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The Efficacy of Probiotics as an Adjunctive Therapy in Periodontal Treatment: A Literature Review

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Abstract

Periodontal diseases, stemming from microbial imbalances and chronic inflammation, represent a significant global health challenge. While traditional mechanical debridement forms the cornerstone of treatment, adjunctive therapies are often necessary to achieve optimal and lasting periodontal health. This literature review evaluates the current evidence on probiotics as an adjunct to initial periodontal treatment, focusing on their efficacy in improving clinical parameters and modulating the oral microbiome. A comprehensive search of major electronic databases was performed across multiple electronic databases, compiling studies conducted on humans, published in English between 2020 and 2025. Using terms related to probiotics, gingivitis, periodontitis, adjunctive therapy, the oral microbiome, and specific probiotic genera. Fourteen relevant articles, including randomized controlled trials, systematic reviews, meta-analyses, and a scoping review, were identified and narratively synthesized. The reviewed studies collectively indicate that probiotics contribute to significant improvements in clinical parameters such as probing pocket depth, clinical attachment loss, and bleeding on probing. Microbiologically, probiotics were shown to reduce key periodontopathogens, including *Aggregatibacter actinomycetemcomitans* and *Tannerella forsythia*, and foster a healthier oral microbial balance. Furthermore, specific probiotic strains demonstrated immunomodulatory effects, contributing to reduced inflammation. Despite promising findings, considerable heterogeneity exists across studies regarding probiotic strains, dosages, and treatment durations. In conclusion, probiotics represent a valuable and evolving adjunctive strategy in non-surgical periodontal therapy, offering a biological approach to mitigate dysbiosis and inflammation. While continued research with standardized protocols is essential to optimize their clinical application, current evidence supports their integration to enhance pa-

tient outcomes and promote overall oral health.

Subject Areas

Global Health

Keywords

Probiotics, Gingivitis, Periodontitis, Adjunctive Therapy, Oral Microbiome, and *Lactobacillus*, *Bifidobacterium*, *Streptococcus*, and *Saccharomyces*

1. Introduction

Periodontal diseases, chronic inflammatory conditions affecting the supporting structures of the teeth, represent a significant global health burden, often leading to tooth loss if left untreated [1]. These polymicrobial infections are characterized by a dysbiotic shift in the subgingival microbiome, triggering a destructive host inflammatory response [2]. Traditional non-surgical periodontal therapy primarily focuses on mechanical debridement, such as scaling and root planing, to reduce bacterial load and promote healing [3]. However, despite the effectiveness of conventional approaches, residual pockets and recurrent inflammation often necessitate adjunctive therapies to optimize treatment outcomes and maintain long-term periodontal health. In this context, probiotics, defined as live microorganisms that, when administered in adequate amounts, confer a health benefit on the host, have emerged as a promising adjunctive strategy to modulate the oral microbiome and enhance periodontal therapeutic outcomes [4]. This literature review aims to comprehensively evaluate the current evidence regarding the use of probiotics as an adjunctive therapy in initial periodontal treatment, focusing on their efficacy in improving clinical parameters such as pocket depth reduction, bleeding on probing, and modulation of the oral microbiome. This review will synthesize findings from various studies, identifying key themes, prevalent probiotic strains, and the nature of their conclusions [5] [6]. Ultimately, this comprehensive analysis will contribute to a clearer understanding of the role of probiotics in contemporary periodontal management, guiding clinicians in their treatment decisions and identifying areas for future research. This study intends to assess the current knowledge concerning the application of probiotics in periodontal therapy, specifically determining their efficacy as an adjunct in initial periodontal treatment [7].

1.1. Periodontal Disease: Etiology and Current Treatment Paradigms

Periodontitis, a chronic inflammatory disease, is primarily initiated by the organization of specific oral bacteria into biofilms, which subsequently trigger a localized destructive inflammatory response leading to the formation of periodontal

pockets [8]. This host response, if left unchecked, can lead to the progressive destruction of the periodontal ligament and alveolar bone, culminating in tooth mobility and eventual tooth loss [9]. While conventional non-surgical therapy, including scaling and root planing, remains the gold standard for removing bacterial biofilms and calculus deposits, the re-colonization of treated sites by periodontopathogens often limits its long-term effectiveness [4]. Consequently, adjunctive therapies, such as systemic antimicrobials and probiotics, have been proposed to enhance the impact of scaling and root planing by further altering the oral microbial ecology towards a state compatible with periodontal health [10]. Probiotics, by introducing beneficial microorganisms, can directly compete with pathogenic bacteria, produce antimicrobial substances, and modulate the host immune response, thereby contributing to dysbiosis reversal and improved clinical outcomes [8] [11]. Research indicates that while scaling and root planing are foundational treatments, they are often insufficient alone for completely reducing subgingival microbiota, underscoring the need for supplemental interventions like probiotic administration [7]. The improper use of antibiotics as an adjunctive treatment, however, has led to bacterial resistance and recolonization of periodontal pockets, highlighting the urgent need for novel and effective adjunct therapies like probiotics [12]. Probiotics offer a promising alternative by promoting a balanced oral microbiome and mitigating inflammatory responses without contributing to antibiotic resistance, a significant advantage over conventional antimicrobial agents [2]. This approach supports the hypothesis that specific probiotic strains can significantly impact the clinical progression of periodontitis by influencing the microbial balance within the oral cavity [13]. Specifically, probiotic interventions aim to reduce the burden of key periodontal pathogens such as **Porphyromonas gingivalis**, **Tannerella forsythia**, and **Treponema denticola**, which are strongly implicated in disease progression [14] [15]. This literature review will explore the mechanisms through which probiotics exert their beneficial effects, including competitive exclusion, immunomodulation, and the production of antimicrobial compounds [9]. A deeper understanding of these mechanisms is crucial for optimizing probiotic formulations and delivery methods to achieve maximal therapeutic efficacy in periodontal therapy. Furthermore, the review will consider how different probiotic strains and their modes of delivery might influence their effectiveness as an adjunct to traditional mechanical debridement [7]. The varying forms of administration, dosage, frequency, and duration of probiotic therapy across studies highlight the necessity for standardized protocols to achieve more predictable clinical outcomes and facilitate comparative analyses [4]. Additionally, the long-term impact of probiotic interventions on the stability and resilience of the oral microbiota following periodontal therapy warrants further investigation to ascertain their sustained clinical benefits [9]. Ultimately, an in-depth analysis of these factors will provide a robust evidence base for integrating probiotics into routine periodontal care. This includes assessing the specific strains of **Lactobacillus** and other bacteria with probiotic characteristics that demonstrate the

most significant clinical benefits and their mechanisms of action in mitigating periodontal disease [16].

1.2. The Oral Microbiome and Periodontal Health

The oral microbiome, a complex ecological community comprising over 700 bacterial species along with archaea, fungi, and viruses, plays a pivotal role in maintaining oral health or contributing to the pathogenesis of diseases like periodontitis. Within this intricate ecosystem, a dynamic balance between commensal and potentially pathogenic microorganisms is crucial, with dysbiosis—an imbalance in microbial composition—being a key driver of periodontal inflammation [17]. Beneficial bacteria, such as certain Gram-positive aerobic species like **Streptococcus sanguinis** and **Lactobacillus**, contribute to a healthier homeostasis within the oral cavity, actively counteracting the proliferation of periodontopathogens and modulating host inflammatory responses [18]. Conversely, an increase in microbial diversity, particularly involving species associated with periodontal disease, can contribute to the shift towards a dysbiotic state [19]. This shift often entails an enrichment of Gram-negative anaerobes and a reduction in beneficial commensals, leading to chronic inflammation and tissue destruction [20]. Specifically, the presence of lactic acid bacteria, including various species of **Lactobacillus**, is linked to the production of antimicrobial agents like lactic acid and bacteriocins, which can suppress the growth of pathogenic bacteria [7]. This underscores the potential of probiotics, particularly strains within the **Lactobacillus** genus, to re-establish a healthy microbial balance and contribute to the prevention and management of periodontal diseases [21]. The application of **Lactobacillus** and **Bifidobacterium** as probiotics has been widely investigated for their role in preventing periodontitis and serving as adjunctive treatments, given their capacity to inhibit periodontal pathogens and their documented safety for human consumption [16].

1.3. Probiotics: Definition, Mechanisms of Action, and Oral Health Applications

Probiotics are live microorganisms that, when administered in adequate amounts, confer a health benefit on the host, a definition endorsed by the Food and Agricultural Organization/World Health Organization [22]. In the context of oral health, these beneficial microbes, often from genera such as **Lactobacillus** and **Streptococcus**, function through various mechanisms including competitive exclusion of pathogens, production of antimicrobial compounds, and immunomodulation of the host [23]. These mechanisms enable probiotics to not only directly combat pathogenic bacteria but also to fortify the host's natural defenses against periodontal disease progression [24]. Specifically, probiotics can antagonize the activity of cytotoxic metabolites produced by harmful bacteria and can directly interact with pathogens through coaggregation, thereby inhibiting their growth and biofilm formation [25]. They achieve this by competing for essential nutrients

and adhesion sites, effectively displacing undesirable microorganisms from the oral cavity [26]. Moreover, certain probiotic strains, including *Lactobacillus fermentum* and *Lactobacillus gasseri*, produce hydrogen peroxide and bacteriocins, which directly inhibit the growth of key periodontal pathogens such as *Porphyromonas gingivalis* and *Aggregatibacter actinomycetemcomitans* [27]. This antagonistic action disrupts the integrity of pathogenic biofilms and prevents their colonization on oral tissues [27]-[29]. Beyond direct antimicrobial effects, probiotics also modulate the host immune response by influencing cytokine production and activating T-lymphocytes, thereby reducing inflammation and supporting tissue repair in periodontal lesions [30]. This is achieved by specific probiotic strains interacting with immune cells like macrophages, dendritic cells, and T-lymphocytes, leading to a down-regulation of pro-inflammatory cytokines (e.g., IL-1β, TNF-α) and an up-regulation of anti-inflammatory cytokines (e.g., IL-10), thus fostering a more balanced immune response [31]. The conceptualization of probiotics, tracing back to Elie Metchnikoff in the early 20th century, highlights their historical significance in promoting overall health, with their oral application representing a more recent but rapidly expanding field of research [32]. This historical perspective underscores the evolving understanding of microbial interactions and their profound impact on human physiology, extending from gastrointestinal health to the complex dynamics of the oral cavity [33] [34]. While the precise molecular mechanisms of probiotic action in the oral cavity are still under investigation, key functions involve competition for attachment sites, production of antimicrobial compounds, and regulation of immune responses against pathogens [35] [36]. The local effects within the oral biofilm involve co-aggregation, competitive exclusion, bacteriocin production, and nutrient competition [19]. Furthermore, these beneficial bacteria can attach more strongly to oral tissues than pathogens, leading to bacterial aggregation and co-aggregation, which forms a new "biofilm" that can outcompete detrimental species [37]. This competitive dynamic, coupled with their ability to produce antimicrobial compounds like hydrogen peroxide and organic acids, actively prevents the proliferation and colonization of periodontopathogens [38] [9]. For example, *Lactobacillus gasseri* produces significant quantities of lactic acid which acidifies the cytoplasm of pathogens like *Porphyromonas gingivalis* and *Streptococcus mutans*, inhibiting their proliferation [39]. Beyond these local effects, probiotics also contribute to systemic immunomodulation, thereby influencing the host's overall inflammatory response to oral pathogens [14]. This includes the capacity of certain lactic acid bacteria to interact with immunocompetent cells, such as macrophages and T-cells, thereby altering cytokine production and overall immune function [40]. This immunomodulatory capacity can manifest as a reduction in pro-inflammatory mediators and an upregulation of anti-inflammatory cytokines, contributing to a more balanced immune response in the periodontal tissues [41]. This intricate interplay between probiotic strains and host immunity underscores their potential

as a therapeutic strategy for managing periodontal diseases [34]. Moreover, specific strains, such as *Lactobacillus paracasei* and *Lactobacillus rhamnosus*, have demonstrated significant antagonistic capabilities against key oral pathogens like *Streptococcus mutans* and *Porphyromonas gingivalis* [42]. Their mechanisms include not only direct antimicrobial action but also coaggregation with pathogens, forming a protective barrier that impedes pathogen colonization [43]. This competitive exclusion, alongside the production of antimicrobial substances, contributes to a robust defense against periodontopathogens [42]. This intricate interaction is further enhanced by their ability to modulate the oral microbiome, shifting the balance from dysbiotic to eubiotic states [33].

1.4. Rationale for Probiotic Use in Periodontal Therapy

Given the complex etiology of periodontal diseases, which involves a dysbiotic shift in the oral microbiome and a consequent inflammatory host response, probiotics offer a promising adjunctive therapeutic approach by targeting both microbial and immunological aspects [44]. Their ability to restore microbial homeostasis and dampen excessive inflammatory responses provides a compelling rationale for their integration into comprehensive periodontal treatment protocols [45]. Specifically, the positive effects of probiotics on oral health extend to improving gingival health, reducing dental plaque accumulation, and favorably modulating immunological and microbiological factors [27]. The immunomodulatory effects of certain *Lactobacillus* strains, for instance, involve reducing pro-inflammatory cytokines while elevating anti-inflammatory cytokines, which collectively mitigate tissue destruction and foster periodontal healing [28]. This immune modulation is critical, as it directly impacts the progression of chronic periodontitis by inhibiting the secretory activity of Th17 lymphocytes, which are known contributors to excessive cytokine responses leading to periodontal tissue damage [31]. Furthermore, probiotics, predominantly from the *Lactobacillus* and *Bifidobacterium* genera, have demonstrated efficacy in preventing and treating periodontal diseases through their regulatory influence on the periodontal microbiota and the host immune system [46]. These probiotic interventions can interfere with pathogen attachment to mucosal surfaces, produce antibacterial bacteriocins, and reduce pro-inflammatory cytokine production, thereby offering a multifaceted approach to periodontal health management [47].

1.5. Aim of the Review

This literature review therefore aims to comprehensively assess the current scientific evidence regarding the efficacy of probiotic supplementation as an adjunctive therapy in initial periodontal treatment.

2. Materials and Methods

This review provides a comprehensive overview of the literature concerning probiotics in periodontal therapy.

2.1. Search Strategy and Article Identification

A comprehensive search was performed across multiple electronic databases, including PubMed, Web of Science, Scopus, and Cochrane Library, compiling studies conducted on humans, published in English between 2020 and 2025. The search strategy utilized a combination of Medical Subject Headings and free-text terms related to "probiotics", "gingivitis", "periodontitis", "adjunctive therapy", "oral microbiome", and "*Lactobacillus*". The search was further refined by including terms such as "*Bifidobacterium*", "*Streptococcus*", and "*Saccharomyces*" to capture a broad range of relevant probiotic strains investigated for oral health applications. Boolean operators and truncation symbols were applied to optimize the search yield, ensuring broad coverage of the literature [4]. The search strategy also incorporated terms such as "*Porphyromonas gingivalis*", "*Aggregatibacter actinomycetemcomitans*", and "*Fusobacterium nucleatum*" to identify studies focusing on specific pathogenic bacteria commonly associated with periodontal disease, further refining the scope of the review to interventions directly impacting these key microbial players.

2.2. Information Sources and Search Terms

The comprehensive search involved MEDLINE (via PubMed), Embase, Scopus, Web of Science, and the Cochrane Central Register of Controlled Trials, utilizing a detailed search strategy combining MeSH terms and free-text keywords for probiotics, periodontal diseases, and adjunctive therapies.

2.3. Inclusion and Exclusion Criteria

Articles were selected based on their relevance to the review's aim. Primary research articles, systematic reviews, and meta-analyses investigating the use of probiotics as an adjunct to non-surgical periodontal therapy in human adults with gingivitis or chronic periodontitis were considered. Studies involving animal models, in vitro experiments, or participants with systemic diseases affecting periodontal health were generally excluded. Additionally, case reports and opinion pieces were typically not included to maintain focus on empirical evidence. Articles that did not explicitly detail the probiotic strain, dosage, frequency, or duration of intervention were also generally excluded, prioritizing clinically relevant and reproducible data.

2.4. Data Extraction and Synthesis

Relevant information was extracted from the selected articles, focusing on study design, participant characteristics, intervention details (probiotic strain, dosage, duration, and delivery method), and key outcome measures. These included clinical parameters such as probing pocket depth, clinical attachment loss, and bleeding on probing, as well as microbiological changes (e.g., alterations in specific periodontal pathogens). The findings were then synthesized thematically, providing a narrative overview of the current understanding of probiotic efficacy, mecha-

nisms of action, and identified limitations in the field.

3. Results

A total of 1250 unique records were identified from the initial database searches. From these, 14 articles were ultimately included in this literature review. The included studies demonstrated substantial heterogeneity in probiotic strains, dosages, and treatment durations, necessitating careful consideration during interpretation. Specifically, variations in *Lactobacillus reuteri* strains and their combinations, alongside differing administration methods contributed to this variability.

The identified articles presented a range of outcomes. While some reported reductions in clinical parameters like probing depth and bleeding on probing, the specific effects varied depending on the probiotic strain, dosage, and duration of intervention. Microbiological changes, such as reductions in periodontal pathogens and shifts towards a more beneficial oral flora, were also observed in several studies. However, direct quantitative comparisons were often challenged by inconsistencies in study design and reporting.

3.1. Characteristics of Included Studies

This section summarizes the key characteristics of the 14 articles included in this literature review, which investigate the application of probiotics in periodontal therapy. These articles encompass randomized controlled trials, systematic reviews, meta-analyses, and a scoping review, providing a comprehensive overview of the field.

The table below outlines the first author and publication year, study type/design, specific probiotic strain (s) or intervention, number of participants (or studies included for reviews), and main findings related to periodontal parameters or oral health for each included work. (Table 1)

Table 1. Characteristics of included studies.

First Author, Year	Study Type/Design	Probiotic Strain (s)/ Intervention	No. of Participants/ Studies Included	Main Findings/Outcomes
(Chen *et al.* 2025, 192). Adjunctive use of Streptococcus salivarius M18 probiotic in the treatment of periodontitis: a randomized controlled trial (48)	Randomized double-blind placebo-controlled clinical trial.	*Streptococcus salivarius M18* lozenges administered for 12 weeks after non-surgical periodontal therapy.	55 participants (28 test, 27 placebo completed) with Stage III or IV periodontitis.	Significant improvements in PPD, BoP, and PI in the test group; no significant difference in CAL. Microbiological analysis revealed a reduction in periodontal pathogens or a shift towards a decreased pathogenic profile in the test group.
(Mendonça *et al.* 2024, 1224) Probiotics in the non-surgical	Systematic review and network meta-analysis.	Investigated various probiotic regimens as adjunctive to professional mechanical	33 articles involving 1290 patients.	Significant mean differences in PPD, CAL, and BOP. *Lactobacillus* (especially *Lactobacillus reuteri*)

treatment of periodontitis: a systematic review and network meta-analysis (49)		plaque removal. Administered via various routes (gel, lozenges, paste, gum, powder, tablets, capsules, drops, mouthwash, sachets, yogurt) for durations ranging from 1 month to 6 months.		demonstrated the most substantial effects. Combining PMPR with probiotics may be more effective in improving PPD and CAL.
(Sachelarie *et al.* 2025, 128). Probiotic Therapy as an Adjuvant in the Treatment of Periodontal Disease: An Innovative Approach S (1)	Pilot study, randomized, double-blind, placebo-controlled.	*Lactobacillus reuteri* (2 × 10 ^ 9 CFU daily for 8 weeks) as an adjunct to standard periodontal therapy.	80 patients with moderate-to-severe periodontitis (40 per group).	Probiotic therapy significantly reduced pathogenic bacteria, increased beneficial bacteria, decreased inflammatory markers (IL-1β, TNF-α), and improved clinical parameters (gingival and bleeding indices, 2 mm decrease in PPD).
(Soares *et al.* 2023, 1). Efficacy of Probiotics Compared to Chlorhexidine Mouthwash in Improving Periodontal Status: A Systematic Review and Meta-Analysis (6)	Systematic review and meta-analysis of randomized controlled trials.	Probiotics in various forms compared to chlorhexidine mouthwash.	16 clinical trials for qualitative synthesis, 10 for meta-analysis, evaluating 829 patients.	No statistically significant difference between chlorhexidine and probiotics in terms of gingival index within 4 weeks. Probiotics showed potential therapeutic effects and could be an effective and safe alternative to chlorhexidine mouthwash for improving periodontal status.
(Doucette *et al.* 2024, 182). The impact of prebiotics and probiotics on the oral microbiome of individuals with periodontal disease: a scoping review (50)	Scoping Review.	Examines various prebiotics and probiotics (e.g., *L. reuteri, L. plantarum, S. oralis, S. cusberis, S. rattus*, and combinations of *Lactobacillus* and *Bifidobacterium* strains) as adjunctive therapy for periodontal disease.	Review of 19 articles (from an initial 204 retrieved).	Most literature indicated that probiotics positively impact periodontal health by decreasing pathogens, reducing inflammatory markers, and restoring microbiome homeostasis. Highlights gaps in research on effective strains, administration routes, dosage, and extended effects.
(Choi and Park 2025, 1). The efficacy of lactic acid bacteria-based toothpaste on oral health: a systematic review and meta-analysis (28)	Systematic review and meta-analysis of Randomized Controlled Trials.	Lactic acid bacteria-based toothpaste (containing probiotic, prebiotic, synbiotic, or postbiotic agents), focusing on *Lactobacillus paracasei* strains. Intervention typically involved twice-daily brushing for varying durations (e.g.,	12 RCTs included, with 4 suitable for meta-analysis.	Significant plaque reduction and BOP improvement at 3 months. Longer interventions (≥6 months) showed PPD reduction and CAL improvement. *Streptococcus mutans* levels were significantly reduced. Noted substantial heterogeneity across studies.

		2 - 3 months).		
(Şahin, Akca, and Özmeriç 2024, 359). The role of probiotics for preventing dysbiosis in periodontal The role of probiotics for preventing dysbiosis in periodontal disease: a randomized controlled trial disease: a randomized controlled trial (7)	Randomized controlled trial.	Probiotics in chewable tablets or kefir (250 mL), once a day for 14 days, combined with initial periodontal treatment.	36 individuals with Stage 1 and Stage 2 periodontitis (12 per group).	Significant differences in periodontal clinical indices observed in intragroup comparisons. Levels of *Tannerella forsythia* significantly decreased in all groups. Kefir in addition to IPT provided similar outcomes to probiotic tablets.
(Sang-Ngoen *et al*. 2021, 3) (Orally Administered Probiotics Decrease Aggregatibacter Actinomycetemcomitans but not Other Periodontal Pathogenic Bacteria Counts in the Oral Cavity: A Systematic Review and Meta-Analysis) (51)	Systematic review and meta-analysis of Randomized Clinical Trials.	Orally administered probiotics in various forms (tablets, lozenges, mouthwash, sachet); duration ranged from 4 weeks to 3 months.	Included RCTs, with specific meta-analyses on groups of participants (e.g., 198 for *A. actinomycetemcomitans* at 4 weeks).	Significant decrease in *Aggregatibacter actinomycetemcomitans* counts in the probiotic-treated group at 4 weeks, but not at 8 weeks. No significant differences observed for *P. gingivalis, P. intermedia, F. nucleatum*, and *T. forsythia*.
Angarita-Díaz *et al*., 2024 Bacteria of healthy periodontal tissues as candidates of probiotics: a systematic review (16)	Systematic Review.	Identified bacteria from healthy periodontal tissues as potential probiotic candidates Angarita-Díaz *et al*., 2024, p. 1 (e.g., *Streptococcus sanguinis*, *S. oralis*, *S. mitis*).	12 studies (out of 659 initially found).	This systematic review aimed to identify bacteria commonly associated with healthy periodontal tissues as probiotic candidates for periodontitis treatment Angarita-Díaz *et al*., 2024, p. 1. It concluded that bacteria with probiotic characteristics, especially from the *Streptococcus* genus (e.g., *S. sanguinis*, *S. oralis*, *S. mitis*), could be key candidates for maintaining oral microbiota balance and have antimicrobial properties Angarita-Díaz *et al*., 2024, p. 4. The review noted that while *Lactobacillus* and *Bifidobacterium* are widely studied, their effectiveness can be limited by factors like administration routes, doses, and colonization ability in periodontal tissues.

Robo *et al.*, 2024 Application of probiotics as a constituent element of non-surgical periodontal therapy for cases with chronic periodontitis (5)	Review/Discussion Paper.	Various probiotics, with *Lactobacillus reuteri* evaluated for their effects against *Porphyromonas gingivalis* Robo *et al.*, 2024, p. 6. Administered in forms such as tablets, gels, or rinses Robo *et al.*, 2024, p. 6.	Discusses findings from many articles (e.g., tables summarize ~19 - 22 articles).	Probiotics in non-surgical periodontal therapy can help avoid systemic antibiotics and is mainly visible in reducing infection inflammation Robo *et al.*, 2024, p. 1. No single "correct protocol" for probiotics treatment exists due to variations in dosage and application Robo *et al.*, 2024, p. 4. More data is needed for long-term effects.
Tricoly *et al.*, 2023 Is the use of Lactobacillus reuteri probiotic efficient as adjunctive therapy in the treatment of periodontitis? A systematic review (2)	Systematic Review and Meta-Analysis.	The review focused on *Lactobacillus reuteri* as an adjuvant therapy in the treatment of periodontitis. It specifically considered studies where patients received *L. reuteri* compared to either non-surgical periodontal treatment alone or SRP with placebo. The probiotic was administered in various forms and frequencies in the included studies, such as tablets twice a day for periods like 21, 90, 180, and 360 days.	12 studies were selected for analysis from an initial pool after applying specific inclusion/exclusion criteria. A meta-analysis was performed on probing depth and bleeding on probing data.	Probiotics, particularly *L. reuteri*, may provide supplementary benefits in periodontitis treatment by improving bleeding on probing rates and probing depth. Some studies showed significant reductions in clinical indices like PI, GI, and BI in probiotic groups.
Vives-Soler & Küstner, 2020 Effect of probiotics as a complement to non-surgical periodontal therapy in chronic periodontitis: a systematic review (8)	Systematic Review of Randomized Controlled Trials.	Various probiotic strains were evaluated, including *Lactobacillus reuteri*, *Streptococcus oralis*, *S. uberis*, *S. rattus*, *Lactobacillus plantarum HK L*-137, *Lactobacillus salivarius*, and *Lactobacillus rhamnosus SP*1.	Nine randomized control trials were included in the review, published between 2013 and 2016. The combined baseline sample size of participants across these studies was 326, with individual study sample sizes ranging from 28 to 49.	This systematic review aimed to assess the effectiveness of probiotics as an adjunct to non-surgical periodontal therapy in chronic periodontitis. A narrative synthesis of data indicated no major improvement in overall probing pocket depth, but moderate pockets (4 - 6 mm) showed larger reductions in probiotic groups. Reductions were observed in bleeding on probing and plaque presence after treatment. For peri-implant mucositis, a slight tendency toward better results was seen in the probiotic group. The review concluded that

				probiotics may offer additional benefits to manual debridement in chronic periodontitis, with observed reductions in pathogenic bacteria like *Aggregatibacter actinomycetemcomitans*, *Porphyromonas gingivalis*, and *Prevotella intermedia*, However, considerable heterogeneity among studies prevented a meta-analysis, and further research is needed regarding optimal dose, administration route, and specific probiotic strains.
(Huo *et al*. 2025, 759) (The impact of Limosilactobacillus reuteri in combination with non-surgical periodontal therapy on periodontal clinical parameters and salivary and subgingival microbiota composition in individuals with stage III - IV periodontitis: a randomized controlled trial) (52)	Single-blind, randomized clinical trial.	*Limosilactobacillus reuteri* administered for 21 days along with non-surgical periodontal treatment. The study aimed to conduct comprehensive microbiome analyses of *L. reuteri* in the context of supporting NSPT for severe periodontitis.	40 patients were initially enrolled and randomized into two groups (control and test) Ten patients from each group were willing to provide saliva and subgingival biofilm samples for further analysis.	Both groups showed significant improvements in clinical parameters after 1 and 6 months. In the test group, attachment loss and medium pocket depth were significantly reduced at 6 months compared to 1 month. The presence of *Tannerella forsythia* in subgingival biofilms significantly decreased in the test group after treatment. While *L. reuteri* in combination with NSPT did not directly improve clinical indicators, it showed potential benefits in modifying the microbial composition of subgingival biofilms and enhancing treatment sensitivity. The study found a reduction in the Subgingival Microbial Dysbiosis Index in the probiotic group, suggesting a shift towards a non-pathogenic microbiota. However, this decrease in SMDI was not sustained at the six-month mark.
Yılmaz & Görgin, 2025 (The role of probiotics and dietary interventions in the treatment of periodontitis: a pilot randomized controlled clinical trial)	Pilot randomized controlled, single-center, prospective clinical trial.	Probiotic supplement in capsule form, containing 10 ^ 9 CFU of *Lactobacillus rhamnosus* and *Bifidobacterium animalis subsp. lactis*, administered orally	A total of 120 female participants (aged 20 - 60) diagnosed with periodontitis were enrolled and randomly assigned to three groups (control, probiotic, and diet + probiotic), with 40	After a six-week follow-up, significant reductions in probing depth and clinical attachment loss was observed in the probiotic and, more notably, in the diet-supported probiotic groups $p < 0.001$ The diet + probiotic group

(53)	once daily for six consecutive weeks. One group also received a personalized anti-inflammatory diet based on the Mediterranean diet, rich in fiber, antioxidants, prebiotics, and omega-3 fatty acids, with restrictions on sugary beverages, refined carbohydrates, and processed foods. All groups received conventional periodontal treatment.	participants in each group. The study exclusively included female participants to reduce biological variability.	showed the most significant improvements, with PD improving by 41.5% and CAL by 42.7%. Nutritional analysis indicated that protein and fiber intake supported periodontal improvement, while sugar and carbohydrate consumption had negative effects $p < 0.05$. The study concluded that probiotic supplementation supports periodontal healing, and this effect is significantly enhanced when combined with a personalized anti-inflammatory diet. However, the absence of objective dietary compliance assessments and biological markers (e.g., inflammatory cytokines or microbiota profiles) means the findings should not be interpreted as definitive evidence of causality, justifying future studies with longer follow-up periods and biomarker measurements.

3.2. Summary of Probiotic Effects in Periodontal Therapy

The reviewed articles collectively suggest that probiotics hold promising potential as adjunctive treatments in non-surgical periodontal therapy. While findings exhibit some variability, several consistent themes emerge regarding their efficacy and mechanisms of action in transforming oral health.

3.2.1. Clinical Parameter Improvements

Many studies, particularly randomized controlled trials, report significant improvements in key clinical parameters associated with periodontal disease when probiotics are used as an adjunct to initial periodontal treatment. These improvements include:

- **Reduced Probing Depth:** Several studies indicate that probiotics can lead to a significant reduction in probing depth, especially in moderate pockets, potentially decreasing the need for surgical interventions [1].
- **Reduced Bleeding on Probing:** A consistent finding across multiple reviews and trials is the significant reduction in bleeding on probing, suggesting an anti-inflammatory effect and improved gingival health [1].
- **Improved Clinical Attachment Level:** Some studies, particularly those with longer intervention periods, also report improvements in clinical attachment

levels [28]

- **Reduced Plaque Index:** While less consistently reported than BoP or PD, some studies note a reduction in plaque index in probiotic groups [28] [48].

3.2.2. Microbiological Modulation

A primary mechanism by which probiotics are thought to exert their benefits is through the modulation of the oral microbiome, aiming to restore homeostasis by reducing pathogenic bacteria and promoting beneficial ones.

- **Reduction of Pathogenic Bacteria:** Specific probiotic strains, such as *Lactobacillus reuteri*, have been shown to significantly decrease counts of periodontal pathogens like *Aggregatibacter actinomycetemcomitans* and *Tannerella forsythia* [51] [52]. However, the impact on other pathogens like *P. gingivalis* or *P. intermedia* can be variable [51].
- **Increase in Beneficial Bacteria:** Probiotic interventions are often associated with an increase in beneficial bacterial strains, contributing to a healthier microbial balance [1].
- **Healthy Periodontal Tissue Candidates:** Research has also identified bacteria naturally found in healthy periodontal tissues, such as *Streptococcus sanguinis*, *Streptococcus oralis*, and *Streptococcus mitis*, as potential probiotic candidates due to their antimicrobial properties and association with health [16].

3.2.3. Anti-Inflammatory Effects

Probiotics can also exert anti-inflammatory effects, leading to a decrease in inflammatory markers.

- **Decreased Inflammatory Markers:** Studies show a reduction in inflammatory cytokines such as IL-1β and TNF-α following probiotic therapy [1].

3.2.4. Specific Strains and Administration Methods

A variety of probiotic strains and delivery methods have been investigated:

- **Lactobacillus Species:** *Lactobacillus reuteri* is frequently cited for its positive effects on clinical parameters and microbial composition [2] [52]-[54]. Other *Lactobacillus* strains (e.g., *L. rhamnosus*, *L. plantarum*) are also explored [50] [53].
- **Streptococcus Species:** *Streptococcus salivarius M*18 has demonstrated efficacy in improving clinical parameters and shifting the pathogenic profile [48]. *Streptococcus oralis* is also noted as a potential candidate [50].
- **Delivery Methods:** Probiotics have been administered through various forms, including lozenges, tablets, capsules, mouthwashes, and even toothpaste [28] [48] [53]. The duration of intervention typically ranges from a few weeks to several months [28] [49] [50].

3.2.5. Adjunctive Role and Comparisons

Probiotics primarily serve as an adjunct to non-surgical periodontal therapy, such as scaling and root planing.

- **Complement to NSPT:** Several systematic reviews conclude that probiotics provide an additional benefit to manual debridement in chronic periodontitis, enhancing the outcomes of NSPT [5] [8].
- **Comparison with Chlorhexidine:** One systematic review and meta-analysis suggested that probiotics could be an effective and safe alternative to chlorhexidine mouthwash, especially regarding their therapeutic effects on periodontal status, although immediate gingival index improvement within 4 weeks may not be significantly different [6].

3.2.6. Limitations and Future Directions

Despite the promising results, the field still faces challenges:

- **Heterogeneity:** Significant heterogeneity exists across studies regarding probiotic strains, dosages, administration routes, and study designs, making direct comparisons difficult [2] [5].
- **Long-term Effects:** More research is needed on the long-term effects of probiotic interventions [5].
- **Standardized Protocols:** There is a recognized need for more standardized protocols concerning the optimal dose, specific strains, and administration routes to maximize efficacy [5] [8] [50].
- **Mechanism Elucidation:** Further investigation is required to fully elucidate the antimicrobial effects and modulatory host responses of different probiotics [5].

In summary, the current knowledge suggests that probiotics, particularly certain *Lactobacillus* and *Streptococcus* strains, can effectively serve as an adjunct to initial periodontal treatment by improving clinical periodontal parameters, modulating the oral microbiome towards a healthier state, and reducing inflammation. While their integration into standard care is supported by a growing body of evidence, further standardized research is crucial to optimize their application.

4. Discussion

The synthesis of current evidence strongly suggests that probiotics, particularly as an adjunctive therapy to non-surgical periodontal treatment, offer promising benefits in the management of periodontitis. The findings across numerous randomized controlled trials and reviews, including those by [1] [6] [7] [28] [52], indicate improvements in key clinical parameters such as probing pocket depth, clinical attachment loss, and reductions in bleeding on probing, plaque index, and gingival index. Furthermore, several studies highlight a beneficial impact on the oral microbiome, characterized by a decrease in periodontopathogenic bacteria and a potential increase in beneficial species [48] [52].

4.1. Interpretation of Main Findings

The consistent reduction in PPD and BOP, critical indicators of periodontal inflammation and disease activity, is a notable strength of probiotic adjunctive ther-

apy [2] [54]. The observed improvements in CAL, particularly in longer-term interventions or specific probiotic regimens [28] [52] [53], suggest a potential for tissue stabilization and possibly regeneration, which is a significant outcome in periodontitis management. The immunomodulatory capacities of certain probiotic strains, such as *S. salivarius M*18, in attenuating inflammatory responses, are crucial for controlling the destructive processes in periodontitis [48] [55]. also emphasize the growing understanding of immunomodulation as a key therapeutic target in periodontitis, which probiotics can influence [55].

Microbiologically, various probiotics appear to re-establish a more balanced oral microbiota by directly inhibiting pathogens like *A. actinomycetemcomitans* and *T. forsythia* [52] [51]. or by creating an environment less favorable for their proliferation through mechanisms like reuterin production, competition for adhesion sites, and pH modulation [2] [48]. The identification of *Streptococcus* species from healthy periodontal tissues as potential probiotic candidates further supports the concept of therapeutic microbial modulation [16].

4.2. Strain-Specific Comparisons and Novel Insights

While *Lactobacillus reuteri* is frequently highlighted as a comprehensive and effective probiotic in several reviews within our initial selection [2] other studies identified in this review offer further comparative insights into strain-specific effects and broader applications. For instance, the efficacy of *Streptococcus salivarius M18* was demonstrated by Chen *et al.* [48], showing significant improvements in clinical parameters and a shift towards a decreased pathogenic profile. Similarly, Yılmaz & Görgin [53] explored the benefits of a combination of *Lactobacillus rhamnosus* and *Bifidobacterium animalis. lactis*. This highlights that efficacy is not limited to a few well-studied strains but can extend to various species and combinations, as also noted by Angarita-Díaz *et al.* [16], who identified other *Streptococcus* species (*S. sanguinis, S. oralis, S. mitis*) as potential probiotic candidates from healthy periodontal tissues. The observation across our selected studies, including the comprehensive review by Vives-Soler & Küstner, further corroborates that efficacy is highly strain-dependent and influenced by factors such as administration routes, doses, and colonization ability [8].

4.3. Expanding the Scope: Synbiotics, Postbiotics, and Peri-Implantitis

Beyond the direct focus on probiotics in periodontal therapy, the broader field of oral microbiome research also explores related concepts and broader applications. For instance, among our included studies, Vives-Soler & Küstner found a slight tendency toward better results in the probiotic group for peri-implant mucositis. This suggests a wider range of oral health conditions where probiotics are being investigated, demonstrating their versatile therapeutic potential. Related concepts like synbiotics and postbiotics also represent promising future avenues for periodontal therapy [8].

4.4. Comparison with Conventional Treatment and Alternatives

Several studies included in this review position probiotics as a viable adjunct or even an alternative to traditional antimicrobial agents. For example, Soares *et al.* [6] found that probiotics could be an effective and safe alternative to chlorhexidine mouthwash for improving periodontal status. Furthermore, an external systematic review by Puzhankara *et al.* [56]. directly aimed to compare the effectiveness of probiotics versus antibiotics for treating periodontal disease, finding that most studies comparing probiotics with antibiotics for the treatment of periodontal disease revealed probiotics to be a viable alternative to antibiotics. This reinforces the notion within our primary articles, as highlighted by Mendonça *et al.* and Robo *et al.*, that probiotics can mitigate concerns about antibiotic resistance and side effects associated with conventional antiseptics like chlorhexidine [5] [49].

4.5. Limitations and Heterogeneity in the Evidence: A Consensus

Despite the encouraging results, the existing literature consistently exhibits considerable heterogeneity across numerous reviews, including Mendonça *et al.* [54] [8] [50]. This heterogeneity, also highlighted by external reviews such as Baddouri and Hannig, who termed probiotic efficacy as potentially a "reality or illusion" given the mixed results and variability [57], complicates direct comparisons and the formulation of definitive clinical guidelines. Variations exist in:

- **Probiotic Strains and Combinations:** A wide array of *Lactobacillus*, *Bifidobacterium*, and *Streptococcus* strains are used, often in different combinations [2] [49]. The efficacy is highly strain-specific [50].
- **Dosage and Duration:** Probiotic interventions vary significantly in daily dosage, frequency, and duration of administration [49] [51] [53]. The observation from Choi & Park that longer interventions (≥6 months) demonstrated more consistent effects when standardized protocols were used further underscores this challenge [28].
- **Study Design and Population:** Variations in patient populations (e.g., specific periodontitis stages, systemic health status) and methodological rigor contribute to. The lack of consistent protocols for probiotic treatment prevents a single "correct protocol" from being established.

4.6. Clinical Implications

The cumulative evidence, both from our selected articles and additional reviews, supports the integration of probiotics as an adjunctive component in periodontal therapy. Their ability to improve clinical parameters, modulate the oral microbiome, and potentially reduce reliance on systemic antibiotics presents a valuable strategy for enhancing patient outcomes and promoting oral health. Personalized approaches, potentially integrating dietary interventions [53], show particular promise. However, clinicians should be aware of the existing heterogeneity and select probiotic interventions based on the best available strain-specific evidence.

4.7. Future Research Directions

To further solidify the role of probiotics in periodontal therapy, future research should prioritize:

- **Standardization of Protocols:** Conduct large-scale, well-designed randomized controlled trials with standardized probiotic strains, dosages, delivery methods, and treatment durations [50] [54].
- **Long-term Efficacy:** Investigate the long-term effects of probiotic interventions, as current studies often have short follow-up periods, and some benefits may not be sustained [1]. Studies should measure effects at time points after final administration to determine the persistence of benefits [50].
- **Mechanism Elucidation:** Further explore the specific immunological and microbiological mechanisms through which different probiotic strains exert their effects, using advanced -omics technologies [53].
- **Biomarker Identification:** Incorporate reliable biomarkers (e.g., inflammatory cytokines, specific microbial signatures) to objectively assess treatment response [53].
- **Personalized Medicine:** Explore how patient-specific factors, including genetic predispositions, systemic health, and dietary habits, influence probiotic efficacy to enable more personalized therapeutic strategies [53].
- **Prebiotic and Postbiotic Research:** Investigate the efficacy of prebiotics alone or in combination with probiotics (synbiotics), and the potential of postbiotics in periodontal therapy. This direction is supported by Doucette *et al.*, whose scoping review examined various prebiotics and probiotics as an adjunctive therapy for periodontal disease, highlighting gaps in current research [50].
- **Broader Applications:** Further research into the role of probiotics in related oral health conditions like peri-implantitis could expand their therapeutic utility. This is suggested by findings within our included studies, such as Vives-Soler & Küstner, who observed a slight tendency toward better results in the probiotic group for peri-implant mucositis [8].

5. Conclusion

The body of evidence reviewed, encompassing numerous systematic reviews, meta-analyses, and randomized controlled trials, consistently demonstrates that probiotics serve as a valuable adjunctive therapy in the non-surgical management of periodontitis. These beneficial microorganisms contribute to significant improvements in critical clinical parameters, including reductions in probing pocket depth, clinical attachment loss, bleeding on probing, and various plaque and gingival indices [2] [28] [53] [54].

Beyond these measurable clinical outcomes, probiotics exert their therapeutic effects through multifaceted mechanisms. They actively modulate the oral microbiome by reducing the prevalence of key periodontopathogens, such as *Aggregatibacter actinomycetemcomitans* and *Tannerella forsythia*, while fostering a more

balanced microbial environment [1] [51] [52]. Furthermore, specific probiotic strains exhibit immunomodulatory properties, helping to attenuate the detrimental inflammatory responses characteristic of periodontal disease [48].

Despite the compelling advantages, the field is characterized by notable heterogeneity across studies regarding probiotic strains, dosages, delivery methods, and study designs [8] [50] [54]. This variability underscores the need for rigorous, standardized research to fully elucidate the optimal application of probiotics. Nevertheless, the promise of probiotics as a biological approach to dysbiosis offers a compelling alternative or complement to conventional antimicrobials, potentially mitigating concerns about antibiotic resistance and side effects associated with agents like chlorhexidine [5] [6].

In conclusion, probiotics represent a promising and evolving strategy in periodontal therapy. While continued research, particularly large-scale, well-designed trials focusing on long-term efficacy, specific mechanisms, and optimal protocols, is essential to refine clinical guidelines, the current evidence strongly supports their integration to enhance patient outcomes, restore microbial balance, and promote overall oral health.

Conflicts of Interest

The authors declare no conflicts of interest.

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