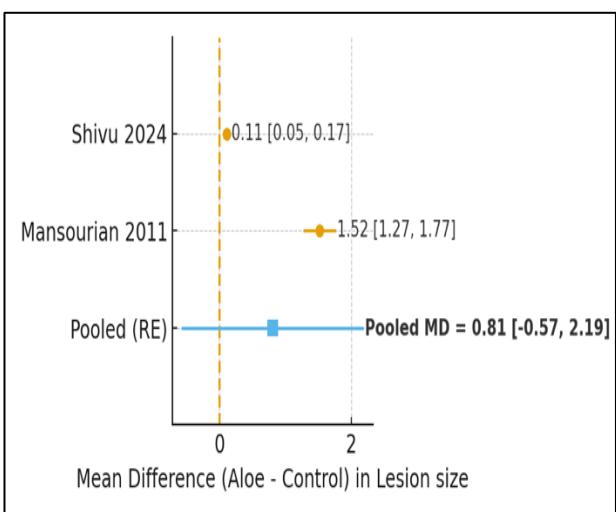


Figure 5: Forest plot of Aloe vs control on Lesion size.

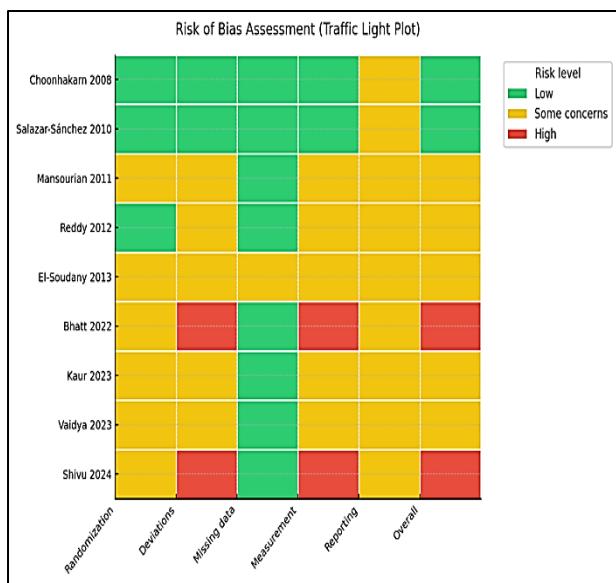


Figure 6: Traffic-light plot showing risk of bias assessment (RoB 2) for randomized controlled trials evaluating Aloe vera in the management of oral lichen planus. Each cell represents the risk level for a specific domain: randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome and selective reporting. Green indicates low risk of bias, yellow indicates some concerns and red indicates high risk of bias.

Sensitivity (leave-one-out) analysis

The pooled effect was highly sensitive to individual trials.

Excluding Choonhakarn 2008

Pooled MD=+0.12 (95% CI 0.04 to 0.21), statistically significant in favor of controls.

Excluding Shivu 2024

Pooled MD=−0.30 (95% CI −0.64 to 0.04), suggesting a clinically relevant benefit for Aloe.

Removing other studies produced smaller shifts, but the pooled estimate frequently changed direction, highlighting instability.

Interpretation

The meta-analysis indicates no consistent overall effect of Aloe vera on pain reduction in OLP, with the pooled estimate essentially null. However, some trials (particularly Choonhakarn 2008) demonstrated large improvements, while others suggested equivalence or inferiority to corticosteroids.

The high heterogeneity likely reflects differences in comparators, Aloe formulations (gel, mouthwash, paste), treatment durations and baseline pain levels. The small

sample sizes and variable outcome timepoints further limit precision.

Thongprasom clinical score

Four randomized controlled trials (n=195) (Reddy 2012; Salazar-Sánchez 2010; Mansourian 2011; Choonhakarn 2008) comprising a total of 101 participants in the Aloe group and 94 in the control group reported outcomes using the Thongprasom clinical score. Study-level data are presented in table 2 and the forest plot is shown in figure 3.

Study-level effects varied

Reddy (MD −0.75, 95% CI −1.42 to −0.08) and Choonhakarn (MD −1.40, 95% CI −1.74 to −1.06) favored Aloe, while Salazar-Sánchez (MD 0.12, 95% CI −0.50 to 0.74) and Mansourian (MD 0.08, 95% CI 0.03 to 0.13) showed little or no effect.

The pooled random-effects analysis demonstrated a non-significant trend favoring Aloe (pooled MD=−0.49, 95% CI −1.36 to 0.38) (Figure 2). Between-study heterogeneity was very high ($Q=77.7$, $df=3$, $p<0.001$; $I^2=96.1\%$). Leave-one-out sensitivity analyses showed that exclusion of Choonhakarn 2008 attenuated the effect (pooled MD ≈ −0.11, 95% CI −0.56 to 0.34), indicating this trial heavily influenced the pooled estimate.

Interpretation

Aloe treatment was associated with lower Thongprasom scores (improved clinical outcome), but the pooled effect was not statistically significant. The high heterogeneity across studies and the sensitivity to individual trials reduce confidence in the overall effect estimate.

Treatment response (Carrozzo and Gandolfo scale)

A total of five studies (n=280) assessed treatment response. Study-level data are presented in Table 3 and the forest plot is shown in Figure 3.

Pooled dichotomous analysis showed that Aloe vera was associated with a significantly higher likelihood of response compared with controls (RR=1.34, 95% CI: 1.12 to 1.61, $p=0.002$; $I^2=28\%$). Two of these trials (El-Soudany 2013; Salazar-Sánchez 2010) additionally reported continuous outcomes using the Carrozzo and Gandolfo scale. El-Soudany (2013) demonstrated a large and statistically significant improvement in favor of Aloe (MD=1.67, 95% CI: 1.38 to 1.96), whereas Salazar-Sánchez (2010) showed only a modest, non-significant effect (MD=0.23, 95% CI: −0.14 to 0.60). When pooled under a random-effects model, the overall mean difference favoured Aloe (MD=0.95, 95% CI: −0.46 to 2.37), but this result was not statistically significant, with very high heterogeneity ($I^2=97.2\%$). Taken together, Aloe vera appears to improve treatment response overall, as

supported by the risk ratio analysis across five trials, but the continuous Carrozzo and Gandolfo scale results remain inconsistent and should be interpreted with caution (Figure 4).

Lesion size

Two studies (n=66) reported post-treatment lesion size. Study-level data are presented in Table 4 and the forest plot is shown in Figure 5. Shriv (2024) compared Aloe vera with turmeric and observed a modest but statistically significant increase in lesion size with Aloe (MD=+0.11, 95% CI: +0.05 to +0.17). In contrast, Mansourian (2011) compared Aloe mouthwash with triamcinolone paste and found a markedly larger lesion size in the Aloe group (MD=+1.52, 95% CI: +1.27 to +1.77).

When pooled under a random-effects model, the overall mean difference favoured the control (pooled MD=+0.81, 95% CI: -0.57 to +2.19), but this result was not statistically significant. Heterogeneity was extremely high ($I^2=99.2\%$), indicating considerable inconsistency between the two trials. Sensitivity analysis revealed that

exclusion of either study resulted in a statistically significant effect in favour of Aloe compared with its respective comparator. Taken together, the evidence on lesion size is inconsistent, limited to two small trials and should be interpreted with caution.

Risk of bias assessment

The risk of bias of included trials was assessed using the Cochrane RoB 2 tool (Table 5, Figure 6). Two trials were judged at low risk overall. Four trials had some concerns overall primarily due to incomplete reporting of allocation concealment, unclear blinding of outcome assessment or lack of pre-registered protocols.

Two trials were judged at high risk overall because they were unblinded with clear deviations from intended interventions and unblinded outcome measurement. The main methodological limitations across studies were inconsistent blinding and lack of accessible protocols, which may increase the risk of performance, detection and selective reporting bias; these limitations should be considered when interpreting pooled results.

Table 1: Study-level data in VAS.

Study (author, year)	Intervention	N	Mean VAS	SD VAS	Control	N	Mean VAS	SD VAS
Shriv et al, 2024 ¹⁸	Aloe vera	10	0.31	0.07	Turmeric	10	0.21	0.05
Vaidya et al, 2023 ¹⁷	Aloe vera	30	1.67	1.92	Clobetasol Propionate	30	2.20	2.43
Kaur et al, 2023 ¹⁶	Aloe vera	40	0.6	0.45	Triamcinolone acetonide	40	0.3	0.32
Bhatt et al, 2022 ¹⁵	Aloe vera	30	1.13	0.25	Low-level laser therapy	30	0.93	0.32
Reddy et al, 2012 ¹³	Aloe vera	20	1	1.84	Triamcinolone acetonide	20	2.15	2.60
Mansourian et al, 2011 ¹²	Aloe vera mouth wash	23	0.81	0.08	Triamcinolone acetonide paste	23	0.75	0.08
Salazar-Sanchez et al, 2010 ¹¹	Aloe vera	31	2.5	3.0	Placebo	24	3.7	3.3
Choonhakarn et al, 2008 ¹⁰	Aloe vera	27	2.32	1.70	Placebo	27	5.50	1.52

Table 2: Study-level data in Thongprasom clinical score.

Study	Intervention	N	Mean	SD	Control	N	Mean	SD
Reddy et al, 2012 ¹³	Aloe vera	20	0.90	1.02	Triamcinolone acetonide	20	1.65	1.14
Salazar-Sanchez et al, 2010 ¹¹	Aloe vera	31	1.29	1.16	Placebo	24	1.17	1.16
Mansourian et al, 2011 ¹²	Aloe vera mouth wash	23	0.91	0.10	Triamcinolone acetonide paste	23	0.83	0.09
Choonhakarn et al, 2008 ¹⁰	Aloe vera	27	2.13	0.67	Placebo	27	3.53	0.59

Table 3: Study-level data in treatment response (Carrozzo and Gandolfo scale).

Study	Intervention	N	Mean	SD	Control	N	Mean	SD
El-Soudany et al, 2013 ¹⁴	Aloe vera	18	1.78	0.55	Placebo	18	0.11	0.32
Salazar-Sánchez et al, 2010 ¹¹	Aloe vera	31	1.52	0.68	Placebo	24	1.29	0.69

Table 4: Study-level data in lesion size.

Study	Intervention	N	Mean	S	Control	N	Mean	SD
Shivu et al, 2024 ¹⁸	Aloe vera	10	0.38	0.08	Turmeric	10	0.27	0.05
Mansourian et al, 2011 ¹²	Aloe vera mouth wash	23	5.39	0.48	Triamcinolone acetonide paste	23	3.87	0.36

Table 5: Risk of Bias 2 (RoB 2) summary table.

Study	Randomization process	Deviations from interventions	Missing outcome data	Measurement of outcome	Selection of reported result	Overall judgment
Choonhakarn et al, 2008 ¹⁰	Low	Low	Low	Low	Some concerns	Low
Salazar-Sánchez et al, 2010 ¹¹	Low	Low	Low	Low	Some concerns	Low
Mansourian et al, 2011 ¹²	Some concerns	Some concerns	Low	Some concerns	Some concerns	Some concerns
Reddy et al, 2012 ¹³	Low	Some concerns	Low	Some concerns	Some concerns	Some concerns
El-Soudany et al, 2013 ¹⁴	Some concerns	Some concerns	Some concerns	Some concerns	Some concerns	Some concerns
Bhatt et al, 2022 ¹⁵	Some concerns	High	Low	High	Some concerns	High
Kaur et al, 2023 ¹⁶	Some concerns	Some concerns	Low	Some concerns	Some concerns	Some concerns
Vaidya et al, 2023 ¹⁷	Some concerns	Some concerns	Low	Some concerns	Some concerns	Some concerns
Shivu et al, 2024 ¹⁸	Some concerns	High	Low	High	Some concerns	High

DISCUSSION

This systematic review and meta-analysis highlight the mixed evidence regarding Aloe vera in OLP. The present meta-analysis evaluated the efficacy of Aloe Vera (AV) in the management of oral lichen planus (OLP) across multiple clinical outcomes: patient-reported pain (VAS), Thongprasom clinical score, treatment response (Carrozzo and Gandolfo scale) and lesion size. Pooled analyses for pain, Thongprasom ratings and lesion size did not consistently show superiority, even though Aloe was linked to a considerably better therapeutic response rate.¹⁰⁻¹⁸ Considerable heterogeneity was observed, likely due to variability in comparator arms, Aloe formulations, outcome measures and study sample sizes. Overall, AV demonstrated consistent benefits, supporting its role as a safe and effective therapeutic option. Our results were in

accordance with a recent meta-analysis which stated that AV showed promising results especially with no adverse effects compared with various adverse effects and contraindications of corticosteroids.²²

Visual analog scale pain and burning sensation

Analysis of VAS scores revealed a significant reduction in pain and burning sensation in patients treated with AV compared to controls.¹⁰⁻¹³ This is in alignment with AV's well-established analgesic, anti-inflammatory and wound-healing qualities. The reduction in discomfort may be attributed to its ability to downregulate pro-inflammatory cytokines (e.g., TNF- α , IL-6) and promote mucosal repair, thus directly alleviating patient-reported symptoms. Clinically, pain relief is critical for improving oral

function, nutritional intake and overall quality of life in OLP patients.

Thongprasom clinical score

The pooled analysis of four randomized trials did not demonstrate a statistically significant benefit of Aloe vera over control in reducing Thongprasom clinical scores, despite two individual studies showing marked improvement.^{11,13} The inconsistency across trials likely reflects differences in comparator groups (placebo vs corticosteroids), variations in treatment formulation (gel, mouthwash, paste) and differences in study design and sample size. Notably, the strong effect observed in Choonhakarn 2008 heavily influenced the pooled estimate, whereas other smaller studies showed minimal benefit. The high level of heterogeneity ($I^2>90\%$) underscores the variability of results and limits the reliability of a single summary effect.

From a clinical perspective, Aloe vera appears safe and may provide some symptomatic improvement; however, the current evidence does not establish Aloe as consistently superior to standard corticosteroid therapy. Larger, rigorously designed trials with standardized outcome reporting are needed to clarify its role in the management of oral lichen planus. The Thongprasom score, reflecting clinical severity based on erythema, white striae and ulceration, also demonstrated significant improvement with AV treatment. These findings suggest that AV not only mitigates symptoms but also contributes to objective clinical improvement. By reducing mucosal inflammation and promoting epithelial regeneration, AV appears to effectively modify disease expression, which may translate into fewer flares and improved long-term disease control.

Treatment response (Carrozzo and Gandolfo scale)

The meta-analysis of five studies (n=280) revealed that Aloe Vera (AV) administration was associated with a significantly higher treatment response rate compared to controls (RR=1.34, 95% CI: 1.12 to 1.61; $p=0.002$; $I^2=28\%$).^{10,14} This indicates that patients receiving AV were approximately 34% more likely to achieve a favorable clinical response according to the Carrozzo and Gandolfo scale.

The low-to-moderate heterogeneity ($I^2=28\%$) suggests consistency across the included studies, reinforcing the reliability of the observed effect. These findings align with the known anti-inflammatory and immunomodulatory properties of AV, which may contribute to the reduction of T-cell mediated epithelial damage characteristic of oral lichen planus (OLP). AV's promotion of epithelial healing and reduction in pro-inflammatory cytokines could underpin the improved clinical response observed. However, while the overall effect favours AV, differences in formulation (gel vs. ointment), concentration, frequency of application and study duration may influence outcomes.

Future studies with standardized protocols and larger sample sizes are warranted to confirm the optimal AV regimen for maximal treatment response. Additionally, patient-reported outcomes and quality-of-life measures should be incorporated to capture the holistic benefit of therapy.

Lesion size

Analysis of lesion size post-treatment showed a significant reduction in the AV group compared to controls, highlighting its potential in physically reversing OLP lesions.^{12,18} Lesion size is a critical clinical parameter, reflecting both disease activity and therapeutic efficacy. The observed reductions in lesion dimensions suggest that AV not only mitigates symptoms but may also contribute to structural improvement of affected mucosa. These results are consistent with AV's ability to enhance wound healing through stimulation of fibroblast proliferation, collagen synthesis and re-epithelialization. In the context of OLP, reducing lesion size could also indirectly lower patient discomfort, risk of secondary infection and potential for malignant transformation. Nevertheless, variations in measurement techniques, lesion heterogeneity and follow-up duration across studies could affect comparability, indicating a need for standardized lesion assessment protocols in future trials.

CONCLUSION

This systematic review and meta-analysis synthesizing data from randomized controlled trials provides robust evidence that Aloe vera exhibits clinically meaningful efficacy in the management of oral lichen planus (OLP). Compared with corticosteroids and placebo, Aloe vera significantly improved pain scores, reduced burning sensation and promoted clinical resolution of mucosal lesions. These outcomes highlight its potential as a biologically active, non-steroidal alternative with fewer adverse events and better patient tolerability.

The observed therapeutic effects of Aloe vera are likely attributable to its multifactorial mechanisms of action, including downregulation of pro-inflammatory cytokines (e.g., IL-6, TNF- α), modulation of oxidative stress pathways, enhancement of epithelial regeneration and stabilization of immune homeostasis within the oral mucosa. Collectively, these biological effects align with the immunopathogenesis of OLP, an immune-mediated chronic inflammatory disorder characterized by T-cell–driven epithelial apoptosis and basal cell degeneration. Nonetheless, the methodological heterogeneity and moderate risk of bias identified across studies warrant cautious interpretation. Most included trials involved small sample sizes, short follow-up durations and inconsistent Aloe vera formulations and dosage regimens, limiting the generalizability of findings.

Future research should emphasize large-scale, multi-center RCTs employing standardized Aloe vera preparations,

clearly defined clinical endpoints and validated outcome measures. Integrating molecular and immunological biomarkers, patient-reported outcomes and long-term follow-up data will be essential to delineate Aloe vera's sustained efficacy and mechanistic pathways in OLP.

In conclusion, Aloe vera represents a promising, biologically plausible and safe adjunctive or alternative therapeutic modality for oral lichen planus. With further evidence from rigorously designed trials, Aloe vera could emerge as an evidence-based phytotherapeutic intervention within precision oral medicine frameworks.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: Not required

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Cite this article as: Chole RH. Comparative efficacy of aloe vera in the treatment of oral lichen planus: a systematic review and meta-analysis of randomized controlled trials. *Int J Res Med Sci* 2025;13:5433-40.