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REVIEW ARTICLE

Effect of probiotic formulations on clinical parameters of gingivitis: A systematic review

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Abstract

Introduction: Gingivitis is a common inflammatory condition associated with dental plaque accumulation and oral microbial dysbiosis, highlighting the need for complementary approaches to support periodontal health.

Objectives: This review examines the effects of oral probiotics on gingivitis, emphasizing clinical outcomes, microbial modulation, specific probiotic strains, administration methods, and their role as adjuncts to professional periodontal care.

Methods: Randomized controlled trials assessing oral probiotic interventions for gingivitis were selected through systematic database searches. Studies were screened based on titles, abstracts, and full texts. The risk of bias of the included studies was assessed using the revised Cochrane risk-of-bias tool for randomized trials. Clinical outcomes such as plaque accumulation, gingival bleeding, and microbiological changes were extracted and summarized qualitatively.

Results: Evidence suggests that oral probiotics can positively influence oral microbiota and reduce gingival inflammation. Certain strains, particularly *Streptococcus salivarius* M18 and *Bifidobacterium animalis* subsp. *lactis* HN019, showed promising clinical effects in individual randomized trials, although results were not uniform across all outcomes or studies. Greater improvements were observed when probiotics were administered over longer periods or alongside professional periodontal therapy. Delivery formulation may influence probiotic exposure and clinical response; however, direct comparisons between lozenges, tablets, and toothpaste are limited. Microbial shifts often preceded measurable clinical improvements. Adverse effects were uncommon and transient. Variability among studies was largely due to differences in strain selection, treatment duration, delivery method, and study design.

Conclusions: Oral probiotics appear to be a promising adjunctive approach for managing gingivitis, with potential benefits for clinical parameters and microbial balance. However, the magnitude and consistency of these effects vary according to strain, formulation, treatment duration, and clinical context. Further adequately powered and standardized trials are needed to determine optimal strains, dosing, delivery systems, and long-term outcomes.

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1. Introduction

In recent years, dentistry has experienced a fundamental transition: from a traditional approach focused solely on pathogen elimination to a biological approach aimed at restoring oral eubiosis. Within this framework, probiotics have emerged as a crucial tool for modulating the oral microbial ecosystem, supporting microbiota resilience during the resolution of inflammatory processes, as demonstrated in experimental gingivitis models.[1-6]

1.1. Mechanisms of action of probiotics

The use of oral probiotics does not aim at surface sterilization, but rather at biological competition. The efficacy of specific strains, such as *Streptococcus salivarius* M18, relies on their dual capacity to reduce plaque accumulation and mitigate gingival inflammation.[7,8] These microorganisms act through multiple mechanisms:

(i) Competition for adhesion sites: preventing pathogenic bacteria from attaching to teeth and gingival surfaces.
(ii) Production of antimicrobial substances: bacteriocins and other metabolites inhibit the growth of pathogenic species.
(iii) Immune modulation: leading to significant reductions in bleeding on probing and pocket depth, particularly in medium-term administration protocols.[9,10]

1.2. Clinical applications as adjuvant therapy

Probiotics appear to provide the greatest clinical benefit when used as adjunctive agents rather than as stand-alone therapies. In gingivitis management, their use has been investigated as a complementary strategy to conventional plaque-control measures, including professional cleaning and routine oral hygiene procedures.[11,12] Unlike traditional antimicrobial approaches aimed primarily at reducing bacterial load, probiotics seek to restore microbial balance through ecological modulation of the oral environment.[13]

Several studies have suggested that selected probiotic strains may contribute to improvements in clinical periodontal parameters, including reductions in gingival inflammation, plaque accumulation, and bleeding on probing. For example, *Bacillus* species have demonstrated beneficial effects on gingival health in adults with gingivitis,[14-28] while other strains, including *Lactobacillus* and *Streptococcus* species, have shown the ability to influence both clinical and microbiological outcomes.[29]

Beyond direct clinical improvements, probiotics may also support the stability and resilience of the oral ecosystem under inflammatory or environmental challenges. This suggests that their therapeutic effect may extend beyond simple symptom reduction and involve broader modulation of the host–microbiota interaction.[30,31]

1.3. Formulations and modes of administration

The delivery vehicle plays a critical role in ensuring microbial viability and effective adherence to oral surfaces. Several formulations have been studied:

(i) Lozenges and orodispersible tablets are among the most frequently investigated delivery systems in the included clinical trials. Their relatively prolonged dissolution may increase the contact time between probiotic microorganisms and the oral environment, potentially facilitating their transient retention on oral surfaces. However, the available evidence does not allow these formulations to be considered a definitive "gold standard," particularly because direct head-to-head comparisons between delivery vehicles are lacking.[32-35]
(ii) Chewing gums: provide simultaneous bacterial release and mechanical stimulation of saliva, improving plaque and gingival indices in short-term interventions, and offering practical home-preventive options.[36,37]
(iii) Toothpastes and daily oral care products: integrating probiotics into toothpaste aims to complement or replace chemical antiseptics, transforming oral hygiene into a "bacterial seeding" phase. Mechanical brushing promotes incorporation of beneficial strains into newly formed biofilm, mitigating effects of dietary stressors such as sugar exposure.[38,39]
(iv) Gels and topical applications: less commonly used at home but valuable professionally, gels allow targeted and viscous application to periodontal pockets or gingival margins, maximizing probiotic concentration in areas affected by acute inflammation and supporting tissue recovery after mechanical therapy.[40-42]

1.4. Safety profile

Oral probiotics generally exhibit a favorable safety profile and are considered well tolerated in individuals with gingival inflammation. Unlike conventional antiseptic agents such as chlorhexidine, probiotic supplementation is not commonly associated with adverse effects including tooth staining, taste alterations, or mucosal irritation, which may negatively affect long-term compliance.[43-48]

Rather than acting through broad antimicrobial elimination, probiotics exert their effects by modulating the oral ecosystem through selective bacterial competition and regulation of host inflammatory responses, helping to maintain microbial balance without disrupting the resident microbiota.[49-54]

Clinical studies investigating probiotics in gingivitis management have reported minimal or no significant adverse events, with occasional mild and transient effects that rarely required treatment discontinuation. Nevertheless, additional long-term studies are still required to further clarify the safety profile of specific probiotic strains and their long-term effects within the oral environment.[55-60]

1.5. Etiopathogenesis of gingivitis

Gingivitis is a reversible inflammatory condition initiated by biofilm accumulation and characterized by alterations in microbial composition and host inflammatory response. The transition from oral eubiosis to dysbiosis contributes to gingival inflammation and may represent a potential target for probiotic modulation.[61-64]

Therefore, the aim of this systematic review was to evaluate the effects of different oral probiotic formulations on clinical and microbiological parameters associated with gingivitis, with particular attention to strain specificity, delivery systems, and their role as adjunctive therapeutic strategies.[36,65-67]

2. Methodology

2.1. Protocol and registration

This systematic review was reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines. The review protocol was registered in the International Prospective Register of Systematic Reviews (registration number CRD420261415386).

2.2. Literature search strategy

A comprehensive literature search was conducted in PubMed, Scopus, and Web of Science to identify clinical studies evaluating the effects of oral probiotic interventions on gingival inflammation and related clinical periodontal outcomes in individuals diagnosed with gingivitis.

The time restriction (2015–2025) was applied to capture the most recent and methodologically consistent evidence, reflecting advances in probiotic formulations, strain selection, delivery systems, and the increasing use of standardized clinical and microbiological outcome measures in periodontal research.

Only English-language studies were included to ensure methodological consistency and accurate interpretation of clinical, microbiological, and patient-related outcomes, while minimizing potential variability associated with translation.

The following search string, incorporating Boolean operators and relevant keywords, was adapted for each database to identify eligible studies:

("probiotics" OR "oral probiotics" OR "Lactobacillus" OR "Bifidobacterium" OR "Streptococcus salivarius") AND ("gingivitis" OR "gingival inflammation") AND ("clinical outcomes" OR "plaque index" OR "bleeding on probing" OR "oral microbiota")

Search strategies were adapted according to the indexing terms and search requirements of each database. Additionally, the reference lists of selected articles were manually screened to identify potentially relevant studies not captured through the initial database search.

Due to substantial heterogeneity among the included studies in terms of probiotic strains, administration protocols, intervention duration, study design, and outcome measures, a quantitative meta-analysis was not considered appropriate; therefore, a qualitative synthesis of findings was performed.

2.3. Inclusion and exclusion criteria

Articles were independently screened and selected by two reviewers according to predefined inclusion and exclusion criteria. The review process followed the Population, Intervention, Comparison, Outcome, and Study design (PICOS) framework.

Studies were included if they met the following criteria:

(i) Human participants diagnosed with gingivitis;
(ii) Randomized controlled trials;
(iii) Studies evaluating oral probiotic interventions administered in different formulations (e.g., lozenges, tablets, toothpaste, or other delivery systems);
(iv) Studies reporting clinical periodontal outcomes and/or microbiological findings.

The exclusion criteria were:

(i) Review articles and meta-analyses;
(ii) Animal and in vitro studies;
(iii) Cross-sectional studies, case reports, and observational studies;
(iv) Articles not written in English;
(v) Studies lacking sufficient clinical outcome data.

The characteristics of the included studies were defined according to the PICOS criteria (Table 1).

Table 1. The components of the PICOS criteria and their use in the evaluation

PICOS element	Description
Population (P)	Systemically healthy adults, aged 18–55 years, diagnosed with mild to moderate gingivitis
Intervention (I)	Oral probiotics administered in various forms, including lozenges, tablets, or toothpaste, containing specific strains such as *Lactobacillus plantarum*, *Lactobacillus brevis*, *Lactobacillus rhamnosus*, *Pediococcus acidilactici*, and *Streptococcus salivarius* M18, administered over periods ranging from 4 weeks to 3 months.
Comparison (C)	Placebo interventions, which were identical in appearance to the active probiotics but contained no live microorganisms
Outcome (O)	Clinical periodontal parameters (PI, GI, BoP, PPD), oral microbiota composition and diversity, and salivary biomarkers such as cytokines, sIgA, and albumin.
Study design (S)	RCTs, including both full-scale and pilot RCTs

Abbreviations: BoP: Bleeding on probing; GI: Gingival index; PI: Plaque index; PICOS: Population, Intervention, Comparison, Outcomes, and Study design; PPD: Probing pocket depth; RCT: Randomized controlled trial; sIgA: Secretory immunoglobulin A.

3. Results

A total of 535 publications were identified through searches of three databases: PubMed (88), Web of Science (198), and Scopus (249). After the removal of 79 duplicate records, 456 records underwent title and abstract screening, of which 58 were excluded. The remaining 398 articles were assessed for eligibility through full-text review, and 387 were excluded for not meeting the inclusion criteria. Ultimately, 11 publications were included in the qualitative synthesis. The selection process is summarized in the PRISMA flow diagram (Figure 1).

The main characteristics and outcomes of the included studies are summarized in Table 2 and described in the following sections.

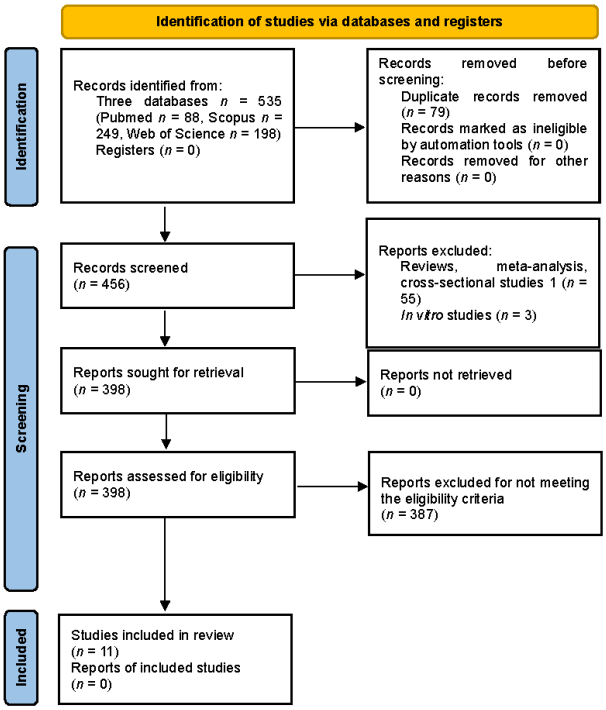


Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram of the literature search and study selection process

Table 2. Characteristics of included studies

Study	Type of study	Aim	Materials and methods	Outcome
Lundtorp Olsen *et al.* [68]	RCT	To evaluate whether probiotic supplementation enhances oral microbiota resilience during the resolution phase following experimentally induced gingivitis.	Healthy adults underwent an experimental gingivitis protocol with suspended oral hygiene. Participants were randomized to probiotic or placebo. Clinical gingival parameters and microbiological profiles (sequencing-based) were assessed.	The probiotic group showed: (i) Faster microbiological recovery toward eubiosis (ii) Lower persistence of pro-inflammatory taxa (iii) Better recovery of gingival indices compared with placebo (iv) Effects were more pronounced during the resolution phase than during induction.
Alkaya *et al.* [19]	Pilot RCT	To evaluate the clinical effects of probiotics containing *Bacillus* species on gingivitis.	(i) Participants: 40 healthy adults with gingivitis (20 test, 20 placebo). (ii) Intervention: Toothpaste, mouthwash, and toothbrush cleanser with *Bacillus* (~5×10^7 total cells). (iii) Clinical outcomes: PI, GI, BoP, PPD.	(i) Both groups showed significant improvements in PI and GI from baseline. (ii) No significant differences between the probiotic and placebo groups for PI, GI, BoP, or PPD. (iii) No adverse effects reported.
Montero *et al.*[23]	RCT	To evaluate the clinical and microbiological effectiveness of adjunctive probiotics in the treatment of gingivitis compared to placebo.	(i) Participants: 59 patients with gingivitis (29 probiotic, 30 placebo). (ii) Intervention: • Test: 2 oral tablets per day containing *Lactobacillus plantarum*, *Lactobacillus brevis,* and *Pediococcus acidilactici*. • Placebo: Identical tablets without live microorganisms.	(i) Both groups showed significant improvement in mean GI after 6 weeks ($p < 0.0001$). (ii) No statistically significant differences between probiotic and placebo groups in overall clinical measures (GI or other indices). (iii) The probiotic group had a significantly greater reduction in sites with baseline GI = 3 (sites with severe inflammation).
Babina *et al.*[13]	RCT	To evaluate whether an oral probiotic containing the *Streptococcus salivarius* M18 strain can improve gingival inflammation, BoP, and dental plaque accumulation in young adults with gingivitis compared with placebo.	(i) Participants: 61 adults aged 18–25 with gingivitis were enrolled; 57 completed the study (27 probiotics, 30 placebo). (ii) Intervention: Oral probiotic containing *Streptococcus salivarius* M18 vs. placebo over 4 weeks. (iii) Followup: Outcomes assessed immediately after the 4-week intervention and after a further 4-week follow-up without probiotic.	(i) Gingival inflammation (GI): After the 4-week intervention, the probiotic group had a significant reduction in GI (effect size 0.58 [95% CI 0.05–1.10]) compared with baseline, and mean GI values were lower in the probiotic group than placebo ($p = 0.045$). This improvement persisted at 4-week follow-up. (ii) Plaque accumulation (TQHPI): The probiotic group showed a significant decrease in plaque scores after 4 weeks (effect size 0.55 [95% CI 0.02–1.07]), while the placebo group showed no significant change. (iii) Gingival bleeding (GBI): GBI decreased significantly in the probiotic group after the intervention (baseline mean 0.127 ± 0.137 vs. post-intervention 0.086 ± 0.086), whereas the placebo group showed a slight increase. However, after follow-up, GBI in both groups did not differ significantly from baseline. Placebo group: No significant improvements in GI, GBI, or TQHPI were seen throughout the study.

(*Cont'd...*)

Table 2. (***Continued***)

Study	Type of study	Aim	Materials and methods	Outcome
Keller *et al.*[36]	RCT	To investigate the clinical effects on gingival inflammation and the composition of the salivary microbiome of oral tablets containing selected probiotic strains in adult patients with moderate gingivitis.	(i) Participants: 47 adults with moderate gingivitis randomized to probiotic or placebo. (ii) Intervention: 4-week administration of tablets containing a mix of *Lactobacillus rhamnosus* PB01 (DSM14869) and *Lactobacillus curvatus* EB10 (DSM32307)vs. placebo.	(i) The probiotic group showed a significant reduction in BoP and GCF flow at 4 weeks compared with baseline ($p < 0.05$), whereas the placebo group did not show similar changes. (ii) Plaque levels tended to decrease in the probiotic group, but differences were not statistically significant (trend $p = 0.05–0.09$). (iii) Selected cytokines in GCF were unaffected by probiotic or placebo.
Babina *et al.*[69]	RCT	To evaluate the effects of three months of daily lozenge supplementation with *Streptococcus salivarius* M18 on gingival bleeding, inflammation, and dental plaque accumulation in adults with gingivitis.	(i) Participants: 62 adults with gingivitis were enrolled; 60 completed the study (31 in the M18 group and 29 in the control/placebo group). (ii) Intervention: Daily probiotic lozenges containing *Streptococcus salivarius* M18 vs. placebo for 3 months, with a 1-month washout follow-up.	(i) Gingival Bleeding (GBI): Probiotic supplementation resulted in significant reductions in BoP compared with baseline at: 1 month: Effect size 1.09 (95% CI: 0.55–1.63) 2 months: Effect size 0.78 (95% CI: 0.26–1.30) 3 months: Effect size 0.67 (95% CI: 0.15–1.18) After the 1-month washout, GBI scores in the probiotic group were not significantly lower than baseline but remained lower than the control group. (ii) Gingival inflammation (GI): No statistically significant differences in GI scores were observed between groups or over time. (iii) Plaque Accumulation (TQHPI): Significant reductions in dental plaque were seen in the probiotic group.
Altamura *et al.*[70]	RCT	To evaluate whether daily supplementation with *Levilactobacillus brevis* CD2 lozenges improves oral health indicators—specifically BoP, PI, and various salivary biomarkers—in otherwise healthy adults.	(i) Participants: 30 healthy adults (15 probiotic, 15 placebo). (ii) Intervention: • Probiotic group: 4 lozenges per day of *Levilactobacillus brevis* CD2 ($\geq 1 \times 10^9$ CFU/lozenge) for 4 weeks. • Placebo group: Identical lozenges without live bacteria.	(i) BoP: After 4 weeks, the probiotic group showed significant reductions in BoP compared with both baseline and placebo. (ii) PI: Significant improvements (reductions) in PI were also seen in the probiotic group relative to placebo and baseline after the 4-week period. (iii) Salivary findings: Salivation rate increased in the probiotic group vs. both baseline and placebo after treatment and was maintained after washout.

(*Cont'd...*)

Table 2. (***Continued***)

Study	Type of study	Aim	Materials and methods	Outcome
Volgenant *et al.*[71]	RCT	To assess the clinical, microbiological, and immunological effects of two oral probiotic strains (*Lactobacillus paracasei* LPc-G110 and *Lactobacillus plantarum* GOS42) delivered in lozenges on the oral ecosystem during an experimental gingivitis challenge, compared with placebo.	(i) Participants: 117 healthy adults (18–55 years old) randomized equally into: • Group A: *Lactobacillus paracasei* lozenges • Group B: Placebo lozenges • Group C: *Lactobacillus plantarum* lozenges (ii) Intervention: One lozenge three times daily after meals for 4 weeks. After a 2-week washin period, subjects refrained from oral hygiene for 2 weeks (experimental gingivitis phase), followed by a 2-week washout phase.	(i) Primary outcome (BOMP): No significant differences among groups in BOMP change after experimental gingivitis. (ii) Gingival health (MGI): Subjects exposed to *Lactobacillus paracasei* or *Lactobacillus plantarum* lozenges showed better recovery of gingival health (improved MGI) after experimental gingivitis compared with placebo (p = 0.021). (iii) Plaque and inflammatory markers: While overall plaque levels and gingival inflammation increased during gingivitis in all groups (expected in the model), the lozenges were associated with dampened pro-inflammatory cytokine (IL-1β) production in saliva during the challenge.
Lundtorp Olsen *et al.*[72]	RCT	To determine whether daily supplementation with probiotic lozenges can counteract oral dysbiosis (perturbations in supragingival microbiota) caused by short-term sugar stress and help restore oral microbiome homeostasis once sugar stress is removed	(i) Participants: 80 healthy adults (19–31 years); 71 completed the study (36 probiotic, 35 placebo). (ii) Intervention: • Probiotic lozenges: Twice daily for 28 days containing *Lacticaseibacillus rhamnosus* PB01 DSM 14870 + *Lactilactobacillus curvatus* EB10 DSM32307 (≈ 1×10^9 CFU/tablet) with xylitol. • Placebo: Identical lozenges without live bacteria. • Sugar challenge: 10% sucrose rinse 6–8 times/day for the first 14 days (sugar stress).	(i) Microbial diversity: (ii) The placebo group showed a significant loss of supragingival microbiota diversity after 14 days of sugar stress (Shannon index ↓). (iii) The probiotic group did not show this decline in diversity, indicating partial protection against sugar-induced diversity loss. However, the difference between groups did not reach statistical significance when directly compared. (iv) Results → Clinical and Biomarkers: • PI and BoP%: No significant differences between probiotic and placebo at any time points (both groups maintained meticulous oral hygiene). • Inflammatory cytokines: No significant differences between groups. • Salivary albumin: Significantly lower at day 28 in the probiotic group compared to placebo, potentially reflecting reduced plasma protein leakage into oral fluids.

(*Cont'd...*)

Table 2. (*Continued*)

Study	Type of study	Aim	Materials and methods	Outcome
Lee *et al.*[39]	RCT	To evaluate whether a toothpaste containing heat-killed *Lacticaseibacillus paracasei* GMNL-143 can improve clinical signs of gingivitis and modulate the oral microbiota in adults with mild to moderate gingivitis.	(i) Participants: 17 adults with mild to moderate gingivitis, each serving as their own control via crossover (toothpaste with GMNL-143 vs. placebo). (ii) Intervention: • Test: Toothpaste containing heat-killed *Lacticaseibacillus paracasei* GMNL-143 at ~0.7×10^9 cells/g. • Control: Matching placebo toothpaste. • Each used for 4 weeks, separated by a 1-week washout before crossover.	(i) Gingival inflammation: • Use of the GMNL-143 toothpaste significantly reduced the GI compared with baseline ($p = 0.0184$). (ii) Plaque and Halitosis: • No statistically significant changes were found in PI, halitosis scores, OHIP, or salivary IgA when compared to placebo. (iii) Microbiota: • Trends suggested a decrease in oral pathogenic bacteria after using GMNL-143 toothpaste, with a notable (but not statistically significant) reduction in *Streptococcus mutans* levels in crevicular fluid (from 1.52 ± 1.82 to 0.61 ± 0.63; $p = 0.0655$). • A shift toward a microbiota composition resembling healthier individuals was suggested, with correlations found between changes in specific taxa (e.g., *Aggregatibacter actinomycetemcomitans*, *Campylobacter*) and GI changes.
Furlaneto *et al.*[57]	RCT	To evaluate whether adjunctive administration of the probiotic *Bifidobacterium animalis* subsp. *lactis* HN019 enhances the clinical and microbiological outcomes in patients with generalized gingivitis undergoing standard periodontal therapy.	Participants: 60 systemically healthy adults with untreated generalized gingivitis, randomly assigned to: • Probiotic group: $n = 30$; received *Bifidobacterium animalis* subsp. *lactis* HN019 lozenges twice daily • Placebo group: $n = 30$; received placebo lozenges	(i) Both groups showed a significant reduction in BOMP at 8 weeks compared with baseline ($p < 0.05$). (ii) Importantly, the probiotic group had a markedly lower percentage of BoP at 8 weeks than the placebo group ($p < 0.0001$), indicating better control of gingival bleeding when *Bifidobacterium animalis* subsp. *lactis* HN019 was used adjunctively with therapy.

Abbreviations: BoP: Bleeding on probing; BOMP: Bleeding on marginal probing; CI: Confidence interval; GBI: Gingival Bleeding Index; GCF: Gingival crevicular fluid; GI: Gingival Index; IgA: Immunoglobulin A; IL-1β: Interleukin-1 beta; MGI: Modified Gingival Index; OHIP: Oral Health Impact Profile; PI: Plaque Index; PPD: Probing pocket depth; RCT: Randomized controlled trial; TQHPI: Turesky modification of the Quigley–Hein Plaque Index.

3.1. Data processing

As part of the screening process, which involved reviewing the titles and abstracts of the articles selected in the previous identification step, the full texts of the included publications were examined after excluding those that did not address the topics under investigation.

3.2. Quality assessment

The methodological quality and risk of bias of the included randomized controlled trials were independently assessed by two reviewers (L.P.Z. and F.E.D.) using the Cochrane Risk of Bias 2 tool. This instrument evaluates potential sources of bias across five domains: (D1) bias arising from the randomization process; (D2) bias due to deviations from intended interventions; (D3) bias due to missing outcome data; (D4) bias in measurement of the outcome; and (D5) bias in selection of the reported results. Each domain was rated as low risk of bias, some concerns, or high risk of bias, leading to an overall risk-of-bias judgment for each

study (Table 3). Any disagreements between reviewers were resolved through discussion and consensus.

4. Discussion

The combined analysis of the included randomized controlled trials indicates that oral probiotic administration shows clinical and microbiological potential in the management of gingivitis, although with heterogeneous effects depending on probiotic strain, intervention duration, delivery vehicle, and clinical setting (experimental models versus real clinical conditions, stand-alone versus adjunctive use). Overall, a consistent trend toward beneficial modulation of the oral microbiota and reduction of gingival inflammatory indices emerges, with variable magnitude of effect.

Table 3. Risk-of-bias assessment of the included RCTs using the Cochrane RoB 2 tool

Study	D1	D2	D3	D4	D5	Overall
Lundtorp Olsen *et al.* [68]	+	+	+	+	-	+
Alkaya *et al.* [19]	-	+	+	+	-	-
Montero *et al.*[23]	+	+	+	+	-	+
Babina *et al.*[13]	+	+	+	+	+	+
Keller *et al.*[36]	+	+	+	+	-	+
Babina *et al.*[69]	+	+	+	+	+	+
Altamura *et al.*[70]	-	+	+	+	-	-
Volgenant *et al.*[71]	+	+	+	+	-	+
Lundtorp Olsen *et al.* [72]	+	+	+	+	-	+
Lee *et al.*[39]	+	+	+	+	-	+
Furlaneto *et al.*[57]	+	+	+	+	+	+

Note: D1: Bias arising from the randomization process; D2: Bias due to deviations from intended interventions; D3: Bias due to missing outcome data; D4: Bias in measurement of the outcome; D5: Bias in selection of the reported result. + indicate low risk of bias; - indicate some concerns; × indicate high risk of bias. The overall column represents the overall risk-of-bias judgment for each study.
Abbreviations: RCT: Randomized controlled trial; RoB 2: Revised Cochrane risk-of-bias tool for randomized trials.

Comparison with previous systematic reviews. Several systematic reviews and meta-analyses have previously evaluated the role of probiotics in periodontal diseases; however, important methodological differences distinguish the present review from the existing literature. Earlier reviews, including those by Akram *et al.*,[33] Benavides-Reyes *et al.*,[73] Hardan *et al.*,[63] and Gruner *et al.*,[74] generally combined patients with gingivitis and periodontitis or included additional oral conditions, thereby increasing clinical heterogeneity and reducing the specificity of conclusions related to gingivitis. Similarly, the comprehensive review by Gheisary *et al.*,[60] despite its robust methodology and large number of included randomized controlled trials, integrated different stages of periodontal disease and incorporated clinical, microbiological, and immunological outcomes in a broader periodontal framework. In contrast, the present review focused exclusively on randomized controlled trials involving patients with gingivitis, allowing a more homogeneous evaluation of clinical and microbiological outcomes associated with the early stage of periodontal disease.

Furthermore, unlike previous reviews that mainly assessed the overall efficacy of probiotics, this review systematically examined clinically relevant variables such as probiotic strain, route of administration, duration of supplementation, and adjunctive use with professional periodontal therapy. Another distinctive aspect is the

emphasis placed on the temporal relationship between microbiological modulation and subsequent clinical improvement, suggesting that ecological changes within the oral microbiota may precede measurable clinical benefits. Consequently, this review provides a more clinically oriented interpretation of the available evidence and helps identify the conditions under which probiotic therapy appears to be most effective for gingivitis.

4.1. Influence of the delivery vehicle on probiotic efficacy

The delivery vehicle appears to be an important determinant of probiotic exposure within the oral cavity, although the available evidence does not permit a definitive ranking of formulations. Among the included trials, lozenges and oral tablets were associated with the most consistent clinical improvements, particularly for gingival bleeding and plaque accumulation. Studies evaluating *Streptococcus salivarius* M18, *Lactobacillus rhamnosus*/*Lactobacillus curvatus*, *Levilactobacillus brevis* CD2, and *Bifidobacterium animalis* subsp. *lactis* HN019 used lozenges or tablets and reported clinically relevant improvements in at least one gingival outcome.[13,36,57,71,72] In contrast, the trial evaluating a probiotic-containing toothpaste reported a significant improvement in gingival inflammation but no significant improvement in plaque, halitosis, oral-health-related quality of life, or salivary immunoglobulin A compared with placebo.[74]

Several formulation-related mechanisms may explain these differences. Lozenges and tablets generally remain in the oral cavity for a longer period than toothpaste during routine brushing, potentially increasing the duration of exposure of probiotic microorganisms to saliva, dental surfaces, and the developing biofilm. Their gradual dissolution may also permit a more sustained release of microorganisms throughout the oral cavity. Toothpaste, in contrast, is exposed to mechanical brushing, expectoration, dilution, and rinsing, which may substantially reduce the effective contact time between viable microorganisms and oral surfaces.

However, these findings should not be interpreted as evidence that toothpaste is intrinsically inferior to lozenges or tablets. The included studies differed not only in delivery vehicle but also in probiotic strain, dose, viability, treatment duration, background oral-hygiene procedures, study population, and outcome assessment. Furthermore, the toothpaste study included heat-killed *Lacticaseibacillus paracasei* GMNL-143 rather than viable probiotic cells,[74] making direct comparison with viable probiotic lozenges or tablets biologically inappropriate. Therefore, the apparent superiority of lozenges and tablets may reflect a combination of vehicle-related effects and differences in probiotic formulation and biological activity.

Overall, the current evidence supports the use of orally retained formulations, particularly lozenges or slowly dissolving tablets, when the objective is to maximize probiotic exposure within the oral cavity. Nevertheless, comparative randomized trials using the same strain, dose, and treatment duration across different delivery vehicles are required before formulation-specific superiority can be established.

4.2. Interpretation of null and non-significant findings

The interpretation of negative or non-significant findings is essential because probiotic efficacy should not be inferred solely from trials reporting statistically significant improvements. Several included studies failed to demonstrate significant between-group differences for their primary or major clinical outcomes. Alkaya *et al.*,[19] for example, reported improvements in plaque and gingival indices in both groups, without significant differences between probiotic and placebo groups. Similarly, Montero *et al.*[23] observed significant improvement in gingival inflammation over time in both groups, while most overall clinical outcomes did not differ significantly between treatment groups. Volgenant *et al.*[71] reported improvements in gingival recovery and selected inflammatory parameters but did not observe a significant between-group difference for the primary bleeding on marginal probing outcome. Olsen *et al.*[68] found that probiotics appeared to partially preserve microbial diversity during experimental sugar stress, although the direct comparison between groups did not reach statistical significance for this outcome. Lee *et al.*[39] observed a significant improvement in gingival inflammation but no significant differences for several secondary clinical and salivary outcomes. These findings indicate that the probiotic effect is neither universal nor consistently detectable across all clinical endpoints. Several explanations are possible, including small sample sizes, limited statistical power, short intervention periods, high baseline oral-hygiene standards, interindividual differences in microbiota, differences in strain and dose, and variability in the sensitivity of clinical endpoints. Importantly, improvements within the probiotic group should not be interpreted as evidence of treatment efficacy when a corresponding between-group comparison is not statistically significant. Future trials should therefore define a primary clinical endpoint a priori, use adequately powered sample sizes, report effect estimates with confidence intervals, and distinguish clearly between within-group changes and treatment effects relative to placebo.

4.3. Long-term monitoring and clinical assessment

Because most included trials followed participants for approximately 4–12 weeks, the available evidence is insufficient to define an optimal long-term duration of probiotic supplementation. Probiotics should therefore be considered an adjunct to, rather than a replacement for, mechanical plaque control and professional preventive care.

In clinical practice, patients receiving probiotic supplementation may be reassessed after approximately 4–8 weeks. Assessment should include gingival bleeding, gingival inflammation, plaque accumulation, adherence to the intervention, patient-reported symptoms, and adverse events. If clinically meaningful improvement is observed and the intervention is well tolerated, continued use may be considered on an individualized basis. However, prolonged administration should not be recommended solely on the basis of short-term trial evidence.

If no clinically relevant improvement is observed, adherence, plaque control, formulation, and other local or systemic risk factors should be reassessed rather than automatically extending probiotic treatment. Future randomized trials should include follow-up periods of at least 6–12 months and evaluate the durability of clinical benefits, persistence of administered strains, changes in the resident oral microbiome, adverse events, and clinical outcomes after discontinuation.

4.4. Limitations

This review has several limitations that should be considered when interpreting the findings. First, only English-language articles were included, which may have introduced language bias. Second, the literature search was limited to three electronic databases, potentially restricting the identification of additional eligible studies. Third, substantial heterogeneity was observed regarding probiotic strains, doses, formulations, intervention duration, background oral-hygiene procedures, and outcome measures, which prevented quantitative meta-analysis.

Furthermore, the included interventions were biologically heterogeneous, including viable and heat-killed preparations and different delivery vehicles. Consequently, the findings should not be generalized to probiotics as a homogeneous therapeutic category. Some studies used experimental gingivitis or controlled ecological challenges, which may not fully reproduce naturally occurring gingivitis. Differences in microbiological sampling and outcome assessment also limited direct comparison across studies.

Finally, most studies included relatively small samples and short follow-up periods. These limitations restrict the assessment of long-term efficacy, persistence of probiotic strains, and long-term safety. The possibility of publication and reporting bias also cannot be excluded. Therefore, the present findings should be interpreted as evidence of potential adjunctive benefit rather than definitive evidence for a universally effective probiotic intervention.

5. Conclusion

The available randomized evidence suggests that oral probiotics may provide an additional benefit in the management of gingivitis, particularly for gingival bleeding, plaque accumulation, and selected microbiological outcomes. However, the magnitude and consistency of these effects vary substantially according to probiotic strain, dose, formulation, duration of administration, and clinical context.

Lozenges and slowly dissolving tablets currently represent the most consistently investigated delivery systems, but the available evidence is insufficient to establish their superiority over probiotic toothpaste or other formulations because direct head-to-head comparisons are lacking and formulation characteristics differ substantially between studies.

Microbiological changes may precede clinical improvement in some settings, but the current evidence supports a temporal association rather than a demonstrated causal pathway. Future longitudinal studies integrating strain-resolved microbiome analysis, metabolomics, and host inflammatory biomarkers are required to clarify the biological mechanisms underlying clinical responses.

Given the predominantly short follow-up periods and small sample sizes of the available trials, long-term efficacy and safety remain insufficiently characterized. Future multicenter randomized trials should therefore use standardized strains, doses, formulations, clinical endpoints, and microbiological methods, together with follow-up periods of at least 6–12 months. Until such evidence becomes available, probiotics should be considered an adjunct to, rather than a replacement for, established plaque-control and professional periodontal care.

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Gaetano Isola and Francesco Inchingolo serve as Associate

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AI tools statement

During the preparation of this manuscript, AI-assisted tools, Grammarly and Claude (Anthropic), were used exclusively to improve the linguistic quality of the text, including grammar, spelling, sentence structure, clarity, and readability. These tools were not used for study design, data collection, statistical analysis, interpretation of results, or generation of scientific conclusions. All AI-assisted suggestions were carefully reviewed and verified by the authors, who take full responsibility for the accuracy, integrity, and final content of the manuscript.

References

1. Lundtorp-Olsen C, Markvart M, Twetman S, Belstrøm D. Effect of Probiotic Supplements on the Oral Microbiota-A Narrative Review. *Pathogens*. 2024;13(5):419.

   doi: 10.3390/pathogens13050419

2. Yu KX, He DW, Fan L, Wang L, Sun J. The role and potential mechanisms of prebiotics in periodontitis treatment: a review. *J Funct Foods*. 2026;139:107221.

   doi: 10.1016/j.jff.2026.107221

3. Zanetta P, De Giorgis V, Barberis E, *et al*. Lactobacillus probiotic cell-free supernatants and vitamin D influence interleukin-6 production and mitigate oral periodontopathogens-induced cytotoxicity in FaDu cells. *Front Microbiol*. 2025;16:1578267.

   doi: 10.3389/fmicb.2025.1578267

4. Inchingolo AM, Inchingolo AD, Fatone MC, *et al*. The effect of periodontal treatment on Helicobacter pylori-infection: a systematic review. *Periodontal and Implant Res*. 2025;9(1):3.

   doi: 10.1007/s41894-025-00146-x

5. Inchingolo F, Inchingolo AD, Palumbo I, *et al*. The Impact of Cesarean Section Delivery on Intestinal Microbiota: Mechanisms, Consequences, and Perspectives-A Systematic Review. *Int J Mol Sci*. 2024;25(2):1055.

   doi: 10.3390/ijms25021055

6. Malcangi G, Patano A, Guglielmo M, *et al*. Precision Medicine in Oral Health and Diseases: A Systematic Review. *J Pers Med*. 2023;13(5):725.

   doi: 10.3390/jpm13050725

7. Salvi GE, Lawrence HP, Offenbacher S, Beck JD. Influence of risk factors on the pathogenesis of periodontitis. *Periodontology 2000*. 1997;14(1):173-201.

   doi: 10.1111/j.1600-0757.1997.tb00197.x

8. Sanz M, Ceriello A, Buysschaert M, *et al*. Scientific evidence on the links between periodontal diseases and diabetes: Consensus report and guidelines of the joint workshop on periodontal diseases and diabetes by the International Diabetes Federation and the European Federation of Periodontology. *J Clin Periodontol*. 2018;45(2):138-149.

   doi: 10.1111/jcpe.12808

9. Sachelarie L, Scrobota I, Romanul I, Iurcov R, Cicalau GIP, Todor L. Probiotic Therapy as an Adjuvant in the Treatment of Periodontal Disease: An Innovative Approach. *MEDICINA-LITHUANIA*. 2025;61(1).

   doi: 10.3390/medicina61010126

10. Saharia NP, Malik M, Jhingan P, Gulati N, Mathur S. Assessment of Interleukin-6 Levels and Lactobacillus casei Counts in Pediatric Stainless Steel and Zirconia Crowns: A Comparative Study. *Int J Clin Pediatr Dent*. 2024;17(4):395-403.

    doi: 10.5005/jp-journals-10005-2813

11. Pietropaoli D, Tatone C, D'Alessandro AM, Monaco A. Possible involvement of advanced glycation end products in periodontal diseases. *Int J Immunopathol Pharmacol*. 2010;23(3):683-691.

    doi: 10.1177/039463201002300301

12. Sgolastra F, Petrucci A, Gatto R, Giannoni M, Monaco A. Long-term efficacy of subantimicrobial-dose doxycycline as an adjunctive treatment to scaling and root planing: a systematic review and meta-analysis. *J Periodontol*. 2011;82(11):1570-1581.

    doi: 10.1902/jop.2011.110026

13. Babina K, Salikhova D, Doroshina V, *et al*. Antigingivitis and Antiplaque Effects of Oral Probiotic Containing the Streptococcus salivarius M18 Strain: A Randomized Clinical Trial. *Nutrients*. 2023;15(18):3882.

doi: 10.3390/nu15183882

14. Iniesta M, Chamorro C, Ambrosio N, Marín MJ, Sanz M, Herrera D. Subgingival microbiome in periodontal health, gingivitis and different stages of periodontitis. *J Clin Periodontol*. 2023;50(7):905-920.

doi: 10.1111/jcpe.13793

15. Ko Y, Lee EM, Park JC, Gu MB, Bak S, Ji S. Salivary microbiota in periodontal health and disease and their changes following nonsurgical periodontal treatment. *J Periodontal Implant Sci*. 2020;50(3):171-182.

doi: 10.5051/jpis.2020.50.3.171

16. Lee R, Park JY, Park Y, Kim K, Ha JW, Lee JS. Microbial Profiling of Saliva, Oral Rinse, Subgingival Plaque and GCF Reveals Site-Specific Dysbiosis in Periodontitis: A Within-Subject Comparison of 150 Participants. *J Clin Periodontol*. 2026;53(2):179-189.

doi: 10.1111/jcpe.70050

17. Ma J, Kageyama S, Takeshita T, *et al*. Clinical utility of subgingival plaque-specific bacteria in salivary microbiota for detecting periodontitis. *PLoS One*. 2021;16(6):e0253502.

doi: 10.1371/journal.pone.0253502

18. Regueira-Iglesias A, Suárez-Rodríguez B, Blanco-Pintos T, *et al*. The salivary microbiome as a diagnostic biomarker of periodontitis: a 16S multi-batch study before and after the removal of batch effects. *Front Cell Infect Microbiol*. 2024;14.

doi: 10.3389/fcimb.2024.1405699

19. Alkaya B, Laleman I, Keceli S, Ozcelik O, Cenk Haytac M, Teughels W. Clinical effects of probiotics containing Bacillus species on gingivitis: a pilot randomized controlled trial. *J Periodontal Res*. 2017;52(3):497-504.

doi: 10.1111/jre.12415

20. Marjani LI, Suharsini M, Fauziah E. Effectiveness of Lactobacillus reuteri Probiotics on Plaque Index, Gingival Index, and Bleeding on Probing in Adolescents with Betel Quid Chewing Habit: Study in Children Aged 13-15 Years in Alor Regency, East Nusa Tenggara. *Int J Clin Pediatr Dent*. 2026;19(2):177-182.

doi: 10.5005/jp-journals-10005-3411

21. Martins AA, Avelino Cassiano L de B, Silva Júnior FL, Caldas SGFR, Lins RDAU, de Aquino Martins ARL. Does Probiotic Therapy Improve Periodontal Treatment Outcomes in Smoking Patients? A Systematic Review of Randomized Clinical Trials. *Probiotics Antimicrob Proteins*. 2026;18(2):3318-3326.

doi: 10.1007/s12602-025-10717-w

22. Michałowski K, Górski B, Brodzikowska A. The Clinical and Antibacterial Effects of a Herbal Toothpaste Containing White Mustard Sinapis alba Extract: A Randomized Clinical Trial. *Dent J (Basel)*. 2025;13(4):165.

doi: 10.3390/dj13040165

23. Montero E, Iniesta M, Rodrigo M, *et al*. Clinical and microbiological effects of the adjunctive use of probiotics in the treatment of gingivitis: A randomized controlled clinical trial. *J Clin Periodontol*. 2017;44(7):708-716.

doi: 10.1111/jcpe.12752

24. Modiri S, Heidari M, Shahmohammadi R, *et al*. A tangible prospect for the treatment of gingivitis using a potentially probiotic strain Lactobacillus plantarum MK06 isolated from traditional dairy products: a triple blind randomized clinical trial. *BMC Oral Health*. 2023;23(1):870.

doi: 10.1186/s12903-023-03494-x

25. Nadelman P, Magno MB, Masterson D, da Cruz AG, Maia LC. Are dairy products containing probiotics beneficial for oral health? A systematic review and meta-analysis. *Clin Oral Investig*. 2018;22(8):2763-2785.

doi: 10.1007/s00784-018-2682-9

26. Niranjan R, Patil S, Dubey A, Lochab B, Priyadarshini R. Small cyclic dipeptide produced by Lactobacillus rhamnosus with anti-biofilm properties against Streptococcus mutans biofilm. *Biofilm*. 2024;8:100237.

doi: 10.1016/j.bioflm.2024.100237

27. Rebelo MB, Oliveira CS, Tavaria FK. Novel Strategies for Preventing Dysbiosis in the Oral Cavity. *Front Biosci (Elite Ed)*. 2023;15(4):23.

doi: 10.31083/j.fbe1504023

28. Sabatini S, Lauritano D, Candotto V, Silvestre FJ, Nardi GM. Oral probiotics in the management of gingivitis in diabetic patients: a double blinded randomized controlled study. *J Biol Regul Homeost Agents*. 2017;31(2 Suppl 1):197-202.

29. Mosaico G, Artuso G, Pinna M, Denotti G, Orrù G, Casu C. Host Microbiota Balance in Teenagers with Gum Hypertrophy Concomitant with Acne Vulgaris: Role of Oral Hygiene Associated with Topical Probiotics. *Microorganisms*. 2022;10(7):1344.

doi: 10.3390/microorganisms10071344

30. Barrea L, Verde L, Auriemma RS, *et al*. Probiotics and Prebiotics: Any Role in Menopause-Related Diseases? *Curr Nutr Rep*. 2023;12(1):83-97.

doi: 10.1007/s13668-023-00462-3

31. Inchingolo AD, Cazzolla AP, Di Cosola M, *et al*. The integumentary system and its microbiota between health and disease. *J Biol Regul Homeost Agents*. 2021;35(2 Suppl. 1):303-321.

doi: 10.23812/21-2supp1-30

32. Agossa K, Dubar M, Lemaire G, *et al*. Effect of Lactobacillus reuteri on Gingival Inflammation and Composition of the Oral Microbiota in Patients Undergoing Treatment with Fixed Orthodontic Appliances: Study Protocol of a Randomized Control Trial. *Pathogens*. 2022;11(2):112.

doi: 10.3390/pathogens11020112

33. Akram Z, Shafqat SS, Aati S, Kujan O, Fawzy A. Clinical efficacy of probiotics in the treatment of gingivitis: A systematic review and meta-analysis. *Aust Dent J*. 2020;65(1):12-20.

doi: 10.1111/adj.12733

34. Arat Maden E, Altun C, Açikel C. The Efficacy of Xylitol, Xylitol-Probiotic and Fluoride Dentifrices in Plaque Reduction and Gingival Inflammation in Children: A Randomised Controlled Clinical Trial. *Oral Health Prev Dent*. 2017;15(2):117-121.

doi: 10.3290/j.ohpd.a37973

35. Boyapati R, Peeta J, Dhulipalla R, Kolaparthy L, Adurty C, Cheruvu RNS. Comparative evaluation of the efficacy of probiotic, Aloe vera, povidine-iodine, and chlorhexidine mouthwashes in the treatment of gingival inflammation: A randomized controlled trial. *Dent Med Probl*. 2024;61(2):181-189.

doi: 10.17219/dmp/156425

36. Keller MK, Brandsborg E, Holmstrøm K, Twetman S. Effect of tablets containing probiotic candidate strains on gingival inflammation and composition of the salivary microbiome: a randomised controlled trial. *Benef Microbes*. 2018;9(3):487-494.

doi: 10.3920/BM2017.0104

37. Nastri L, De Rosa A, De Gregorio V, Grassia V, Donnarumma G. A New Controlled-Release Material Containing Metronidazole and Doxycycline for the Treatment of Periodontal and Peri-Implant Diseases: Formulation and In Vitro Testing. *Int J Dent*. 2019;2019:9374607.

doi: 10.1155/2019/9374607

38. Inchingolo F, Inchingolo AM, Malcangi G, *et al*. The Benefits of Probiotics on Oral Health: Systematic Review of the Literature. *Pharmaceuticals (Basel)*. 2023;16(9):1313.

doi: 10.3390/ph16091313

39. Lee MK, Chen IH, Hsu IL, *et al*. The impact of Lacticaseibacillus paracasei GMNL-143 toothpaste on gingivitis and oral microbiota in adults: a randomized, double-blind, crossover, placebo-controlled trial. *BMC Oral Health*. 2024;24(1):477.

doi: 10.1186/s12903-024-04251-4

40. de Brito Avelino L, Rodrigues KT, da Silva Cruz NT, Martins AA, de Aquino Martins ARL. Effectiveness of Probiotic Therapy in the Management of PeriodontalDisease in Diabetic Patients: A Scoping Review. *Curr Diabetes Rev*. 2024;20(9):e281123223961.

doi: 10.2174/0115733998271193231108054254

41. Puzhankara L, Banerjee A, Chopra A, Venkitachalam R, Kedlaya MN. Effectiveness of probiotics compared to antibiotics to treat periodontal disease: Systematic review. *Oral Dis*. 2024;30(5):2820-2837.

doi: 10.1111/odi.14781

42. Rajasekaran JJ, Krishnamurthy HK, Bosco J, *et al*. Oral Microbiome: A Review of Its Impact on Oral and Systemic Health. *Microorganisms*. 2024;12(9):1797.

doi: 10.3390/microorganisms12091797

43. Bakkeren E, Piskovsky V, Lee MNY, Jahn MT, Foster KR. Strain displacement in microbiomes via ecological competition. *Nat Microbiol*. 2025;10(12):3122-3135.

doi: 10.1038/s41564-025-02162-w

44. Doucette H, Ward R, Wheeldon C, Whelan A. The impact of prebiotics and probiotics on the oral microbiome of individuals with periodontal disease: a scoping review. *Can J Dent Hyg*. 2024;58(3):182-195.

45. Inchingolo AD, Cosola MD, Inchingolo AM, *et al*. Correlation between occlusal trauma and oral microbiota: a microbiological investigation. *J Biol Regul Homeost Agents*. 2021;35(2 suppl 1)):295-302.

doi: 10.23812/21-2supp1-29

46. Çelik MN, Dazıroğlu MEÇ, Pınar BA, *et al*. Microbiome crosstalk and nutrition: the interplay between gut microbiota-organ axis and dietary factors. *Food Res Int*. 2026;232:118945.

doi: 10.1016/j.foodres.2026.118945

47. Chen WJ, Sharma LA, Shao P, *et al*. Adjunctive use of Streptococcus salivarius M18 probiotic in the treatment of periodontitis: a randomized controlled trial. *3 BIOTECH*. 2025;15(6).

doi: 10.1007/s13205-025-04363-w

48. Chugh P, Dutt R, Sharma A, Bhagat N, Dhar MS. A critical appraisal of the effects of probiotics on oral health. *J Funct Foods*. 2020;70:103985.

doi: 10.1016/j.jff.2020.103985

49. Inchingolo AD, Malcangi G, Inchingolo AM, *et al*. Benefits and Implications of Resveratrol Supplementation on Microbiota Modulations: A Systematic Review of the Literature. *Int J Mol Sci*. 2022;23(7):4027.

doi: 10.3390/ijms23074027

50. Salah AN, Doghish YA, Abbass SO, *et al*. Microbiota-based therapies in oral health and disorders. *Folia Microbiol (Praha)*. 2025;70(6):1217-1240.

doi: 10.1007/s12223-025-01324-x

51. Santacroce L, Muzio EL, Bottalico L, *et al*. Subversion of the Oral Microbiota and Induction of Immune-Mediated Systemic Inflammation with Special Reference to Periodontitis: Current Knowledge and Perspectives. *Endocr Metab Immune Disord Drug Targets*. 2023;23(4):470-484.

doi: 10.2174/1871530322666220629101357

52. Schlagenhauf U, Rehder J, Gelbrich G, Jockel-Schneider Y. Consumption of Lactobacillus reuteri-containing lozenges improves periodontal health in navy sailors at sea: A randomized controlled trial. *J Periodontol*. 2020;91(10):1328-1338.

doi: 10.1002/JPER.19-0393

53. Sedghi LM, Bacino M, Kapila YL. Periodontal Disease: The Good, The Bad, and The Unknown. *Front Cell Infect Microbiol*. 2021;11:766944.

doi: 10.3389/fcimb.2021.766944

54. Sharma H, Ruikar M, Verma S. Probiotic Supplementation for Periodontal Diseases - An Umbrella Review. *Indian J Dent Res*. Published online November 28, 2024.

doi: 10.4103/ijdr.ijdr_905_23

55. Inchingolo F, Inchingolo AM, Avantario P, *et al*. The Effects of Periodontal Treatment on Rheumatoid Arthritis and of Anti-Rheumatic Drugs on Periodontitis: A Systematic Review. *Int J Mol Sci*. 2023;24(24):17228.

doi: 10.3390/ijms242417228

56. Ferrillo M, Giudice A, Migliario M, *et al*. Oral-Gut Microbiota, Periodontal Diseases, and Arthritis: Literature Overview on the Role of Probiotics. *Int J Mol Sci*. 2023;24(5):4626.

doi: 10.3390/ijms24054626

57. Furlaneto F, Levi YL de AS, Sávio D de SF, *et al*. Microbiological profile of patients with generalized gingivitis undergoing periodontal therapy and administration of Bifidobacterium animalis subsp. lactis HN019: A randomized clinical trial. *PLoS One*. 2024;19(11):e0310529.

doi: 10.1371/journal.pone.0310529

58. García HC, Orona VU, Méndez LF, Coronado AA, Garza MAG. Diet and nutrition key factors for oral microbiota composition: a systematic review. *Food Nutr Res*. 2025;69.

doi: 10.29219/fnr.v69.11956

59. Gatej S, Gully N, Gibson R, Bartold PM. Probiotics and Periodontitis - A Literature Review. *J Int Acad Periodontol*. 2017;19(2):42-50.

60. Gheisary Z, Mahmood R, Harri Shivanantham A, *et al*. The Clinical, Microbiological, and Immunological Effects of Probiotic Supplementation on Prevention and Treatment of Periodontal Diseases: A Systematic Review and Meta-Analysis. *Nutrients*. 2022;14(5):1036.

doi: 10.3390/nu14051036

61. Inchingolo AD, Malcangi G, Semjonova A, *et al*. Oralbiotica/Oralbiotics: The Impact of Oral Microbiota on Dental Health and Demineralization: A Systematic Review of the Literature. *Children*. 2022;9(7):1014.

doi: 10.3390/children9071014

62. Hamilton A, Barnes M, Hutto T. The Effects Of Oral Probiotics on Gingival and Periodontal Health: A Literature Review. *Dent Rev*. 2024;4(3):100101.

doi: 10.1016/j.dentre.2024.100101

63. Hardan L, Bourgi R, Cuevas-Suárez CE, *et al*. The Use of Probiotics as Adjuvant Therapy of Periodontal Treatment: A Systematic Review and Meta-Analysis of Clinical Trials. *Pharmaceutics*. 2022;14(5):1017.

doi: 10.3390/pharmaceutics14051017

64. Huo P, Deng L, Lu J, Kan P, Jing R, Luo L jun. 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. *BMC ORAL HEALTH*. 2025;25(1).

doi: 10.1186/s12903-025-06084-1

65. Boyeena L, Koduganti RR, Panthula VR, Jammula SP. Comparison of efficacy of probiotics versus tetracycline fibers as adjuvants to scaling and root planing. *J Indian Soc Periodontol*. 2019;23(6):539-544.

doi: 10.4103/jisp.jisp_590_18

66. Iniesta M, Herrera D, Montero E, *et al*. Probiotic effects of orally administered Lactobacillus reuteri-containing tablets on the subgingival and salivary microbiota in patients with gingivitis. A randomized clinical trial. *J Clin Periodontol*. 2012;39(8):736-744.

doi: 10.1111/j.1600-051X.2012.01914.x

67. Kamianowski C, Kamianowski A, Nikitiuk J, *et al*. The Effect of Probiotic Lactobacillus Strains on Porphyromonas gingivalis, the Etiological Factor of Periodontal Diseases-A Systematic Review. *Probiotics Antimicrob Proteins*. 2026;18(2):3055-3093.

doi: 10.1007/s12602-025-10607-1

68. Lundtorp Olsen C, Massarenti L, Vendius VFD, *et al*. Probiotics Support Resilience of the Oral Microbiota during Resolution after Experimental Gingivitis-A Randomized, Double-Blinded, Placebo-Controlled Trial. *Nutrients*. 2023;15(22):4805.

doi: 10.3390/nu15224805

69. Babina K, Salikhova D, Makeeva I, *et al*. A Three-Month Probiotic (the Streptococcus salivarius M18 Strain) Supplementation Decreases Gingival Bleeding and Plaque Accumulation: A Randomized Clinical Trial. *Dent J (Basel)*. 2024;12(7):222.

doi: 10.3390/dj12070222

70. Altamura S, Lombardi F, Augello FR, *et al*. Levilactobacillus brevis CD2 as a multifaceted probiotic to preserve oral health: results of a double-blind, randomized, placebo-controlled trial in healthy adults. *J Transl Med*. 2025;23(1):128.

doi: 10.1186/s12967-024-06000-1

71. Volgenant CMC, van der Waal SV, Brandt BW, *et al*. The Evaluation of the Effects of Two Probiotic Strains on the Oral Ecosystem: A Randomized Clinical Trial. *Front Oral Health*. 2022;3:825017.

doi: 10.3389/froh.2022.825017

72. Lundtorp Olsen C, Massarenti L, Vendius VFD, *et al*. Probiotics Partly Suppress the Impact of Sugar Stress on the Oral Microbiota-A Randomized, Double-Blinded, Placebo-Controlled Trial. *Nutrients*. 2023;15(22):4810.

doi: 10.3390/nu15224810

73. Benavides-Reyes C, Cabello I, Magán-Fernández A, Rodríguez-Barranco M, Usta SN, Mesa F. Clinical effects of probiotics on the treatment of gingivitis and periodontitis: a systematic review and meta-analysis. *BMC Oral Health*. 2025;25(1):490.

doi: 10.1186/s12903-025-05888-5

74. Gruner D, Paris S, Schwendicke F. Probiotics for managing caries and periodontitis: Systematic review and meta-analysis. *J Dent*. 2016;48:16-25.

doi: 10.1016/j.jdent.2016.03.002