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REVIEW ARTICLE

EVALUATING THE EFFICACY OF PROBIOTICS IN TREATING ORAL LICHEN PLANUS: A SYSTEMATIC REVIEW OF CURRENT EVIDENCE

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Abstract

Objective: To systematically evaluate the clinical effectiveness, immunological outcomes, and safety of probiotic therapy in the management of oral lichen planus.

Methods: A systematic review of randomized controlled trials was conducted following the PRISMA 2020 guidelines and registered with PROSPERO **(**CRD42024550624**).** Electronic searches were performed across multiple databases from January 2001 to March 2025. Trials assessing probiotic interventions in patients with clinically and/or histopathological diagnosed oral lichen planus were included. Risk of bias was assessed using the Cochrane RoB 2 tool with domain-level judgments, and certainty of evidence was evaluated using the GRADE approach.

Results: Four randomized controlled trials involving 110 participants were included. Substantial heterogeneity was observed in probiotic strains, formulations, treatment regimens, and outcome measures. Probiotic monotherapy did not demonstrate consistent improvement in pain or lesion severity compared with placebo or standard therapy. In contrast, adjunctive probiotic use alongside topical corticosteroids were associated with greater pain reduction, improved lesion scores. Immunological assessments showed non-significant trends toward reduced inflammatory markers**.** All probiotic interventions were well tolerated, with no serious adverse events reported.

Conclusion: Probiotics do not appear to provide consistent clinical benefit when used as monotherapy in oral lichen planus. Their role may be limited to adjunctive use, particularly in patients receiving topical corticosteroids, where benefits related to microbial balance and treatment tolerability may be observed**.** Given the low to very low certainty of evidence**, s**mall sample sizes, and methodological limitations, further well-designed randomized controlled trials are required.

Keywords: immunomodulation, oral lichen planus, probiotics

1.INTRODUCTION

Oral lichen planus (OLP) is a chronic immune-mediated inflammatory disorder of the oral mucosa and was classified by the World Health Organization as an oral potentially malignant disorder in 2005. The disease commonly affects middle-aged women and

presents with symptoms such as pain, burning sensation, and mucosal discomfort, significantly impairing quality of life[1,2].Topical and systemic glucocorticoids remain the gold standard for OLP management due to their anti-inflammatory and immunosuppressive effects.[1,3] However, prolonged use is associated with adverse effects, disease recurrence, and limited suitability for long-term management. These limitations highlight the need for safer, sustainable therapeutic approaches that can modulate immune responses without significant systemic toxicity.[4] The pathogenesis of OLP primarily involves a T-cell–mediated immune response that targets basal keratinocytes, leading to epithelial damage and chronic inflammation. At the immunological level, OLP is characterized by activation of $CD4^+$ and $CD8^+$ T cells, resulting in excessive production of pro-inflammatory cytokines,

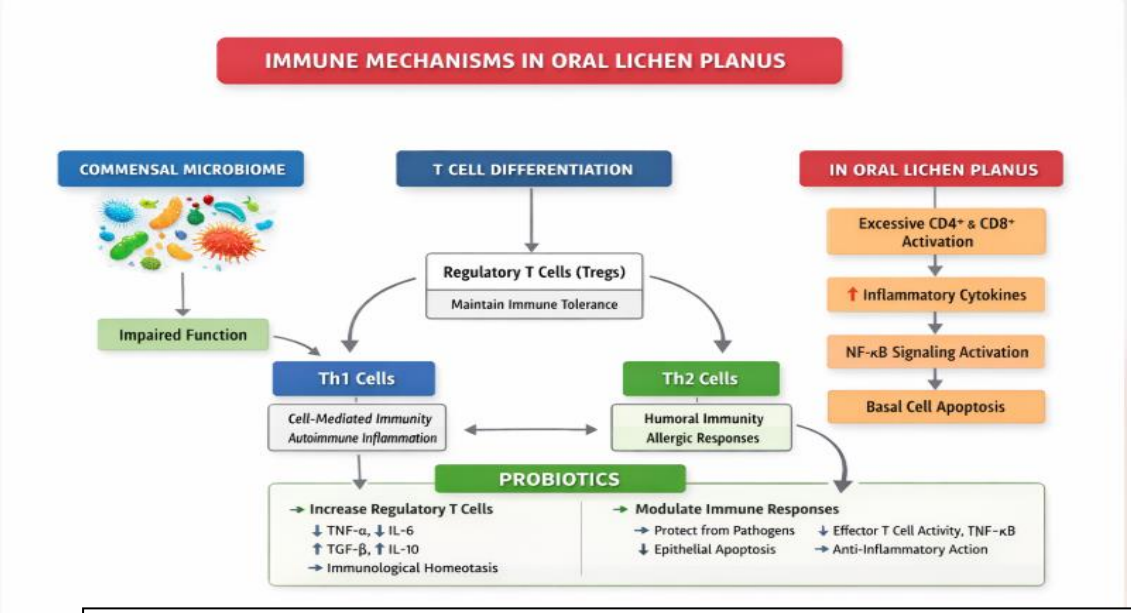

Figure 1. Schematic representation of immune dysregulation in Oral lichen planus and putative probiotic modulatory effects.

up-regulation of nuclear factor-kappa B (NF-κB) signalling, and abnormal apoptosis of basal epithelial cells.[2,4] dysregulation of regulatory T cells (Tregs), which normally maintain immune tolerance and suppress excessive immune activation, further contributes to disease persistence and progression. The oral cavity harbours a complex and dynamic microbiome that plays a critical role in maintaining mucosal immunity and immune homeostasis. Alterations in the composition of this commensal flora, characterized by an imbalance between beneficial and pathogenic microorganisms, have been implicated in the development and progression of immune-mediated and inflammatory oral diseases. Modulation of the oral microbiome has therefore emerged as a potential therapeutic strategy for conditions driven by immune dysregulation.[5,6]

Probiotics are defined as live microorganisms that confer health benefits when administered in adequate amounts. Their therapeutic potential lies in restoring microbial balance and exerting immunomodulatory effects.[6,7] Probiotics interact with epithelial cells, dendritic cells, and T lymphocytes to influence cytokine production, regulate immune signaling pathways, and maintain mucosal barrier integrity. Specific oral probiotic strains, such as *Streptococcus salivarius* an early colonizer of the oral conditions. Mechanistically, probiotics enhance the proliferation and function of regulatory T cells, leading to reduced levels of pro-inflammatory cytokines such as TNF-α and IL-6, and increased production of anti-inflammatory cytokines including IL-10 and TGF-β [8,10]. They also attenuate excessive effector T-cell responses,

down-regulate NF-κB signaling, and reduce apoptosis of basal keratinocytes. Through these mechanisms, probiotics help shift the mucosal immune environment toward an anti-inflammatory and immunotolerant state[10,11]. Despite growing interest in probiotics as an adjunctive immunotherapeutic approach for OLP, existing clinical evidence remains limited. The absence of evidence regarding their clinical efficacy necessitates a systematic evaluation of available evidence. Therefore, this systematic review aims to critically assess the effectiveness of probiotics in the management of oral lichen planus and to synthesize current clinical evidence supporting their immunomodulatory role.

METHODS

Protocol and registration

This systematic review was prospectively registered in the International Prospective Register of Systematic Reviews (PROSPERO; CRD42024550624) and conducted in accordance with the PRISMA 2020 guidelines. (Table 1) Randomized clinical trials published in English between January 2001 and March 2025 were included. Eligible studies involved patients clinically and/or histopathologic ally diagnosed with oral lichen planus. Case reports, case series, observational studies, narrative or systematic reviews, animal and in vitro studies were excluded. Studies involving lichenoid drug reactions were excluded, reactions, graft-versus-host disease, or other clinically similar lichenoid lesions were excluded to avoid diagnostic overlap. Trials with unclear, non-standardized, or unspecified diagnostic criteria for oral lichen planus, as well as studies that did not evaluate probiotics as an intervention, were also excluded.

Table 1. PICO Framework and Search Strategy

No.	PICO		Term	Search Terms
1	P(Population)	Patient's aged 18 years and above diagnosed with oral lichen planus based on clinical and/or histopathological examination	Oral lichen planus	"Oral lichen planus" OR OLP OR "oral mucosal lichen planus" OR "lichen planus oral" MeSH: *Lichen Planus, Oral*
2	I (Intervention)	Probiotic preparations	Probiotic intervention	Probiotic OR "probiotic therapy" OR "probiotic treatment" OR "probiotic supplement" OR "live bacteria" OR "beneficial bacteria"MeSH: *Probiotics*
3	I		Specific probiotic strains	Lactobacillus OR "Lactobacillus reuteri" OR "L. reuteri" OR "Lactobacillus rhamnosus" OR Bifidobacterium OR "Bifidobacterium animalis" OR "B. lactis HN019" OR "VSL#3" OR "multi-strain probiotic"OR"Streptococcus salivarius" OR

				"Lacticaseibacillus" MeSH: *Lactobacillus*; *Bifidobacterium*
4	C (Comparison)	Other pharmacotherapeutic agents or placebo	Comparators	PlaceboOR corticosteroid OR clobetasol OR "topical steroid"OR "conventional treatment" OR "standard care" MeSH: *Glucocorticoids*; *Anti-Inflammatory Agents*
5	O (Outcomes)	Clinical and symptomatic improvement Primary: 1.Pain reduction assessed - Visual Analog Scale or Numeric Rating Scale 2.Clinical improvement of oral lichen planus lesions assessed using Thongprasom score, Oral Disease Severity Score, or reduction in lesion size and severity Secondary outcomes: 1. Safety and tolerability of probiotic therapy 2. Recurrence of oral lichen planus lesions 3.Improvement in oral health–related quality of life assessed using Oral Health Impact Profile	Outcomes	Pain OR "pain reduction" OR VAS OR NRS OR "Visual Analog Scale" OR "Numeric Rating Scale" OR "lesion size" OR Thongprasom OR "Oral Disease Severity Score" (ODSC) OR "candida load" OR recurrence OR "disease severity" OR "quality of life" OR OHIP MeSH: *Pain Measurement*; *Quality of Life*
6	Study designs (S):	Randomized clinical trials		
7	Timeframe (T):	Studies published between 2001 and March 2025**.** No restrictions were applied regarding study setting.		

A comprehensive literature search was conducted to identify relevant studies published from January 2001 to March 31, 2025, across PubMed/MEDLINE, Cochrane Library, ProQuest, Clinical Key, Scopus, OpenGrey, Library Hub Discover, and institutional repositories, without restrictions on study setting. The search was independently performed by two reviewers (NS and SC) using a combination of Medical Subject Headings (MeSH) and free-text terms related to oral lichen planus and probiotics (Table 1). Key terms included “oral lichen planus,” “probiotics,” “Lactobacillus,” “Streptococcus salivarius,” “Bifidobacterium,” and “Lacticaseibacillus rhamnosus GG.” The search was limited to human studies published in English. Certainty of evidence for primary outcomes (pain, lesion size, microbial load) was graded using GRADE pro GDT software across five domains (RoB, inconsistency, indirectness, imprecision, publication bias), starting from high (RCTs) and downgraded accordingly. Sensitivity analyses explored adjunctive vs. monotherapy effects qualitatively.

RESULTS

Study selection

The literature search is summarized in the PRISMA flowchart in figure 2. A total of 990 records were initially identified through database and manual searches. After removing duplicates, 69 records remained for title and abstract screening. Of these, 64 were excluded for not meeting the inclusion criteria. Five full-text articles and theses were then assessed for eligibility. Following full-text evaluation, 1 study of oral microbiome in oral lichen planus during a 1-year randomized clinical trial Thomsen et all This microbiome was excluded as it represented observational 16S rRNA analysis without clinical OLP endpoints, where probiotics served as a secondary adjunct rather than primary intervention. Four RCTs were included in the qualitative synthesis. The study characteristics were discussed in results section and in table 2.

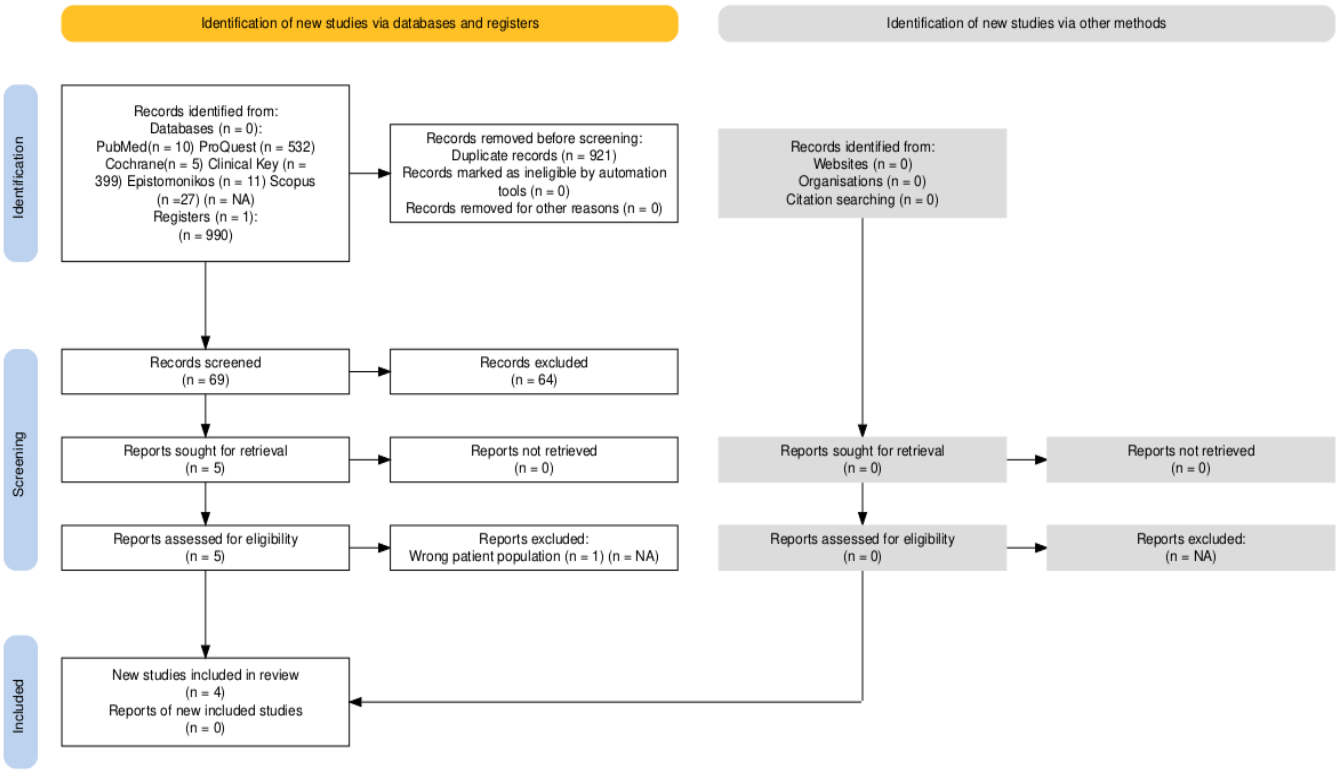

Figure 2. PRISMA 2020 flow diagram

Table 2 Study Characteristics

Study (Author, Year)	Sample Size (n)	Study Design	Intervention	Comparator	Primary Outcome	Secondary Outcomes	Key Findings	Certainty of Evidence (GRADE)
Ana Carolina Fragoso Motta et al., 2022	22	Randomized double-blind controlled trial	*Bifidobacterium animalis* subsp. *lactis* HN019	Placebo	Pain reduction (VAS/NRS)	Cytokine levels (IL-6, IFN-γ), histopathology	No statistically significant clinical improvement; borderline reduction in IL-6 and IFN-γ ($p = 0.052$)	Medium
Erni Marlina, Richard N. Goodman et al., 2022	30	Randomized double-blind parallel-group trial	Multi-strain probiotic (VSL#3)	Placebo	Pain reduction (VAS/NRS)	Cytokine levels, symptom scores	No significant difference in pain reduction; non-significant immunological trend ($p = 0.082$)	High
Mette K. Keller et al., 2018	22	Randomized placebo-controlled trial	*Lactobacillus reuteri* lozenges	Placebo	Oral candidiasis recurrence	OLP symptom severity	No significant difference in candidiasis recurrence or OLP symptoms between groups	Medium
Amira Abdel et al., 2025	36	Randomized controlled trial	Probiotic capsules + topical clobetasol	Clobetasol alone	Lesion size reduction (Thongprasom score)	Pain reduction, Candida load	Significant improvement in lesion size and pain reduction with adjunctive probiotic therapy; reduced Candida colonization	Low

The four randomized clinical trials exhibited heterogeneity in participant demographics, probiotic formulations, outcome assessment methodologies, and overall methodological rigor. Across the included trials, participant ages ranged approximately from 25 to 65 years, with reported mean ages between 48 and 52 years [7-10]. Female-to-male ratios ranged from 1.8:1 to 2.5:1 across studies. All participants were adults aged 18 years and older and were diagnosed based on comprehensive clinical examination; histopathological confirmation was performed in three studies to exclude clinically similar conditions, including lichenoid drug reactions and graft-versus-host disease[13-15]. Sample sizes ranged from 22 to 60 participants per study arm (total 110). Exclusion criteria were largely consistent across the studies. Clinical outcomes were assessed using a range of validated instruments appropriate for the multidimensional clinical presentation of OLP. Patient-reported pain and burning sensation were evaluated using either the 11-point Numeric Rating Scale (NRS; 0 = no pain, 10 = worst imaginable pain) or the 100-mm Visual Analog Scale (VAS), with assessments conducted at baseline and at predefined follow-up intervals.

Lesion severity and extent were quantified using objective clinical indices, including the ODSS, which incorporates measures of disease activity and chronicity, and the Thongprasom scale, which grades lesion size, erythema, and ulceration. In most studies, clinical assessments were supported by calibrated intraoral examination and standardized photographic documentation to enhance reliability. Microbiological outcomes primarily focused on salivary *Candida* colonization, quantified as colony-forming units per millilitre using chromogenic agar culture. This endpoint was clinically relevant given the increased susceptibility of OLP patients particularly those receiving corticosteroid therapy to opportunistic candidiasis. Immunological outcomes were evaluated in two studies using enzyme-linked immunosorbent assay (ELISA) on serum or salivary samples to quantify pro-inflammatory cytokines, including interferon-γ (IFN-γ), interleukin-6 (IL-6), and CXCL10 [7-10]. Selected studies additionally incorporated histopathological and immunohistochemical analyses, assessing basal keratinocyte apoptosis and $CD8^+$ T-cell infiltration within the sub epithelial inflammatory infiltrate. Health-related quality of life was assessed in one study using the Oral Health Impact

Profile-14 (OHIP-14). Methodological quality varied across studies. One study of Marlina,2022[7] reported a formal sample size calculation, powered at 80% with a two-sided α of 0.05 to detect a clinically meaningful 30% reduction in pain scores. The remaining trials were pilot studies., studies reported recruitment challenges or attrition, including an 18% dropout rate documented by Keller et al.[8] Follow-up durations ranged from ultra–short-term assessments (15–30 days for pain to short- and medium-term follow-up periods (4–16 weeks for lesion severity. [11-15]None of the included studies evaluated long-term disease recurrence or sustained remission beyond six months. The probiotic interventions investigated varied in formulation, strain composition, dosage, and route of administration. These included multi-strain powder formulations[9-10] (VSL#3, containing *Lactobacillus* spp., *Bifidobacterium* spp., and *Streptococcus thermophiles* at a total dose of 450 billion CFU/day), single-strain topical suspension (*Bifidobacterium animalis* subsp. *lactis* HN019), dissolvable lozenge (*Lactobacillus reuteri* DSM 17938/ATCC PTA 5289), [10]and oral probiotic capsules administered as adjunctive therapy with topical clobetasol[14].Comparator groups consisted of identical placebo formulations in monotherapy trials or clobetasol 0.05% monotherapy in adjunctive studies. In all the selected studies double-blinding of participants and outcome assessors was implemented where feasible.[10-15]

Primary outcomes

Pain reduction

Pain reduction was the most consistently reported primary outcome across all included studies and was assessed using either the 11-point Numeric Rating Scale (NRS) or the Visual Analog Scale (VAS). Assessments were conducted at baseline and at predefined follow-up intervals ranging from 15 days to 16 weeks. The study by Marlina et al. (2022) demonstrated no statistically significant difference in pain reduction between the VSL#3 probiotic group and placebo at 30 days (mean NRS change −0.5 vs −0.7; p = 0.82). Similarly, Keller et al. (2018) reported no benefit of probiotic lozenges over placebo, with pain scores paradoxically favoring the placebo group (p = 0.037); however, interpretation of these findings is limited by high attrition rates and the study's primary focus on recurrent candidiasis rather than oral lichen planus activity. In contrast, Kamal et al. (2025) demonstrated significantly greater pain reduction in the adjunctive probiotic plus clobetasol group compared with clobetasol monotherapy at both two weeks (mean NRS change −4.2 vs −3.1; p = 0.01) and four weeks, indicating a clinically relevant additive effect. Motta reported improvement in pain scores in the probiotic arm; however, overall clinical response, particularly lesion resolution, was inferior to corticosteroid therapy [15]

Lesion size reduction

Lesion severity was evaluated using the Thongprasom score or the ODSS. Among the included studies, only the adjunctive probiotic trial demonstrated statistically significant superiority, with a 72% reduction in lesion severity in the probiotic plus clobetasol group compared with a 55% reduction in the clobetasol-only group at four weeks (p = 0.02).[13,15]

Other studies reported no significant intergroup differences, with comparable lesion improvement observed in both probiotic and control arms.[13,15] Motta demonstrated inferior lesion resolution with probiotic monotherapy compared with topical clobetasol, indicating that probiotics alone are insufficient for effective mucosal healing.[13,15]

Pathogenic microbial load and recurrence

One study assessed salivary *Candida* load as a measure of pathogenic microbial burden. Adjunctive probiotic therapy resulted in a significantly greater reduction in candida counts compared with corticosteroid monotherapy (88% vs 62%; p < 0.001), suggesting a potential protective effect against steroid-associated candidiasis.[14]In contrast, the Keller study reported no significant differences in candida load or recurrence between probiotic and placebo groups. None of the included studies provided long-term data on disease recurrence, as follow-up durations were limited to a maximum of

16 weeks. Consequently, the effect of probiotics on sustained remission or relapse prevention remains undetermined.[16]

Secondary outcomes

Quality of life

Quality of life was evaluated in only one study using the Oral Health Impact Profile-14 (OHIP-14). Marlina et al. reported small, non-significant improvements in both probiotic and placebo groups, with changes below the minimal clinically important difference. These findings indicate no perceptible quality-of-life benefit attributable to probiotic therapy.[15]

Immunological and microbiological markers

Two studies assessed inflammatory cytokines using enzyme-linked immunosorbent assays. [12,15]Probiotic therapy was associated with non-significant reductions in IFN-γ and IL-6 levels, suggesting possible immunomodulatory trends without consistent clinical translation. [13,15]One study further demonstrated reduced basal keratinocyte apoptosis and decreased $CD8^+$ T-cell infiltration on histopathological and immunohistochemical analysis following probiotic treatment. Microbiome analysis using 16S rRNA sequencing revealed modest shifts in bacterial composition favouring *Firmicutes* in the probiotic arm; however, alpha and beta diversity indices did not reach statistical significance, limiting conclusions regarding microbiome restructuring.

Safety and compliance

All probiotic interventions were well tolerated, with no serious adverse events reported. Minor adverse effects, including transient gastrointestinal discomfort or taste disturbances, were self-limiting and did not require treatment discontinuation. Compliance rates were between 82% –100%.

Risk of bias

Risk of bias was independently assessed by two reviewers (NS and VJ) using the Cochrane RoB 2 tool, with disagreements resolved by consensus (Figure 3). One study was judged to have a low risk of bias across all domains, reflecting adequate randomization and allocation concealment, minimal deviations from intended interventions, complete outcome data, blinded outcome assessment, and outcomes. In contrast, the remaining studies demonstrated either some concerns or a high risk of bias, primarily due to inadequate reporting of randomization and allocation concealment, limited or unclear blinding of outcome assessors, reliance on subjective outcome measures, attrition with uncertain intention-to-treat analysis, and selective outcome reporting. Overall, three of the four included trials (75%) exhibited important methodological limitations, highlighting the need for more rigorously designed randomized controlled trials with robust allocation concealment, objective outcome measures, appropriate blinding, and transparent reporting.

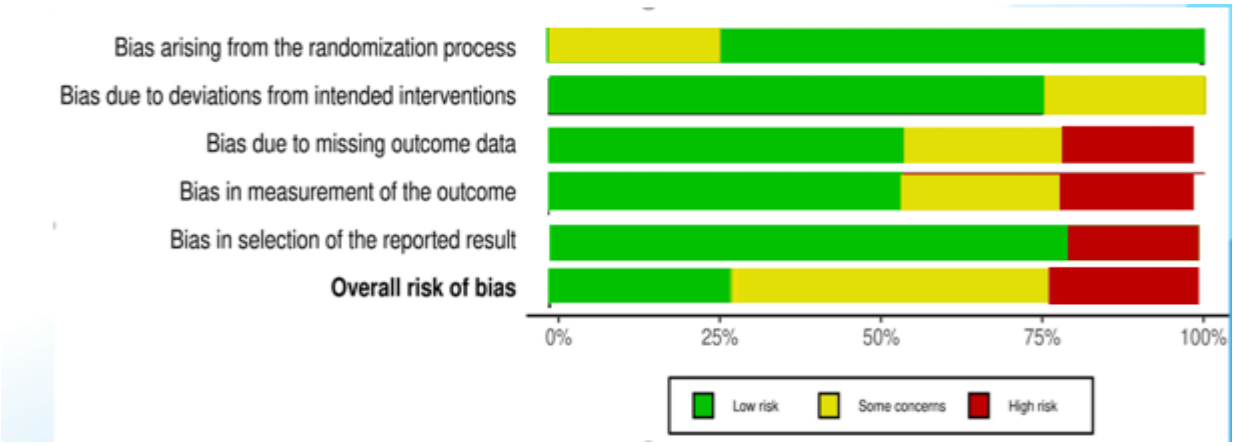

Figure 3. Risk of Bias Assessment

Meta-analysis:

A meta-analysis was not undertaken because of substantial clinical and methodological heterogeneity among the included studies. Key sources of heterogeneity included marked variation in probiotic strains (multi-strain formulations such as VSL#3 versus single-strain preparations including *Lactobacillus reuteri* and *Bifidobacterium animalis* subsp. *lactis* HN019), treatment paradigms (probiotic monotherapy versus adjunctive use with topical corticosteroids), routes and formulations of administration (sachets, lozenges, capsules, and topical suspensions), outcome assessment instruments (NRS, VAS, Thongprasom score, and ODSS), and duration of follow-up (ranging from 30 days to 16 weeks). Furthermore, heterogeneity in study design, sample size, and overall risk of bias introduced additional uncertainty that could have compromised the validity and interpretability of pooled effect estimates.

Statistical heterogeneity (I^2) could not be calculated, as pooling of results was not appropriate due to the lack of comparable outcome measures and insufficient uniform data reporting across studies. In addition, effect size estimation was not feasible**,** as studies reported outcomes using different scales, endpoints, and time points, preventing meaningful quantitative synthesis.

Grading of the evidence (GRADE)

The certainty of evidence for each critical outcome was evaluated using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach.The certainty of evidence for each included study was evaluated across the four GRADE domains: risk of bias, inconsistency, indirectness, and imprecision. The study by Ana Carolina Fragoso Motta et al. (2022) was rated as having low certainty of evidence. This was due to concerns regarding risk of bias arising from unclear reporting of randomization and allocation concealment, as well as inconsistency between outcomes, where reductions in immunological markers such as interleukin-6 and interferon-γ did not translate into significant clinical improvement in pain or lesion severity .[15]Although indirectness was not a major concern, imprecision was evident due to the small sample size (n = 22) and borderline statistical significance (p = 0.052). Similarly, the study by Erni Marlina and Richard N. Goodman et al. (2022**)** was also graded as low certainty of evidence. While the study demonstrated relatively low risk of bias with appropriate blinding, inconsistency was observed due to the absence of statistically significant clinical benefit despite trends in immunological outcomes. [13,16] .Imprecision was also present due to the limited sample size (n = 30) and non-significant findings (p = 0.082), although indirectness was minimal as outcomes directly addressed oral lichen planus symptoms. In contrast, the study by Mette K. Keller **et** al. (2018) was

rated as very low certainty of evidence.[14] This was primarily due to high risk of bias related to attrition, lack of intention-to-treat analysis, and incomplete outcome reporting. Additionally, indirectness was significant, as the primary outcome focused on oral candidiasis recurrence rather than core oral lichen planus clinical outcomes. Imprecision further reduced confidence due to the small sample size (n = 22) and absence of significant findings. Finally, the study by Amira Abdel et al. (2025) was rated as moderate certainty of evidence. This study demonstrated relatively low risk of bias and consistent improvements across clinically relevant outcomes, including lesion size reduction, pain relief, and decreased Candida colonization when probiotics were used as adjunctive therapy. Indirectness was minimal, as outcomes directly addressed oral lichen planus management. However, the certainty was downgraded by one level due to imprecision associated with the relatively small sample size (n = 36). Overall, the certainty of evidence across studies ranged from very low to moderate, with most studies downgraded due to imprecision, inconsistency, and methodological limitations, supporting the conclusion that probiotics may have a limited but potentially beneficial adjunctive role in the management of oral lichen planus.

DISCUSSION

This systematic review provides a comprehensive and PRISMA-compliant synthesis of randomized controlled trials evaluating the efficacy of probiotics in the management of oral lichen planus (OLP). It addresses a clinically relevant and insufficiently explored question. By integrating rigorous risk-of-bias (RoB2) and GRADE assessments across heterogeneous probiotic strains, formulations, and treatment paradigms, this review offers an evidence-based framework for the selective incorporation of probiotics into OLP management rather than their routine clinical use. Evidence from four randomized controlled trials involving 110 participants indicates that probiotic monotherapy does not confer consistent clinical superiority over conventional treatment modality [13,15]. Pain reduction outcomes were noted and were statistically significant in study of Erni marlina. In the studies by Fragoso Motta et al. and Marlina, the effects of probiotic therapy were seen in immunological biomarkers, particularly interferon-γ and interleukin-6 levels.[13,15]These immunological changes were not seen with clinical improvement in pain, lesion severity, or disease progression. These findings suggest that probiotics alone are insufficient to alter the clinical course of OLP when compared with established anti-inflammatory therapies. In contrast, adjunctive probiotic therapy combined with topical corticosteroids demonstrated more favourable and clinically relevant outcomes. Adjunctive use resulted in significantly greater lesion improvement as assessed by the Thongprasom score, superior pain relief and marked suppression of oral candidal load (88% vs 62%; $p < 0.001$) compared with corticosteroid monotherapy[14]. These findings are particularly relevant in routine OLP care, where long-term topical steroid use is frequently complicated by secondary candidiasis. Despite these results, the overall certainty of evidence was graded as low due to imprecision, heterogeneity, and methodological limitations in three of the four trials. Among the included studies, Marlina et al. had low overall risk of bias[13]. This study established the safety and tolerability of the multi-strain formulation VSL#3 but demonstrated clinical superiority over conventional treatment outcome. However, favourable trends in salivary IFN-γ levels suggest early immunomodulatory effects, which may require longer treatment duration or adjunctive use to translate into clinical benefit [15]. The trial by Kamal and Amira Abdel ,[14]provided the strong evidence

supporting adjunctive probiotic use. The combination of probiotic capsules with topical clobetasol resulted in superior clinical and microbiological outcomes, underscoring the potential of probiotics to mitigate steroid-associated symbiosis rather than act as primary anti-lichenoid agents. Motta's study ,[9] offered unique histopathological and immunological insights, including reductions in CD8+ lymphocytes and NF-κB expression. However, its classification as grey literature, unclear randomization procedures, and selective outcome reporting substantially limit the reliability and generalizability of its findings. Similarly, Keller's trial evaluating *Lactobacillus reuteri* lozenges was constrained by high attrition, lack of intention-to-treat analysis, and a primary focus on candidiasis rather than OLP disease activity,[16] resulting in largely null OLP-specific outcomes. The adjunctive benefits observed are biologically plausible given the immunopathogenesis of OLP [1-3], which involves T-cell–mediated epithelial damage, cytokine dysregulation, and emerging evidence of oral microbial imbalance characterized by reduced *Lactobacillus* and *Firmicutes* abundance. Probiotics may exert beneficial effects through competitive exclusion of pathogenic microorganisms, enhancement of regulatory T-cell activity, modulation of pro-inflammatory cytokines, and stabilization of mucosal barrier function. Importantly, these mechanisms are more consistent with supportive microbial homeostasis than with direct suppression of lichenoid inflammation.

Beyond OLP, probiotics have demonstrated clinical utility across a range of oral conditions, including reduction of cariogenic bacteria, improvement in periodontal parameters (mean pocket depth reduction of approximately 1 mm), suppression of halitosis-associated pathogens, and reduction of oral *Candida* colonization[22-24]. These broader oral health benefits further reinforce the biological plausibility of probiotics as adjunctive agents in chronic inflammatory oral mucosal disorders. [13,15]No systematic review has specifically evaluated probiotic therapy in OLP, rendering this review the first to synthesize evidence in this domain. However, the findings are concordant with systematic reviews assessing other non-steroidal adjunctive therapies in OLP, which similarly conclude that such interventions rarely outperform topical corticosteroids but may enhance overall disease control when used adjunctively. This pattern parallels observations in other immune-mediated disorders, where probiotics demonstrate modest but supportive effects rather than disease-modifying efficacy. Unlike inflammatory bowel disease or rheumatoid arthritis, where probiotic evidence is more robust, OLP research remains constrained by small sample sizes, heterogeneity, and limited follow-up. Based on current evidence, probiotics should not be recommended as monotherapy for OLP [18,21]. However, selective adjunctive use may be justified in specific clinical scenarios, particularly in patients with mild-to-moderate symptomatic OLP receiving topical corticosteroids, those with recurrent steroid-associated candidiasis, or individuals seeking supportive, non-immunosuppressive adjuncts. Probiotics may be most appropriately applied as short-term adjuncts (approximately 4 weeks), preferably using multi-strain formulations such as VSL#3 or well-characterized strains like *Bifidobacterium animalis* HN019. Their role appears to be supportive rather than curative, with treatment success influenced by strain selection, disease phenotype, treatment duration, and clinician adherence to standardized protocols. As with dentin preservation being more critical than liner selection in restorative dentistry, careful patient selection and treatment context appear to outweigh universal application in determining probiotic efficacy in OLP.

Limitations and future directions

The evidence base is limited by small sample sizes, short follow-up durations (≤16 weeks), substantial heterogeneity in probiotic strains and outcome measures, and methodological weaknesses in most trials. Key outcomes such as recurrence rates, quality-of-life translation, malignant transformation risk, and cost-effectiveness remain unaddressed. These limitations underscore the need for adequately powered, multicentre randomized trials with standardized diagnostic criteria, uniform outcome measures, and long-term follow-up. However, the absence of strong evidence does not imply a lack of clinical utility in all contexts.

Clinical implications:

Probiotic monotherapy has not demonstrated consistent superiority over placebo or established corticosteroid treatment in reducing pain or achieving meaningful lesion resolution.

Probiotics may be considered as adjunctive agents in selected clinical scenarios, particularly in patients receiving long-term topical corticosteroids, where they may help reduce oral candidiasis, support microbial homeostasis, and improve overall treatment tolerability. Their favourable safety profile and high patient acceptability further support selective adjunctive use. Whether specific multi-strain or so-called "immunomodulatory" probiotic formulations confer greater benefit than single-strain preparations remains an open question and warrants further investigation.

CONCLUSION

The findings of this systematic review suggest that probiotic therapy may not consistently provide superior clinical outcomes compared with placebo or standard corticosteroid treatment when used as monotherapy in oral lichen planus. While adjunctive probiotic use alongside topical corticosteroids may be associated with potential supportive benefits, particularly in relation to reduced *Candida* colonization and improved patient-reported comfort, the current evidence base remains limited and heterogeneous**.**

Given the low to moderate certainty of evidence**,** small sample sizes, and methodological limitations of the included studies, definitive clinical recommendations cannot be made at this stage**.** Further well-designed, adequately powered randomized controlled trials with standardized outcome measures are required to better clarify the role of probiotics in the management of oral lichen planus.

DECLARATION

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Competing Interests
The authors declare that there are no competing interests related to this manuscript.

Ethics Statement
As this study is a systematic review of previously published literature and does not involve human participants or animals directly, ethical approval was not required.

Data Availability
All data generated or analyzed during this study are included within this published article. Additional data can be obtained from the corresponding author upon reasonable request.

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