GRADUATION PROJECT

Degree in Dentistry

THE USE OF PROBIOTICS IN PERIODONTAL THERAPY

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RESUMEN

Introducción: Las enfermedades periodontales son afecciones inflamatorias de alta prevalencia asociadas a un biofilm dental disbiótico y a la progresión de la destrucción tisular; su manejo se ha basado principalmente en la terapia periodontal no quirúrgica, aunque se han explorado estrategias adyuvantes para optimizar los resultados clínicos y favorecer el equilibrio microbiano. **Objetivo:** Evaluar la eficacia de los probióticos como complemento al raspado y alisado radicular en la mejora de la profundidad de sondaje, el nivel de inserción clínica y el sangrado al sondaje, así como analizar las cepas, las formas farmacéuticas, la duración del tratamiento y los efectos microbiológicos descritos. **Material y método:** Se realizó una revisión documental en Medline, Dentistry & Oral Sciences Source y Scopus entre octubre de 2025 y abril de 2026, limitada a estudios revisados por pares, en inglés, con texto completo, en adultos y publicados en los últimos diez años. Se incluyeron ensayos clínicos aleatorizados que compararon el raspado y alisado radicular con y sin probióticos. **Resultados:** Se incluyeron once ensayos clínicos aleatorizados. La suplementación con probióticos mostró tendencias favorables en los parámetros clínicos, especialmente en la reducción del sangrado al sondaje, mientras que la profundidad de sondaje y el nivel de inserción clínica presentaron resultados variables. Las cepas más estudiadas fueron *Limosilactobacillus reuteri* y *Bifidobacterium animalis* subsp. *lactis*. **Conclusiones:** Los probióticos constituyen un complemento prometedor de la terapia periodontal no quirúrgica, aunque la heterogeneidad metodológica limita la definición de protocolos óptimos y la evidencia sobre beneficios a largo plazo.

PALABRAS CLAVE

Odontología, Periodontología, Probióticos, Raspado y Alisado Radicular, Microbioma Oral

ABSTRACT

Introduction: Periodontal diseases are highly prevalent inflammatory conditions associated with a dysbiotic dental biofilm and progressive tissue destruction; their management has been primarily based on non-surgical periodontal therapy, although adjunctive strategies have been explored to optimize clinical outcomes and promote microbial balance; **Objective:** To evaluate the efficacy of probiotics as an adjunct to scaling and root planing in improving probing depth, clinical attachment level, and bleeding on probing, as well as to analyze the strains, pharmaceutical forms, treatment duration, and microbiological effects reported in the literature; **Materials and Methods:** A literature review was conducted using Medline, Dentistry & Oral Sciences Source, and Scopus between October 2025 and April 2026, limited to peer-reviewed studies in English, with full text available, involving adult humans, and published within the last ten years. Randomized clinical trials comparing scaling and root planing with and without probiotic administration were included; **Results:** Eleven randomized clinical trials were included. Probiotic supplementation showed favorable trends in clinical periodontal parameters, particularly in reducing bleeding on probing, while results for probing depth and clinical attachment level were variable. The most studied strains were *Limosilactobacillus reuteri* and *Bifidobacterium animalis* subsp. *Lactis*; **Conclusions:** Probiotics appear to be a promising adjunct to non-surgical periodontal therapy; however, methodological heterogeneity limits the definition of optimal protocols and the strength of evidence regarding long-term benefits.

KEY WORDS

Dentistry, Periodontology, Probiotics, Scaling and Root Planing, Oral Microbiome

INDEX

1.INTRODUCTION 6

1.1. Periodontal disease 6
1.1.1. Definition and affected tissues 6
1.1.2. Characteristics of a healthy periodontium 6
1.1.3. Gingivitis: a reversible inflammation 6
1.1.4. Periodontitis: an irreversible tissue destruction 6
1.1.5. Pathogenesis and risk factors 7
1.1.6. 2017 Classification: staging and grading 7
1.1.7. Clinical manifestations 7
1.1.8. Global prevalence 7

1.2. Conventional Periodontal therapy 8

1.3. Probiotics and periodontal health 8

1.4. The oral microbiome and periodontal dysbiosis 9

1.5. Justification for the use of probiotics in periodontal therapy 10

2. OBJECTIVES 11

2.1. Primary objective 11

2.2. Secondary objective 11

2.3. Tertiary objective 11

3. MATERIAL AND METHOD 12

3.1. Search strategy 12

3.2. PICO question 13

3.3. Eligibility criteria 13

3.4. Source of evidence selection 13

3.5. Presentation of results 14

4.RESULTS 15

4.1. Selection process 15

4.2. Synthesis of the results 16

5. DISCUSSION 26

5.1. Interpretation of clinical improvements and comparison with literature 26

5.2. Explaining discrepancies between trials 27

5.4. Microbiological outcomes: partial alignment with clinical changes 30

5.5. Immunological outcomes and mechanistic plausibility 31

5.7. Limitations of this review and consequences for interpretation 32

6. CONCLUSIONS 34

7. SUSTAINABILITY 35

8. REFERENCES 36

1.INTRODUCTION

1.1. Periodontal disease

1.1.1. Definition and affected tissues

Periodontal disease is a chronic inflammatory illness affecting the hard and soft tissues supporting the teeth, including alveolar bone, the gingiva, periodontal ligament, and cementum (1). It is initiated by the accumulation of a dysbiotic bacterial biofilm on the tooth surface, which triggers a host-mediated immune-inflammatory response leading to a progressive destruction of the periodontal attachment apparatus (2).

1.1.2. Characteristics of a healthy periodontium

According to the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions, a clinically healthy periodontium is characterized by an absence of visible inflammation, minimal bleeding on probing, and physiological probing depths (<3mm), which may occur on an intact or reduced periodontium. In this state, the microbial biofilm and host immune response exist in harmony, maintaining tissue homeostasis (1,2).

1.1.3. Gingivitis: a reversible inflammation

In contrast to this healthy state, gingivitis is described as a reversible, plaque-induced inflammatory lesion confined to the gingival tissues without loss of clinical attachment or alveolar bone. Clinically, it presents with erythema, edema, and bleeding on probing, however these signs resolve with proper plaque control and improved oral hygiene (2).

1.1.4. Periodontitis: an irreversible tissue destruction

Following gingivitis, periodontitis is defined as a chronic, multifactorial inflammatory disease related to dysbiotic plaque biofilms, which progressively causes the destruction of the alveolar bone and periodontal ligament. Unlike gingivitis, periodontitis provokes an irreversible tissue destruction ,which lead to a clinical attachment loss (CAL), pocket formation, gingival recession, and potential tooth loss (2,3).

1.1.5. Pathogenesis and risk factors

Periodontal disease therefore encompasses a spectrum of conditions ranging from reversible gingival inflammation to advanced, destructive periodontitis. The underlying pathogenesis involves a complex interplay between microbial dysbiotic and host-mediated immune-inflammatory mechanisms, modulated by genetic, environmental, and behavioural risk factors such as diabetes, stress, smoking, and poor oral hygiene (1,2).

1.1.6. 2017 Classification: staging and grading

The 2017 World Workshop introduced a staging and grading framework to classify periodontitis according to its severity (amount of attachment loss and bone destruction), complexity (pocket depth, tooth loss, and furcation involvement), and rate of progression. The grading system further considers risk factors and their impact on disease trajectory, emphasizing a personalized approach to diagnosis and management (2).

1.1.7. Clinical manifestations

Clinically, periodontitis manifests as deep periodontal pockets bleeding on probing, radiographic bone loss, and tooth mobility. Once established, it can be stabilized but not fully reversed; thus, individuals with a history of periodontitis are considered periodontally susceptible and require ongoing maintenance. Beyond its oral implications, periodontitis is recognized as a chronic non-communicable disease sharing biological mechanisms and risk factors with systemic conditions such as diabetes mellitus, cardiovascular disease, and rheumatoid arthritis. Chronic periodontal inflammation contributes to the overall systemic inflammatory burden, strengthening the link between oral and general health (1).

1.1.8. Global prevalence

The global burden of periodontal disease continues to rise, with incidence and prevalence rates having increased steadily over the past three decades. Periodontitis now ranks among the top 15 most prevalent health conditions worldwide, affecting approximately 50% of adults, and severe cases occur in around 11% of the population (4–6).

1.2. Conventional Periodontal therapy

The main goal of conventional periodontal therapy focuses on the mechanical removal of bacterial biofilm and calculus through mechanical debridement, commonly termed non-surgical periodontal therapy (NSPT), which includes scaling and root planing (SRP) (7,8); and can be accompanied by adjunctive antimicrobial or antiseptic treatments such as chlorhexidine rinses and systemic antibiotics (4,9).

These approaches aim to reduce bacterial load and inflammation, allowing periodontal tissues to heal.

However, in many patients, particularly those with deep pockets or systemic comorbidities, complete microbial and inflammatory control remains difficult to achieve (7,10). However, despite their effectiveness in reducing pathogenic bacteria, traditional methods do not restore the natural microbial balance of the oral cavity. Repeated mechanical debridement may be required due to biofilm reformation, and long-term or repeated antibiotic use raises concerns about bacterial resistance and the disruption of beneficial commensal species (6,10,11).

As a result, novel therapeutic strategies targeting the re-establishment of a symbiotic oral microbiota have gained growing attention. Among these, probiotic therapy represents a promising biological approach (7,11).

1.3. Probiotics and periodontal health

In this context, probiotics have emerged as a promising adjunctive approach in periodontal therapy. First introduced by Lilly and Stillwell in 1965, the term “probiotics” refers to “live microorganisms which, when administered in adequate amounts, confer a health benefit on the host” (7,11) . Originally studied in gastrointestinal health, probiotics have gained recognition for their potential role in maintaining oral microbial equilibrium (5,9). Their application in periodontology represents a shift from traditional antimicrobial approaches toward a more biological and ecological concept of disease control, one which focuses on restoring harmony within the oral microbiome rather than simply eradicating bacteria.

In periodontal therapy, probiotics aim to restore microbial balance, reduce pathogenic bacterial colonization, and modulate host inflammatory responses (3,11). Most dental probiotics belong to the genera *Lactobacillus* and *Bifidobacterium*, with *Lactobacillus reuteri* being the most studied strain due to its proven antimicrobial and anti-inflammatory properties (5,12–18).

Probiotics may act through multiple mechanisms, including competition for adhesion sites and nutrients**,** production of antimicrobial compounds (bacteriocins and hydrogen peroxide), inhibition of biofilm formation, modulation of local conditions (such as pH), and regulation of host immune responses (7,19).

Experimental studies have demonstrated that the introduction of health-compatible bacterial species into periodontal pockets after SRP can reduce inflammation and delay recolonization by periodontopathogens, a process referred to as "guided recolonization" (7,20). Clinical trials have shown that *Limosilactobacillus reuteri* supplementation following non-surgical therapy can reduce bleeding on probing and gingival inflammation, even though its effect on pocket depth is modest (18).

1.4. The oral microbiome and periodontal dysbiosis

The oral cavity harbors one of the most complex and diverse microbial communities in the human body, just after the gut microbiome (21). A key factor in the pathogenesis of periodontal disease is microbial dysbiosis, it is an imbalance in the composition of the oral microbiota that favors pathogenic species. In health, the oral microbiome consists of over 700 microbial species, forming a stable ecosystem that supports oral homeostasis (6,20,22).

When this balance is disrupted, opportunistic pathogens such as *P. gingivalis, T. forsythia*, and *A. actinomycetemcomitans* can overgrow, triggering an exaggerated host inflammatory response and tissue destruction (5).

The review by Siddiqui *et al.* (2023) emphasizes that dysbiosis not only alters the diversity but also the metabolic activity of the biofilm, leading to chronic inflammation and a self-sustaining pathogenic cycle (6). This imbalance contributes to increased production of pro-inflammatory cytokines (IL-1β, TNF-α) and destruction of the periodontal ligament and alveolar bone (5,7,8,10,11,20–22).

Recent evidence also suggests a reciprocal relationship between the oral and gut microbiomes, termed the "oral–gut axis"(22). Oral pathobionts can translocate to the gastrointestinal tract through saliva ingestion, influencing gut microbial composition and systemic inflammation (23). Conversely, gut dysbiosis may alter immune regulation, exacerbating periodontal inflammation (3,20).This bidirectional connection supports the concept of periodontitis as not merely a local infection but a manifestation of systemic dysbiosis (6). The relationship between oral dysbiosis and systemic health is increasingly recognized; periodontal inflammation has been linked to

diabetes, cardiovascular disease, rheumatoid arthritis, and even neurodegenerative conditions (3,6).

Restoring microbial balance is therefore a critical goal in modern periodontal therapy. Probiotic approaches may support this objective by competing with periodontopathogens for adhesion sites and nutrients, producing antimicrobial substances, and modulating host immune responses (5,6,11). By targeting dysbiosis rather than focusing solely on bacterial elimination, probiotic therapy aligns with an ecological approach to oral disease management, aiming to re-establish a symbiotic relationship between the host and its microbiota.

1.5. Justification for the use of probiotics in periodontal therapy

Traditional mechanical debridement effectively removes biofilm but does not correct the dysbiotic microbial composition or fully restore homeostasis. In contrast, probiotics offer a biological solution to rebalance the oral ecosystem, reduce the virulence of pathogenic species, and support a stable health-associated microbiota (3,11). Moreover, probiotics are safe, cost-effective, and non-invasive, with minimal risk of side effects compared to antibiotics (7,21).

The inclusion of probiotics in periodontal therapy aligns with the modern understanding of periodontitis as a dysbiosis-driven inflammatory condition rather than a purely infectious disease (22). As such, the therapeutic goal shifts from bacterial eradication to ecological balance restoration (6). Furthermore, the oral–gut microbiome interaction underscores the need for a holistic approach to managing chronic inflammation, whole probiotics may serve as a bridge between oral and systemic health (23).

Despite promising results, several questions remain unresolved, including the optimal strain, dosage, duration, and delivery method for probiotic administration in periodontal therapy (5,12,24). Long-term randomized controlled trials are required to validate current findings and to integrate probiotics into evidence-based clinical guidelines (7,8).

2. OBJECTIVES

2.1. Primary objective

To evaluate the effectiveness of probiotics as an adjunct to conventional non-surgical periodontal therapy (scaling and root planing) in improving clinical parameters such as probing depth, bleeding on probing, and clinical attachment level.

2.2. Secondary objective

To identify the most effective probiotic strains, dosage forms, and treatment durations reported in the literature, and to discuss their potential integration into evidence-based periodontal therapy protocols.

2.3. Tertiary objective

To examine how probiotic administration influences the composition of the oral microbiome and contributes to the re-establishment of microbial homeostasis in periodontal sites.

3. MATERIAL AND METHOD

This study corresponds to a documentary research design, focused on the collection, analysis, and synthesis of scientific literature concerning the use of probiotics as adjuncts in periodontal therapy. The research was descriptive and qualitative in nature with the goal of summarising the available data and identifying the key conclusions, constraints, and future directions of probiotic use in periodontology.

3.1. Search strategy

Information was retrieved from scientific databases including Medline, Dentistry & Oral Sciences Source, and Scopus. The search focused specifically on randomized clinical trials evaluating the adjunctive use of probiotics in non-surgical periodontal therapy.

The documentary research was conducted between October 2025 and April 2026 using three different databases. For each database consulted, the following filters were systematically applied: full text**,** humans**,** adults**,** publication date restricted to the last 10 years**,** peer-reviewed journals, and English language. The search was performed using the following keywords and combinations:

For MEDLINE: (probiotics or probiotic therapy or probiotic supplement) AND (periodontal disease or periodontitis or gingivitis or periodontal health) AND (non-surgical treatment or management or therapy) AND (outcomes or benefits or effects)

For Dentistry & Oral Sciences Source: (probiotics or probiotic therapy or probiotic supplement) AND (periodontal disease or periodontitis or gingivitis or periodontal health) AND (non-surgical treatment or management or therapy) AND (outcomes or benefits or effects)

For Scopus: TITLE-ABS-KEY(probiotics and periodontal therapy) AND (LIMIT-TO (SUBJAREA,"DENT")) AND (LIMIT-TO (DOCTYPE,"ar")) AND (LIMIT-TO (EXACTKEYWORD,"Human")) AND (LIMIT-TO (LANGUAGE,"English")) AND (LIMIT-TO (PUBSTAGE,"final"))

3.2. PICO question

The methodology was structured according to the PICO framework using the Population, Intervention, Comparison, Outcome.

In adults with chronic periodontitis or gingivitis (P), is probiotic supplementation as an adjunct to conventional non-surgical periodontal therapy (I) more effective than conventional therapy alone (C) in improving clinical periodontal parameters and promoting beneficial modulation of the oral microbiome (O)?

3.3. Eligibility criteria

Inclusion Criteria	**Exclusion criteria**
Human adults Gingivitis or untreated periodontitis stage I–IV (2017 classification) Healthy individuals Non-smokers.	Animals, in vitro Children/adolescents (<18 years). Presence of systemic diseases (e.g., diabetes, autoimmune disorders) Smokers.
Probiotics used as an adjunct to conventional non-surgical periodontal therapy (SRP/NSPT), with a control/comparator group (SRP alone, placebo).	Concomitant adjunctive treatments that confound the probiotic effect (systemic/local antibiotics, LAD, dietary interventions).
Reports at least one clinical outcome (PD, CAL, BOP, PI) and/or microbiological/inflammatory outcomes (e.g., IL-1β). with a probing depth ranging from 3 to 7 mm for periondontitis patients.	Studies lacking clinical or microbiological outcomes with use of medications affecting periodontal tissues (phenytoin, cyclosporin, nifedipine, chronic NSAIDs).
Clearly identified probiotics strains.	Studies using non-defined microbial mixtures.
Articles with a timeframe of 2015-2025.	Articles published before 2015 were excluded.

Table 1. Inclusion and Exclusion criteria.

3.4. Source of evidence selection

All citations identified through the database search were imported into a reference manager, and duplicates were removed. Titles and abstracts were screened for relevance using the Rayyan

software. Studies that appeared eligible were retrieved in full and assessed according to the predefined inclusion criteria, with a focus on randomized clinical trials investigating probiotics as adjuncts to non-surgical periodontal therapy. Reasons for excluding full-text articles were systematically documented.

3.5. Presentation of results

The results are presented in a narrative format, summarising the main findings of the selected studies. Emphasis is placed on the types of probiotic strains used, their administration protocols, clinical outcomes, and the consistency of evidence regarding their effectiveness as adjuncts to non-surgical periodontal therapy.

4.RESULTS

4.1. Selection process

The database search identified 304 records. After removing 127 duplicates using Rayyan, 177 records remained for title and abstract screening. Of these, 132 records were excluded based on title/abstract, and 45 full-text articles were assessed for eligibility. Following full-text review, 34 articles were excluded for predefined reasons, and 11 randomized controlled trials were included in this documentary literature review.

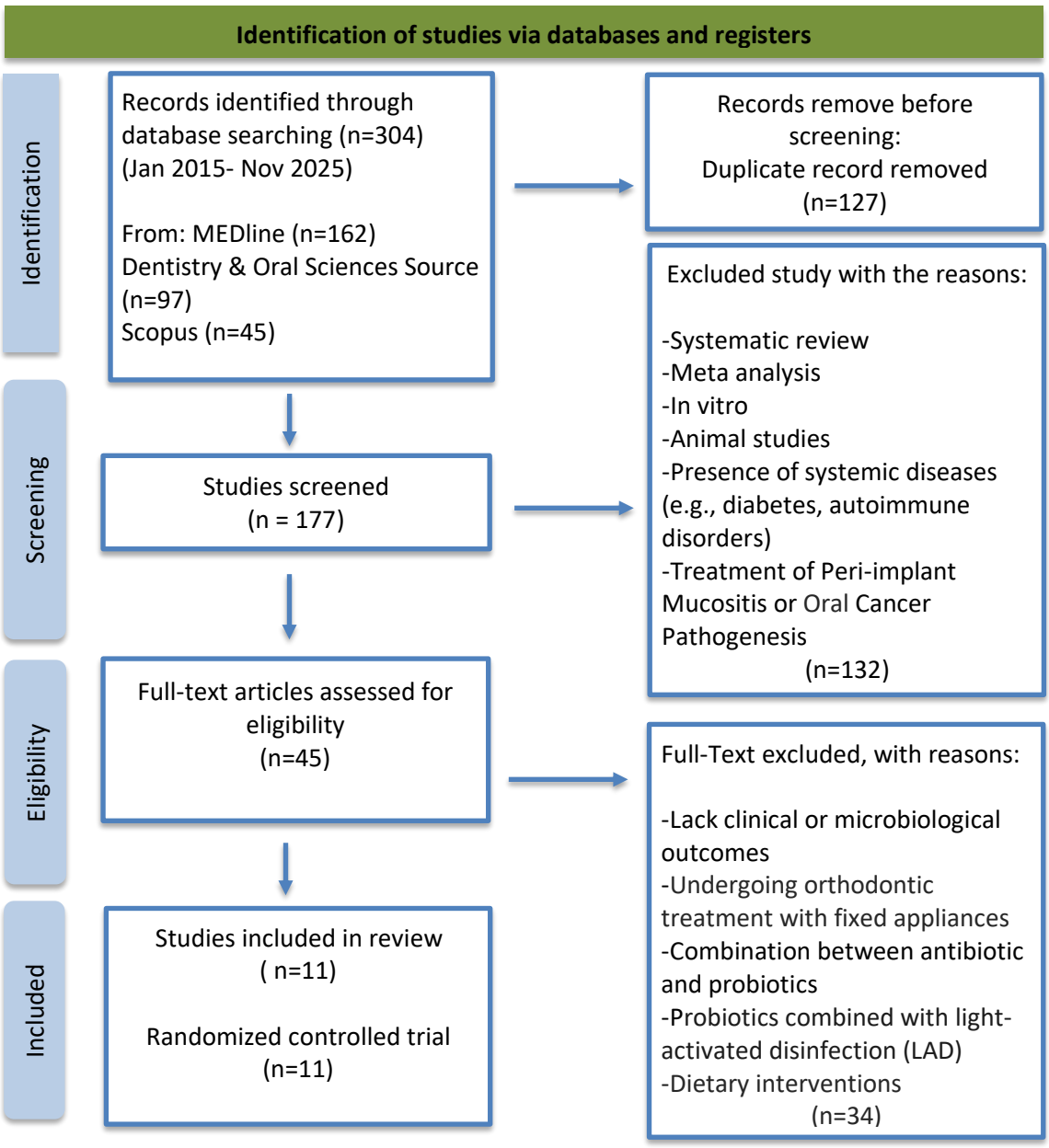


Figure 1. PRISMA 2020 flowchart (25).

4.2. Synthesis of the results

Authors (year)	Study Type	Disease	Sample, Groups, and Timepoint	Probiotic Used	Clinicals Outcomes (baseline → follow-ups) Reported as mean ± SD
Mensi *et al.* (2025) **(17)**	Quadruple-blind, placebo-controlled Randomized controlled trial	Periodontitis Stage III/IV Grade B/C	44 patients 2 groups: Probiotic (n=22) and Control (n=22) Timepoint: Baseline, 3 months, 6 months	*Limosilactobacillus reuteri DSM 17938* + *L. reuteri ATCC PTA 5289* lozenges	<u>Probing Depth (PD, mm)</u> **Probiotic**: Baseline: 5.45 ± 0.41 3 months: 4.03 ± 0.30 6 months: 3.97 ± 0.30 **Control**: Baseline: 5.63 ± 0.40 3 months: 4.01 ± 0.32 6 months: 3.92 ± 0.32 <u>Clinical Attachment Level (CAL, mm)</u> **Probiotic**: Baseline: 5.79 mm 3 months: 4.41 mm 6 months: 4.41 mm **Control**: Baseline: 5.92 mm 3 months: 4.28 mm 6 months: 4.17 mm <u>Bleeding on Probing (BOP, %)</u> **Probiotic**: Baseline: 83.5 3 months: 49.7 6 months 42.3 **Control**: Baseline: 89.0 3 months: 50.9 6 months: 38.8 <u>Plaque Index (PI, %)</u> **Probiotic**: Baseline: 38.6. 3 months: 31.4 6 months: 33.6 **Control**: Baseline: 52.1 3 months: 32.4 6 months 26.8
Huo *et al.* (2025)	Randomized Controlled Trial	Periodontitis	40 patients	*Limosilactobacillus reuteri DSM 17938* +	<u>Probing Depth (PD, mm)</u> **Probiotic**: Baseline: 4.32 ± 0.76

(15)		Stage III–IV	2 groups: Probiotic (18) and Control (16) Timepoint: Baseline, 1 month, 6 months	*Limosilactobacillus reuteri ATCC PTA 5289*	1 month: 3.24 ± 0.46 6 months: 2.90 ± 0.44 **Control**: Baseline: 4.30 ± 0.88 1 month: 3.19 ± 0.59 6 months: 2.90 ± 0.47 <u>Clinical Attachment Level (CAL, mm)</u> **Probiotic**: Baseline: 3.57 ± 0.97 1 month: 2.87 ± 0.98 6 months: 2.54 ± 1.18 **Control**: Baseline: 3.30 ± 1.15 1 month: 2.56 ± 0.99 6 months: 2.45 ± 0.99 <u>Plaque Index</u> **Probiotic:** Baseline:1.29 ± 0.58 1 month: 1.13 ± 0.44 6 months: 1.12 ± 0.40 **Control** Baseline:1.37 ± 0.54 1 month: 1.07 ± 0.46 6 months: 0.96 ± 0.42
Özener *et al.* (2023) **(26)**	Randomized placebo-controlled clinical study	Periodontitis Stage III, Grade B	30 Patients 2 groups: Probiotic (15) and Control (15) Timepoint: Baseline, 28 days, 3 months	*Bifidobacterium animalis subsp. Lactis*	<u>Probing Depth (PD, mm)</u> **Probiotic:** Baseline: 2.76 ± 0.38 28 days: 1.92 ± 0.34 3 months: 2.05 ± 0.36 **Control:** Baseline: 2.59 ± 0.43 28 days: 1.95 ± 0.34 3 months: 2.06 ± 0.35 <u>Clinical Attachment Level (CAL, mm)</u> **Probiotic:** Baseline: 2.93 ± 0.37 28 days: 2.12 ± 0.45 3 months: 2.26 ± 0.45 **Control:** Baseline: 2.67 ± 0.46 28 days: 2.05 ± 0.42 3 months: 2.16 ± 0.43 <u>Bleeding on Probing (BOP %)</u>

					Probiotic: Baseline: 52.70 ± 21.98 28 days: 6.42 ± 1.80 3 months: 10.58 ± 3.16 **Control:** Baseline: 49.16 ± 15.09 28 days: 17.48± 3.58 3 months: 22.34 ± 5.23 <u>Plaque Index</u> **Probiotic**: Baseline: 1.81±0.23 28 days: 0.17±0.08 3 months: 0.18±0.08 **Control:** Baseline: 1.79±0.36 28 days: 0.34±0.21 3 months: 0.35±022
Silva Levi *et al.* (2023) **(27)**	Randomized double blind, placebo-controlled trial	Plaque-induced generalized gingivitis	60 patients 2 groups: probiotic (25) and control (28) Timepoint: baseline 2 weeks 8 weeks	*Bifidobacterium animalis* subsp. *lactis HN019*	<u>Probing Depth (PD, mm)</u> **Probiotic** Baseline: 1.98 ± 0.68 2 weeks: 2.05 ± 0.63 8 weeks: 1.93 ± 0.49 **Control**: Baseline: 1.96 ± 0.55 2 weeks: 1.89 ± 0.47 8 weeks: 2.02 ± 0.40 <u>Clinical Attachment Level (CAL, mm)</u> **Probiotic**: Baseline: 0.02 ± 0.28 2 weeks: 0.03 ± 0.28 8 weeks: 0.03 ± 0.27 **Control**: Baseline: 0.02 ± 0.13 2 weeks: 0.04 ± 0.17 8 weeks: 0.03 ± 0.27 <u>Bleeding on Probing. (BOP, %)</u> **Probiotic**: Baseline: 62.48 ± 19.64 2 weeks: 30.56 ± 17.7 8 weeks: 18.79 ± 10.39 **Control**: Baseline: 53.38 ± 18.02 2 weeks: 35.85 ± 12.57 8 weeks: 35.36 ± 12.59

					Plaque Index (PI, %) **Probiotic**: Baseline: 77.83 ± 19.13 2 weeks: 55.01 ± 21.57 8 weeks: 48.29 ± 20.48 **Control**: Baseline 71.57 ± 18.34 2 weeks: 54.45 ± 16.64 8 weeks: 49.96 ± 16.40
Jebin *et al.* (2021) **(28)**	Double-blinded randomized controlled clinical trial	Chronic Periodontitis Stage II/III, Grade A/B	27 patients 2 groups: Probiotic (14), And Control (13) Timepoint: Baseline 1month 3 months	*Lactobacillus reuteri UBLRu-87*	Probing Depth (PD, mm) **Probiotic:** Baseline: 5.27 ± 0.49 1 month: 4.31 ± 0.52 3 months: 3.60 ± 0.56 **Control:** Baseline: 5.20 ± 0.40 1 month: 4.80 ± 0.42 3 months: 4.35 ± 0.38 Clinical Attachment Level (CAL, mm) **Probiotic:** Baseline: 3.99 ± 0.56 1 month: 3.43 ± 0.41 3 months: 2.97 ± 0.35 **Control :** Baseline: 4.17 ± 0.20 1 month: 3.84 ± 0.23 3 months: 3.50 ± 0.21 Plaque Index (PI) **Probiotic**: Baseline: 1,69±0,36 1 month 0,79± 0,23 3 months: 0,95± 0,19 **Control**: Baseline 1,80± 0,32 1 month 1,11 ± 0,12 3 months: 1,28± 0,23
Ghasemi *et al.* (2020) **(29)**	Randomized double-blind, placebo-controlled trial	Stage III, Grade A Generalized Periodontitis	36 patients 2 groups: Probiotics (18) and Control (18)	*Bifidobacterium lactis* + *Lactobacillus acidophilus* + *Lactobacillus rhamnosus* + *Bifidobacterium bifidum*	Probing Depth (PD, mm) **Probiotic**: Baseline 5.65 ± 0.57 1 month 4.29 ± 0.71 3 months 4.29 ± 0.71 **Control** : Baseline 5.78 ± 0.57, 1 month 5.33 ± 0.67 3 months 4.97 ± 0.68

			Timepoint: Baseline 1month 3 months		<u>Clinical Attachment Level (CAL, mm)</u> **Probiotic**: Baseline: 5.31 ± 0.58 1 month: 4.67 ± 0.63 3 months: 4.25 ± 0.76 **Control**: Baseline: 5.33 ± 0.69 1 month: 4.96 ± 0.71 3 months: 4.69 ± 0.69 <u>Bleeding on Probing (BOP, %)</u> **Probiotic**: Baseline: 48.95 ± 7.73 1 month: 30.56 ± 9.89 3 months: 19.46 ± 10.97 **Control**: Baseline: 47.55 ± 8.14 1 month: 35.77 ± 7.68 3 months: 23.45 ± 9.17 <u>Plaque Index (PI)</u> **Probiotic**: Baseline :50.76±7.8 1 month: 30.57±11.84 3 months: 19.59±10.79 **Control**: Baseline: 48.72±7.71 1 month:33.34±10.09 3 months: 20.11±7.54
Alkaya *et al.* (2017) **(30)**	Pilot Randomized Controlled Trial	Generalized Gingivitis	40 patients 2 groups: Probiotic group (20) Control group (20) Timepoint: Baseline 8 weeks	*Bacillus subtilis* + *Bacillus megaterium* + *Bacillus pumilus*	<u>Probing Depth (PD, mm)</u> **Probiotic**: Baseline: 2.20 ± 0.22 8 weeks: 1.92 ± 0.19 **Control**: Baseline: 2.17 ± 0.35, 8 weeks: 1.87 ± 0.25 <u>Bleeding on Probing (BOP, %)</u> **Probiotic** Baseline: 37 ± 14, 8 weeks: 15 ± 5 **Control**: Baseline: 34 ± 9, 8 weeks: 13 ± 6

Table 2. Baseline and follow-up clinical periodontal outcomes (Probing Depth, Attachment Level, and Bleeding Indices) in probiotic versus control groups: evidence from randomized controlled clinical trials in periodontitis and gingivitis patients.

Authors (year)	Study Type	Probiotic Used	Duration of intake, Form, and Groups	Formulation Dose	Microbiological outcomes
Sachelarie *et al.* (2025) **(5)**	Randomized controled trial	*Lactobacillus reuteri*	Duration of intake: 8 weeks Form: 1 capsule daily 2 groups: Probiotic group (20) Control group (20)	2×10^9 CFU	<u>*Porphyromonas gingivalis*</u> **Probitic:** Baseline: 4.8×10^6 CFU 8 weeks: 1.2×10^6 CFU **Control:** Baseline: 4.7×10^6 CFU 8 weeks: 3.9 × × 10^6 CFU <u>*Aggregatibacter actinomycetemcomitans*</u> **Probitic:** Baseline: 3.1×10^5CFU 8 weeks: 0.9×10^5CFU **Control:** Baseline:3.2×10^5CFU 8 weeks: 2.7×10^5CFU <u>*Lactobacillus* spp.</u> **Probitic:** Baseline: 1.5×10^5 CFU 8 weeks: 4.6×10^5 CFU **Control:** Baseline: 1.4×10^5 CFU. 8 weeks: 1.7×10^5 CFU <u>*Bifidobacterium* spp.</u> **Probitic:** Baseline: 2.2×10^5 CFU 8weeks: 5.1×10^5 CFU **Control:** Baseline: 2.3×10^5 CFU 8 weeks: 2.5×10^5 CFU
Huo *et al.* (2025) **(15)**	Randomized controled trial	*Limosilactobacillus reuteri* DSM 17938 *Limosilactobacillus reuteri* ATCC PTA 5289	Duration of intake: 21 days Form: 1 lozenge twice daily	Each lozenge: 1×10^8 CFU of each strain 2×10^8 total per lozenge	16S rRNA sequencing <u>*Tannerella forsythia:*</u> **Probiotic:** Baseline: 1.72 ± 0.28. 1 month: 0.89 ± 0.12. 6 months: 1.11 ± 0.13. **Control**:

			2 groups: Probiotic (18) Control (16)		Baseline: 1.62 ± 0.31 1 month: 1.11 ± 0.15 6 months: 1.35 ± 0.19 <u>*Streptococcus constellatus:*</u> **Probiotic**: Baseline: 0.88 ± 0.22 1 month: 0.65 ± 0.19 6 months: 0.70 ± 0.20. **Control :** Baseline: 0.87 ± 0.19 1 month: 0.77 ± 0.17 6 months: 0.79 ± 0.21 <u>*Prevotella nanceiensis:*</u> **Probiotic** Baseline: 1.02 ± 0.18 1 month: 1.04 ± 0.17 6 months: 1.23 ± 0.16. **Control**: Baseline: 1.00 ± 0.20 1 month: 1.12 ± 0.15 6 months: 1.15 ± 0.18
Poulose *et al.* (2024) **(31)**	Randomized controled trial	*Streptococcus faecalis*, *Clostridium butyricum*, *Bacillus mesentericus,* *Lactobacillus sporogenes*, *Saccharomyces boulardii*	Duration of intake: Single local subgingival application after SRP Form: Paste of 1 gm powder in 0.5 ml saline 2 groups: Probitioc (31) Control (31)	1g probiotic powder mixed with 0.5 mL saline and delivered subgingivally (once) Streptococcus faecalis (30 million spores), Clostridium butyricum (30 million), Bacillus mesentericus (3 million), Lactobacillus sporogenes. (30 million), Saccharomyces boulardii (40 million yeast cells)	<u>*Porphyromonas gingivalis.*</u> **Probiotic:** Baseline: 6.60 ± 0.63 Day 4: 3.35 ± 0.34 Day 8: 3.94 ± 0.33. **control:** Baseline: 6.43 ± 0.64 Day 4: 3.84 ± 0.66 Day 8: 4.54 ± 0.49 <u>*Tannerella forsythia:*</u> **Probiotic:** Baseline: 1.72 ± 0.28 Day 4: 0.89 ± 0.12 Day 8: 1.11 ± 0.13. **control**: Baseline: 1.62 ± 0.31 Day 4: 1.11 ± 0.15 Day 8: 1.35 ± 0.19. <u>*Fusobacterium nucleatum*</u> **Probiotic:** Baseline: 2.45 ± 0.34 Day 4: 1.80 ± 0.25

					Day 8: 1.50 ± 0.22 **control :** Baseline**:** 2.43 ± 0.31 Day 4: 2.10 ± 0.30 Day 8: 2.25 ± 0.35 <u>*Prevotella intermedia:*</u> **Probiotic:** Baseline: 2.10 ± 0.25 Day 4: 1.60 ± 0.18 Day 8: 1.20 ± 0.15. **Control:** Baseline: 2.05 ± 0.28 Day 4: 1.95 ± 0.20 Day 8: 2.05 ± 0.30
Jebin *et al.* (2021) **(28)**	Randomized controled trial	*Lactobacillus reuteri* UBLRu-87	Duration of intake: 4 weeks Form: 1 chewable probiotic tablet/day 2 groups: Probitioc (14) Control (13)	0.5 billion CFU/day	<u>*Porphyromonas gingivalis*</u> <u>(qPCR,*mean log CFU/mL)*</u> **Probiotic:** Baseline: 6.60 ± 0.63 1 month: 3.35 ± 0.34 3 months: 3.94 ± 0.33 **Control :** Baseline: 6.43 ± 0.64 1 month: 3.84 ± 0.66 3 months: 4.54 ± 0.49
Montero *et al.* (2017) **(32)**	Randomized controled trial	*Lactobacillus plantarum CECT 7481,* *Lactobacillus brevis CECT 7480,* *Pediococcus acidilactici CECT 8633*	Duration of intake: 6 weeks (42 days) Form: 2 oral tablet/day 2 groups: Probiotic (30) Control (29)	Tablets containing strains at 1.00×10^3 CFU for each strain	qPCR; Cq values converted to CFU/mL using standard curves; results reported as log-transformed counts/mL (mean (SD)) <u>*Tannerella forsythia*</u> **Probiotic:** Baseline: 4.40 ± 1.4 6 weeks: 3.34 ± 1.5 **Control:** Baseline: 4.04 ± 1.9 6 weeks: 3.53 ± 1.6 <u>*Aggregatibacter actinomycetemcomitans*</u>

					Probiotic: Baseline: 2.25 ± 1.3 6 weeks: 1.29 ± 1.6 **Control :** Baseline: 2.24 ± 1.0 6 weeks: 1.18 ± 1.3 *Fusobacterium nucleatum* **Probiotic:** Baseline: 4.89 ± 0.7 6 weeks: 4.79 ± 0.6 **Control**: Baseline: 4.81 ± 0.8 6 weeks: 4.53 ± 0.8 *Porphyromonas gingivalis* **Probiotic:** Baseline: 2.61 ± 1.5 6 weeks: 2.24 ± 0.9 **Control**: Baseline: 3.02 ± 2.2 6 weeks: 2.44 ± 1.2 *Campylobacter rectus* **Probiotic:** Baseline: 3.31 ± 1.1 6 weeks: 3.32 ± 0.8 **Control**: Baseline: 3.23 ± 1.2 6 weeks: 2.61 ± 1.3

Table 3. Microbiological outcomes of probiotic interventions in periodontal and gingival diseases: probiotic strains, formulation/dose, duration, and changes in targeted periodontal pathogens or microbial markers (as reported in included randomized controlled trials).

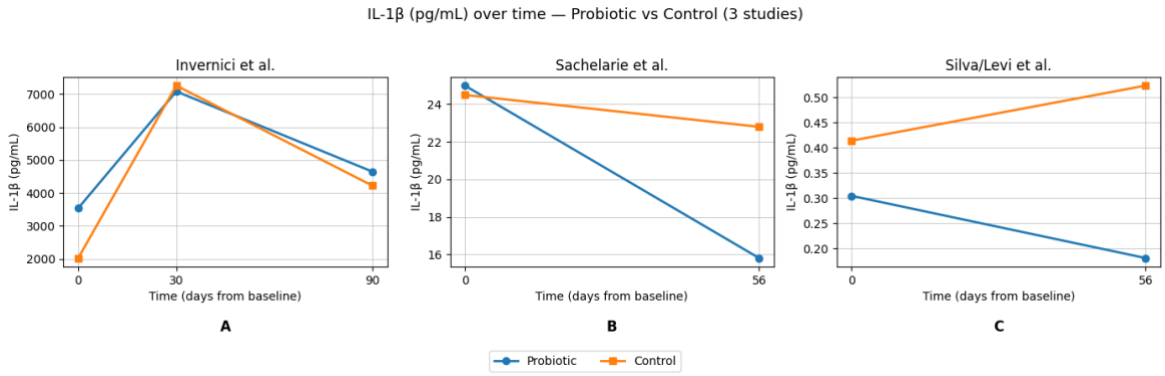


Figure 2. Comparison of gingival crevicular fluid IL-1β (pg/mL) over time (Baseline Day 0 to Days 30, 56 and 90) between probiotic and control groups across three randomized controlled trials: (A) Invernici et al. (16), (B) Sachelarie et al. (5) , and (C) Silva Levi et al. (27).

5. DISCUSSION

Across the 11 randomized controlled trials included in this review, namely Sachelarie *et al.;* Mensi *et al*.; Huo *et al*.; Özener *et al*.; Silva Levi *et al*.; Jebin *et al*.; Ghasemi *et al*.; Alkaya et *al.*; Poulose *et al*.; Montero *et al*.; Invernici *et al*., the overall pattern suggests that adding probiotics to non-surgical periodontal therapy tends to improve clinical recovery beyond mechanical debridement alone, but the magnitude and consistency of benefit varies meaningfully between studies (5,15,16,26–33). The key clinical outcomes are summarized in Table 2, while the microbiological outcomes are summarized in Table 3. In addition, inflammatory marker trends (IL-1β) from the three studies reported by Invernici *et al.*; Sachelarie *et al*.; Silva Levi *et al.* are synthesized in Figure 2 (5,18,27).

This section provides a critical analysis of the results obtained in the current review of studies examining the use of probiotics as adjuncts to non-surgical periodontal therapy. The focus is on comparing the findings of this study with previous research, exploring areas of agreement, highlighting discrepancies, and providing explanations for these variations.

This variability is important clinically because it implies that probiotics should not be interpreted as a single interchangeable intervention; rather, outcomes likely depend on strains, delivery method, treatment duration, baseline disease severity, and the outcomes selected for evaluation (Table 2) (5,15,16,26–33).

5.1. Interpretation of clinical improvements and comparison with literature

Most included trials reported improvements in probing depth and clinical attachment when probiotics were used as an adjunct to scaling and root planing (Table 2), particularly in the studies by Jebin *et al.* and Ghasemi *et al.* This direction of effect is consistent with the wider periodontal literature which suggests that probiotics may support post-debridement healing by competing with periodontopathogens, influencing biofilm recolonization, and modulating host inflammatory responses, potentially resulting in reduced pocket inflammation and improved tissue stability (28,29).

A key point emerging from the comparison of included studies is that disease severity likely influences how detectable the probiotic effect is. In trials enrolling more advanced periodontitis populations (stage III–IV), additional effects beyond mechanical therapy were more variable and sometimes limited ,as illustrated by Mensi *et al.* and Huo *et al.* , where both groups improved

strongly but between group separation was small. In contrast, in studies with less severe or more moderate disease profiles such as those reported by Jebin *et al.* and Ghasemi *et al*., incremental improvements were more frequently measurable (15,28,29,33).

Within the present evidence base, several studies illustrate clinically detectable adjunctive benefit (Table 2) (5,15,16,26–33). For example, Jebin *et al.* reported lower probing depth and clinical attachment loss values at follow-up in the probiotic group compared with SRP alone, and Ghasemi *et al*. similarly observed more favorable clinical parameters in the probiotic group than placebo after non-surgical therapy (Table 2) (28,29).

At the same time, not all included studies demonstrated the same magnitude of added benefit, indicating that probiotic effects are likely context-dependent rather than uniformly reproducible with any strain, regimen, or population (Table 2) (5,15,26–33). A key factor influencing detectability appears to be baseline disease severity**.** In trials enrolling more advanced stage III–IV periodontitis, additional effects beyond mechanical therapy were more variable and sometimes limited (15,33). By contrast, studies including less severe or more moderate disease profiles more frequently reported measurable incremental improvements (16,28,29). In severe cases, residual deep pockets, complex anatomy, and higher inflammatory burden may constrain the additional clinical improvements achievable through microbiome modulation alone, especially when probiotic exposure is short or dosing is not optimized (Table 2) (15,33).

When comparing the included periodontitis RCTs directly, the overall pattern suggests that trials reporting clearer PD/CAL benefits , notably by Jebin *et al.*, Ghasemi *et al.*, tend to be those where protocol conditions allow separation between groups (follow-up duration, baseline severity, and strong strain-specific effects), whereas in trials where SRP alone produces very large improvements or where study conditions differ (follow-up, dosing, baseline characteristics), the extra probiotic effect becomes harder to detect (Table 2) (15,26–30).

5.2. Explaining discrepancies between trials

Where only marginal differences were reported between probiotic and control groups particularly in Mensi *et al.* and Huo *et al.,* and for structural outcomes in Özener *et al.* The most plausible explanations relate to heterogeneity in protocols rather than a true absence of biological potential (Table 2) (5,15,16,26–33).

First, treatment duration and follow-up timing appear decisive: short intake periods or limited follow-up windows may underestimate benefits that require time to consolidate, particularly for outcomes like attachment gain or sustained reductions in inflammation (26,33). This may help

explain why studies with short probiotic exposure, such as those reported by Mensi *et al.* and Huo *et al.* , show limited between-group separation compared with trials where follow-up and protocols differ, such as Jebin *et al*. , Ghasemi *et al.* (15,18,28,29,33).

Second, strain selection is likely critical. Even within commonly used genera (*Lactobacillus/Limosilactobacillus* and *Bifidobacterium*), strains differ in adherence capacity, antimicrobial metabolite production, and immunomodulatory effects, which could produce real differences in clinical response (Table 2) (15,16,26,28–33). For example, Ghasemi *et al.* used a multi-strain combination ,Özener *et al.* used *B. animalis* subsp. *lactis* , and Jebin *et al.* used a specific *L. reuteri* strain , which may partly contribute to heterogeneity in outcomes (26,28,29).

Third, delivery route may affect whether probiotics can meaningfully influence subgingival ecosystems: systemic oral consumption may have limited direct access to periodontal pockets compared with local subgingival delivery, but local delivery may be short-lived unless repeated or supported by ongoing ecological change (table 2) (31). This is relevant when contrasting systemic lozenges/tablets in Mensi *et al*. and Huo *et al.* with the local approach described by Poulose *et al.*(15,31,33).

Another source of apparent discrepancy is the strength of the control intervention. Scaling and root planing alone often produces substantial clinical improvement, meaning adjunctive effects can be difficult to detect unless the study is adequately powered and includes sufficiently challenging baseline conditions (15,33). This may explain why Mensi *et al.* and Huo *et al.* show improvements in both arms with only small between-group differences, even when probiotics are biologically plausible (15,33).

This interpretation is consistent with external randomized evidence in stage III periodontitis showing that adjunctive probiotics may fail to provide measurable added benefit when SRP already produces substantial improvements. In a placebo-controlled, parallel-arm RCT, Morales *et al.* randomized stage III periodontitis to receive either a placebo or *Lactobacillus rhamnosus SP1*. At 12 months, all groups improved significantly, but no significant inter-group differences were found, and the authors concluded that probiotics failed to provide additional benefits beyond SRP (34). Overall, comparing the RCTs showing stronger added benefit , for example Jebin *et al.*; Ghasemi *et al*.; Invernici *et al.* ; with those that do not , such as Mensi *et al*.; Huo *et al.;* Özener *et al.* , suggests that protocol heterogeneity (strain, dose, duration, delivery route, baseline severity, and follow-up) is a plausible explanation for mixed findings, rather than a simple “effective/ineffective” conclusion for probiotics as a general category (Table 2) (15,26,29,33).

5.3. Inflammation control and bleeding on probing as a consistent signal

Among reported clinical endpoints, bleeding on probing appears to show one of the most consistent improvements with probiotic adjuncts, particularly in Ghasemi *et al.,* Özener *et al.,* and Silva Levi *et al.* (Table 2) (26,27,29).

Supportive evidence from gingivitis trials also suggests that probiotics may produce clearer effects on inflammation-sensitive indices (GI/BOP) than on structural parameters over short follow-up periods, reinforcing that the most reproducible signal may be anti-inflammatory rather than regenerative. This is clinically meaningful because BOP reflects inflammatory activity and is sensitive to changes in gingival immune response. The pattern observed in Silva Levi *et al.* (clear BOP improvement and cytokine differences), contrasted with the more modest or non-significant mean-index differences reported by Montero *et al.* and Alkaya *et al.*, supports the interpretation that endpoint choice and study context strongly influence detectability (27,30,32).

Taken together, the evidence indicates that probiotics may be most reliably beneficial as anti-inflammatory adjuncts, with structural parameters improving in some but not all contexts (Table 2) (5,15,16,26–33).

Evidence from gingivitis trials supports the idea that probiotic interventions, when effective, tend to produce clearer effects on inflammation-sensitive indices (GI/BOP) than on structural parameters over short follow-up periods. In the double-blind RCT by Silva Levi *et al., subsp Bifidobacterium animalis. lactis HN019* was used as an adjunct to professional supragingival scaling, and the probiotic group showed lower BOP, a higher proportion of sites with GI ≤ 1 at 8 weeks compared with placebo, and lower GCF levels of IL-1α, IL-1β, and MCP-1, supporting an anti-inflammatory effect (27).

However, gingivitis findings are not uniform across formulations and strains. In a 6 weeks placebo-controlled trial with tablets containing *L. plantarum*, *L. brevis* and *P. acidilactici*, Montero *et al.* reported improvement in mean GI in both groups with no clear between-group differences for mean clinical indices; the probiotic group mainly showed a reduction in the number of severely inflamed sites and a microbiological signal (reduction of *T. forsythia* in the test group) (32). In addition, Alkaya *et al.* in a pilot RCT testing bacilli-containing toothpaste/mouthrinse/toothbrush cleaner, reported significant intra-group improvements over 8 weeks but no inter-group differences at any time point, indicating that probiotics may not provide added benefit when hygiene/prophylaxis effects are already strong or when the selected probiotic regimen is not optimal (30).

These gingivitis trials illustrate how study outcomes can differ depending on which endpoint is

used: Silva Levi *et al.* shows clearer differences on inflammation markers and cytokines, whereas Montero *et al.* reports stronger changes at the level of severe sites rather than in mean GI , and Alkaya *et al.* suggests that improvements can occur in both arms without inter-group separation when prophylaxis/hygiene effects are strong . This reinforces the importance of endpoint selection when interpreting benefit in gingivitis studies (27,30,32).

5.4. Microbiological outcomes: partial alignment with clinical changes

As shown in Table 3, microbiological findings vary notably depending on the study and the analytical method used**.** Sachelarie *et al.* reported clear reductions in targeted periodontopathogens (*P. gingivalis* and *A. actinomycetemcomitans*) in the probiotic group compared with controls, together with increased counts of *Lactobacillus* spp. and *Bifidobacterium* spp., supporting an ecological shift consistent with probiotic exposure (Table 3) (5). Poulose *et al.* also reported rapid reductions in multiple targeted pathogens following a single local subgingival probiotic application (Table 3) (31). In addition, Jebin *et al.* reported a decrease in *P. gingivalis* over time, with lower values in the probiotic group than in the control group at follow-up (Table 3) (28).

This aligns with the intended rationale for using probiotics in periodontal therapy: supporting recolonization dynamics after debridement and limiting pathogen re-establishment (3,11). However, a discrepancy becomes apparent when clinical improvement is observed without a parallel, consistent microbial shift. In the sequencing-based study by Huo *et al.* (Table 3), microbial composition changed over time in both the probiotic and control groups, with limited between-group separation for several taxa, while Table 2 shows substantial clinical improvement in both arms. This pattern suggests that, in some protocols, clinical benefits may reflect enhanced resolution of inflammation or host-response modulation rather than a clearly detectable and durable restructuring of the subgingival microbiome (15).

Methodological differences likely contribute to these mixed microbiological findings. Studies focusing on a small set of pathogens , for example, CFU/qPCR reporting in Sachelarie *et al.,* Jebin *et al.*, and Montero *et al.* ,may detect targeted pathogen reductions more readily than community-level sequencing approaches as and Huo *et al.* (Table 3) (5,15,28,32). Therefore, apparent “microbiological inconsistency” should be interpreted cautiously; it may reflect measurement limitations as much as biological variability (Table 3) (15,16,26,28–32).

5.5. Immunological outcomes and mechanistic plausibility

The review also highlights evidence that probiotics may reduce inflammatory mediators in gingival crevicular fluid (GCF). This supports a mechanistic pathway whereby probiotics contribute to improved periodontal outcomes by modulating host inflammatory response, potentially reducing cytokine-driven tissue breakdown and promoting repair (Figure 2) (5,18,27).

Figure 2 was created to make the IL-1β findings easier to interpret visually. It includes only the three studies in this review that reported comparable IL-1β cytokine outcomes namely Invernici *et al.,* Sachelarie *et al*. and Silva Levi *et al.* The figure is separated into three panels (A–C), one panel per study, rather than combining them into a single graph, because absolute IL-1β values and measurement ranges were not the same between studies. In each panel, the probiotic group is plotted against the control/placebo group over time from baseline (Day 0) to follow-up (Days 30, 56 or 90 depending on the study). Lower IL-1β values indicate reduced inflammatory activity in GCF (5,18,27).

As summarized in Figure 2, IL-1β showed a clearer probiotic-associated reduction in two of the three included trials with cytokine outcomes. In Sachelarie *et al*. ,IL-1β decreased substantially in the probiotic group (reported 37% reduction) compared with minimal change in controls (5). In Silva Levi *et al*., the control group presented higher IL-1β levels than the probiotic group at 8 weeks ,supporting an anti-inflammatory effect (27). In Invernici *et al.* cytokine patterns also favored probiotics when results were expressed relative to baseline, with the control group showing a higher IL-1β ratio at 30 and 90 days (18).

However, immunological effects were not consistently detected across all trials, and several methodological factors can influence whether cytokine shifts are measurable. Between-study variability in probiotic strain and delivery**,** follow-up timing**,** sampling procedures**,** and biomarker processing/assay methods may contribute to heterogeneous findings. This mixed pattern reinforces the possibility that probiotic benefits are context-dependent and suggests that future trials should standardize biomarker methodology and align sampling timepoints with plausible time courses of immune modulation (5,18,27).

5.6. Clinical implications

Overall, the included evidence suggests that probiotics can be considered a low-risk adjunct to non-surgical periodontal therapy, particularly when the clinical goal is improved inflammation

control after mechanical debridement (Table 2) (5,15,16,26–33). This interpretation is mainly supported by studies showing clearer improvements in inflammation-sensitive endpoints such as BOP. For example**,** Ghasemi *et al.* reported a marked reduction in BOP from baseline to 3 months in both groups, with numerically greater improvement in the probiotic arm (29). Özener *et al.* also showed strong improvement in BOP in the probiotic group compared with control at follow-up, despite similar PD/CAL values between groups (26). In gingivitis, Silva Levi *et al.* showed a clinically relevant reduction in BOP and inflammatory mediator trends favoring the probiotic group, supporting the idea that probiotic effects may be more consistently detectable in inflammatory outcomes than in structural parameters over short periods (27).

By contrast, other studies reported limited additional benefit beyond SRP alone. Mensi *et al.* and Huo *et al.* reported strong clinical improvement over time in both probiotic and control groups, with minimal inter-group separation for key parameters (15,33).This suggests that when SRP produces major improvements ,the extra probiotic effect may be difficult to detect. This cautious interpretation is reinforced by external evidence: in a triple-blind RCT, Morales *et al*. found that *Lactobacillus rhamnosus* SP1 did not provide additional clinical benefits beyond SRP at 12 months in stage III periodontitis (35).

Clinically, the most defensible interpretation is therefore not that probiotics replace established therapy, but that they may provide incremental benefit in selected contexts, particularly when inflammation remains persistent or the risk of dysbiosis rebound is high, and when strains and protocols appear effective in controlled trials such as those by Ghasemi *et al*., Özener *et al.*, Silva Levi *et al.*, and (for PD/CAL) Jebin *et al.* However, because protocol heterogeneity remains substantial (strain, formulation, dose, delivery, duration), probiotics cannot yet be recommended as a standardized universal adjunct for all periodontal patients (Table 2) (26–29). From an antibiotic stewardship perspective, probiotic adjuncts are attractive because they represent a non-antibiotic approach. However, the evidence remains provisional until long-term trials confirm whether probiotics reduce relapse, maintenance needs, or the real-world reliance on antimicrobials.

5.7. Limitations of this review and consequences for interpretation

Several limitations constrain the strength of conclusions that can be drawn. The included trials are heterogeneous in design, strains, formulations**,** dosing regimens, and follow-up duration, limiting direct comparability and makes it difficult to define an optimal probiotic protocol (Table

2 and Table 3) (24–26). For example, the probiotic composition differs substantially between trials (single-strain *L. reuteri* in Jebin *et al.* vs multi-strain combinations in Ghasemi *et al.*), and delivery approaches vary from systemic lozenges/tablets (Mensi et al., Huo et al., and Ghasemi et al.) to local subgingival application (Poulose et al.) (15,29,31,33). These differences likely contribute to why some studies show clearer added benefits (Jebin *et al*., Ghasemi *et al.* , Invernici *et al.*) while others show minimal inter-group differences (Mensi *et al*., Huo *et al.*) (15,28,29,31,33).

Second, follow-up duration is often limited, which restricts interpretation about durability. Even when short-term inflammatory or clinical improvements are observed , for example BOP improvement in Silva Levi and Özener *et al.*, it remains uncertain whether these effects persist long-term or translate into reduced recurrence and improved maintenance outcomes (26,27).

Third, microbiological and immunological outcomes are not measured in a standardized way, complicating mechanistic interpretation. The studies Sachelarie *et al*., Jebin *et al*., Montero *et al.* studies report targeted pathogens using CFU/qPCR approaches while others like Huo *et al.* use sequencing-based profiling, and this influences what change can be detected (Table 3). This variability may partly explain why clinical and microbial outcomes do not always align (5,15,28,32).

Fourth, the included evidence covers both periodontitis and gingivitis, which naturally differ in expected outcomes. Structural parameters (PD/CAL) are more relevant for periodontitis studies, whereas gingivitis trials are more likely to show detectable changes in inflammation-sensitive indices (GI/BOP), as illustrated by clearer BOP improvement in Silva Levi *et al.*, mixed results in Montero *et al.*, and no inter-group differences in Alkaya *et al.* This means that conclusions must be interpreted according to disease category and endpoint selection (26,29).

Finally, the eligibility criteria restricted included evidence to systemically healthy, non-smoking adults (Table 1). Therefore, applicability to common periodontal risk groups (smokers and patients with diabetes or other systemic conditions) remains uncertain. This is clinically relevant because these groups often show poorer response to conventional therapy and may respond differently to microbiome modulation. Future trials should include higher-risk groups, standardize confounders (smoking exposure, HbA1c/metabolic control), and report subgroup analyses to clarify whether probiotic effects are similar, reduced, or differential.

6. CONCLUSIONS

Probiotic supplementation as an adjunct to scaling and root planing appears to provide additional clinical benefit, with the most consistent added improvement observed in inflammatory control, particularly bleeding on probing. Improvements in probing depth and clinical attachment level are generally favourable but more variable across trials.

No single probiotic regimen can be recommended at present because the included trials used heterogeneous strains, delivery formats, dosages, and treatment durations. *Lactobacillus/Limosilactobacillus* and *Bifidobacterium-b*ased products are the most recurrent in the literature, but differences in protocols and follow-up limit direct comparison and prevent firm evidence-based standardization for routine clinical integration.

Microbiological evidence suggests a tendency toward reduced levels of key periodontopathogens and a shift toward a more balanced periodontal ecosystem in some studies; however, this is not consistently demonstrated across all trials. Clinical improvement can occur even when compositional changes are limited, suggesting probiotics may act through both ecological mechanisms and host-response modulation. Standardized long-term trials with comprehensive microbiome analysis are required to confirm durability and identify the most effective strategies.

Future studies should prioritize protocol standardization clearly defining strain, dose, delivery route, and duration so that findings can be compared and pooled more meaningfully. Long-term trials are especially needed to determine whether benefits persist, whether probiotics reduce relapse or maintenance needs, and whether prolonged use raises any unforeseen risks. Additionally, more comprehensive microbiome approaches (e.g., sequencing-based community profiling) would help clarify whether probiotics primarily act through microbial restructuring, immune modulation, or both, and which microbial changes predict clinical response. Finally, strain-specific comparisons are essential, as the current evidence strongly suggests that efficacy is not uniform across probiotic candidates.

7. SUSTAINABILITY

In line with RD822/2021, this project has sustainability implications because periodontal disease is highly prevalent and long-term management consumes clinical time, materials, and financial resources. Probiotics, if confirmed as a safe adjunct to scaling and root planing, could improve inflammation control and support periodontal stability, potentially reducing relapse, discomfort, and tooth loss over time.

This aligns with SDG 3 (Good Health and Well-Being) by supporting preventive, low-risk strategies that may improve quality of life.

It may also contribute to SDG 10 (Reduced Inequalities), as populations with limited access to continuous care could benefit from approaches which help maintain stability between visits, reducing productivity losses and supporting fairer oral health outcomes. Economically, a low-cost adjunct that yields incremental benefits could reduce repeat visits and the need for more invasive treatments, improving efficiency for patients and services.

Environmentally and socially, encouraging non-antibiotic adjuncts supports antimicrobial stewardship and relates to SDG 12 (Responsible Consumption and Production) by limiting unnecessary antibiotic exposure and emphasizing responsible consumption practices (including packaging and supply chains).

Any future implementation should be guided by evidence-based indications and long-term trials that confirm effectiveness and safety across diverse patient groups.

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