The impact of prebiotics and probiotics on the oral microbiome of individuals with periodontal disease: a scoping review

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PRACTICAL IMPLICATIONS OF THIS RESEARCH

- Probiotics have been shown to reduce the prevalence of pathogenic bacteria, inflammatory markers, and dysbiosis within oral microbiomes found in periodontal disease.
- Probiotics may have potential as an adjunct treatment for periodontal disease.
- Oral health professionals should be aware of possible adjunct modalities for the treatment of periodontal disease in their clients.

ABSTRACT

Background: The influence of prebiotics and probiotics on oral microbiome composition, addressing dysbiosis, and aiding in the regulation of the immune–inflammatory response has recently been discussed. The objective of this scoping review is to explore current literature that examines the use of prebiotics and probiotics as adjunctive therapy for the treatment of periodontal disease with the intent to identify gaps in the literature to inform future research and dental hygiene practice. **Methods:** This review was conducted from December 2022 to August 2023 using the Arksey and O'Malley approach and PRISMA-ScR guidelines. Three databases were searched using combinations of keywords. Only peer-reviewed human/in vitro studies published in the last 10 years were included. **Results:** The search retrieved 204 articles. Duplicates were removed, titles and abstracts screened, and the full text of 80 articles examined, resulting in the inclusion of 19 articles. **Discussion and Conclusion:** Most of the included literature indicated that probiotics have a positive impact on periodontal health as evidenced by changes in periodontal disease parameters. Future research should further examine various modes of administration and dosages. The effects of specific prebiotic and probiotic strains on specific pathogenic bacteria in conjunction with non-surgical periodontal therapy should also be further explored.

RÉSUMÉ

Contexte : Le rôle des prébiotiques et des probiotiques dans la composition du microbiome buccal, dans la lutte contre la dysbiose et dans la régulation de la réponse immuno-inflammatoire a récemment fait l'objet de discussions. L'objectif du présent examen de la portée est d'explorer la documentation courante qui examine l'utilisation de prébiotiques et probiotiques à titre de traitement auxiliaire au traitement de la maladie parodontale avec l'intention de trouver les lacunes dans la documentation et de guider les prochaines recherches et la pratique de l'hygiène dentaire. **Méthodes :** Cette revue a été réalisée de décembre 2022 à août 2023 en utilisant l'approche d'Arksey et O'Malley et les lignes directrices de PRISMA-ScR. Des recherches ont été effectuées dans 3 bases de données en utilisant une combinaison de mots clés. Seules les études humaines ou in vitro évaluées par les pairs et publiées dans les 10 dernières années ont été incluses. **Résultats :** Au total, la recherche a donné lieu à 204 articles. Les doublons ont été supprimés, les titres et les résumés ont été vérifiés et le texte intégral de 80 articles a été examiné, ce qui a entraîné l'inclusion de 19 articles. **Discussion et conclusion :** Selon la plupart des publications incluses, les probiotiques ont des effets positifs sur la santé parodontale, comme en témoignent les changements dans les paramètres de la maladie parodontale. Les recherches futures devraient examiner les différents modes d'administration et de doses. Il faut aussi explorer les effets des prébiotiques et des probiotiques particuliers sur des bactéries pathogéniques spécifiques en conjonction avec la thérapie parodontale non chirurgicale.

Keywords: dysbiosis; non-surgical periodontal therapy; oral microbiome; oral microbiota; periodontal disease; prebiotics; probiotics
CDHA Research Agenda category: risk assessment and management

INTRODUCTION

Periodontal disease is a biofilm-induced chronic inflammatory disease affecting the periodontium.[1,2] The periodontium is composed of the gingiva, the underlying connective tissue, cementum, alveolar bone, and the periodontal ligament.[1] A key feature of periodontitis is the activation of osteoclasts resulting in the destruction of the alveolar bone leading to tooth mobility.[1] There are conflicting estimates of the prevalence of periodontal disease globally, with ranges reported from 50%[1] to 90%[3]. Non-surgical periodontal therapy (NSPT) is the conventional initial treatment for periodontal disease.[1] A key component of NSPT is mechanical debridement (scaling and root planing) via hand or powered instruments by an oral health professional. In addition to mechanical debridement, NSPT may include oral medications or rinses to decrease bacterial pathogens.[1] The primary goal

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Manuscript submitted 16 January 2024; revised 8 May 2024; accepted 29 May 2024

of mechanical debridement is to remove calculus, biofilm, and toxins to reduce inflammation and subsequently halt the progression of tissue destruction.[1,3] However, mechanical debridement is technique-sensitive, with complete calculus and biofilm removal being difficult to achieve.[1,3] Specific tooth morphology, such as furcations or the presence of periodontal pockets greater than 5 mm, have been shown to decrease the ability to effectively remove all calculus by scaling and root planing.[4] This residual calculus provides a surface conducive to the adherence of plaque biofilm, thereby initiating the host's immune response leading to dysbiosis, inflammation, and destruction of periodontal tissues.[4]

The oral cavity harbours over 700 different microbiota species, making it one of the largest and most diverse hosts of bacteria, fungi, viruses, and protozoa in the human body.[5] This symbiotic community of microorganisms is referred to as the oral microbiome, or oral microbiota.[6] While bacteria that are embedded in dental biofilm have been associated with the initiation and progression of periodontal disease, very few of the 700+ species that live within the oral microbiome can be considered pathogenic.[6,7] A shift towards increases in gram-negative bacteria has been identified within the microbiome during the progression of oral diseases, such as periodontitis. Concurrently, the number of gram-positive bacteria decreases to accommodate this dynamic balance within the oral cavity.[8]

While the presence of bacteria is critical in the initiation of periodontal disease, there are additional contributing factors such as age, gender, ethnicity, socioeconomic status, smoking, diabetes mellitus, metabolic syndrome, and obesity, which have an impact on the host's response to the bacteria.[1,2] Although plaque biofilm has a causative effect on the development of gingivitis (a reversible form of periodontal disease), gingivitis does not always progress to periodontitis.[2] This would indicate that, in some cases, the host's response to the bacteria prevents the progression. Conversely, the progression of gingivitis to periodontitis is likely due to plaque biofilm inducing gingival inflammation, which then exerts selective pressure for the development of a dysbiotic and inflammatory microbiota that are able to evade the host's immune response.[2] When pathogenic bacteria are present in the oral environment, pro-inflammatory cytokines or proteolytic enzymes are activated, aiding in the destruction of the periodontium.[9]

Current literature indicates that alterations in the oral microbiome homeostasis, or dysbiosis, play a key role not only in periodontal disease progression, but also in systemic health.[6,7] The oral cavity is not only a gateway into the body's internal environment, but it is also a complex microbiome providing the specific conditions needed to support the colonization of microbes.[6] In an ideal balanced oral microbiome, homeostasis is achieved between interbacterial and host-bacterial interactions.[8] It has been found that individuals with both systemic disease and periodontal disease have alterations within their oral microbiota when compared to individuals without disease.[8] It is important to note that periodontal pathogens are present in the interdental microbiota of young adults who do not have signs of such pathogens, therefore placing them at risk of periodontal and systemic disease.[10] This evidence has led to further studies and a better understanding that an imbalance between "good" and "bad" bacteria in the oral cavity contributes to both oral and systemic disease.[8] Oral disease etiology is multifactorial, with nutrition having been shown to have an impact on the development of periodontal and systemic disease.[11] When lifestyle changes occur, the oral microbiome may favour the colonization of bacteria associated with disease, which can have negative implications for both periodontal and systemic health.[8] Therefore, changing the composition of bacteria present in the oral microbiome may reduce the risk for both periodontal disease and systemic health conditions.[8]

Recently, researchers have explored the potential prebiotics and probiotics may have to influence the composition of the microbiota by adding or promoting the growth of beneficial microbes, thus aiding in the regulation of the immune-inflammatory response.[9] Probiotics have been defined as live microorganisms that provide a health benefit to the host when consumed in sufficient quantity.[12] The adequate dose to provide health benefits is dependent on both the strain and the product. Prebiotics have been defined as selectively fermentable ingredients that cause a change in the activity or composition of the microbiota and allow these health benefits to occur.[12] Currently, prebiotics and probiotics are being considered as an adjunct treatment to help with diseases associated with microbial dysbiosis.[13] Studies have demonstrated that probiotics produce positive outcomes as an adjunct to traditional mechanical debridement by influencing the composition of bacterial biofilm.[9]

With recent evidence supporting the link between systemic disease and periodontal disease,[14] it is important that novel treatments for periodontal disease be explored and that oral health professionals be knowledgeable about evidence-based treatment modalities. This scoping review explores current literature on the use of prebiotics and probiotics as an adjunctive therapy for the treatment of periodontal disease, with the intent to identify gaps in the literature to inform future research and dental hygiene practice.

METHODS

A scoping review was conducted over an 8-month period, from December 5, 2022, to August 2023, with the aim of identifying literature that discusses the impact of prebiotics and probiotics as an adjunctive therapy for the treatment of periodontal disease. This review adhered to Arskey and O'Malley's 5-stage framework for conducting a scoping

review[15] and the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses for Scoping Reviews (PRISMA-ScR).[16] The stages outlined are 1) identifying the research question; 2) identifying relevant studies; 3) study selection; 4) charting the data; and 5) collating, summarizing, and reporting the results.[15]

Stage 1: This scoping review sought to answer the question: "What literature exists that discusses the impact of the use of probiotics and prebiotics as an adjunct to non-surgical periodontal therapy on the oral microbiome of individuals with periodontal disease?"

Stage 2: Relevant articles were identified through a search conducted in the electronic databases CINAHL, DOSS, and PubMed between December 5, 2022, and January 23, 2023. Various combinations of keywords (periodontal disease, prebiotics, probiotics, oral microbiome, oral microbiota, dysbiosis, non-surgical periodontal therapy) were utilized in the search strategies for each of the 3 databases (Table 1). Duplicates were screened and excluded using Covidence.

Stage 3: The titles and abstracts of the articles that remained after Stage 2 were divided among 3 research team members (AW, RW, CW) such that each abstract and title were reviewed by 2 team members for consistency. In instances where there were differing opinions, the articles were discussed and, when necessary, a third researcher would determine the final decision. Three team members (AW, RW, CW) then reviewed and confirmed that each of the selected articles met the inclusion criteria and ensured that there were no remaining articles to be excluded. The inclusion criteria were free articles published within the last 10 years, written in English, peer-reviewed primary or secondary research, and human/in vivo studies. Implant, in vitro, and animal studies were excluded as the review was focussed on the use of prebiotics and probiotics as an adjunctive therapy for individuals with periodontal disease, not peri-implant disease. The full text of each remaining article was then screened by 3 research team members (AW, RW, CW). Articles that did not adhere to the inclusion criteria were eliminated.

Stage 4: Relevant information including the author(s), publication year, methods, clinical data collected, probiotic(s) studied, mode and frequency of delivery, results, and conclusion was charted using Google Tables (Table 2) for each of the included articles by all 4 research team members (HD, AW, RW, CW).

Stage 5: The findings from each article were compiled and summarized. Each article was categorized (Table 2) following the Arskey and O'Malley approach for scoping reviews.[14] Four researchers (HD, AW, RW, CW) reviewed and confirmed the information included in the summary of findings.

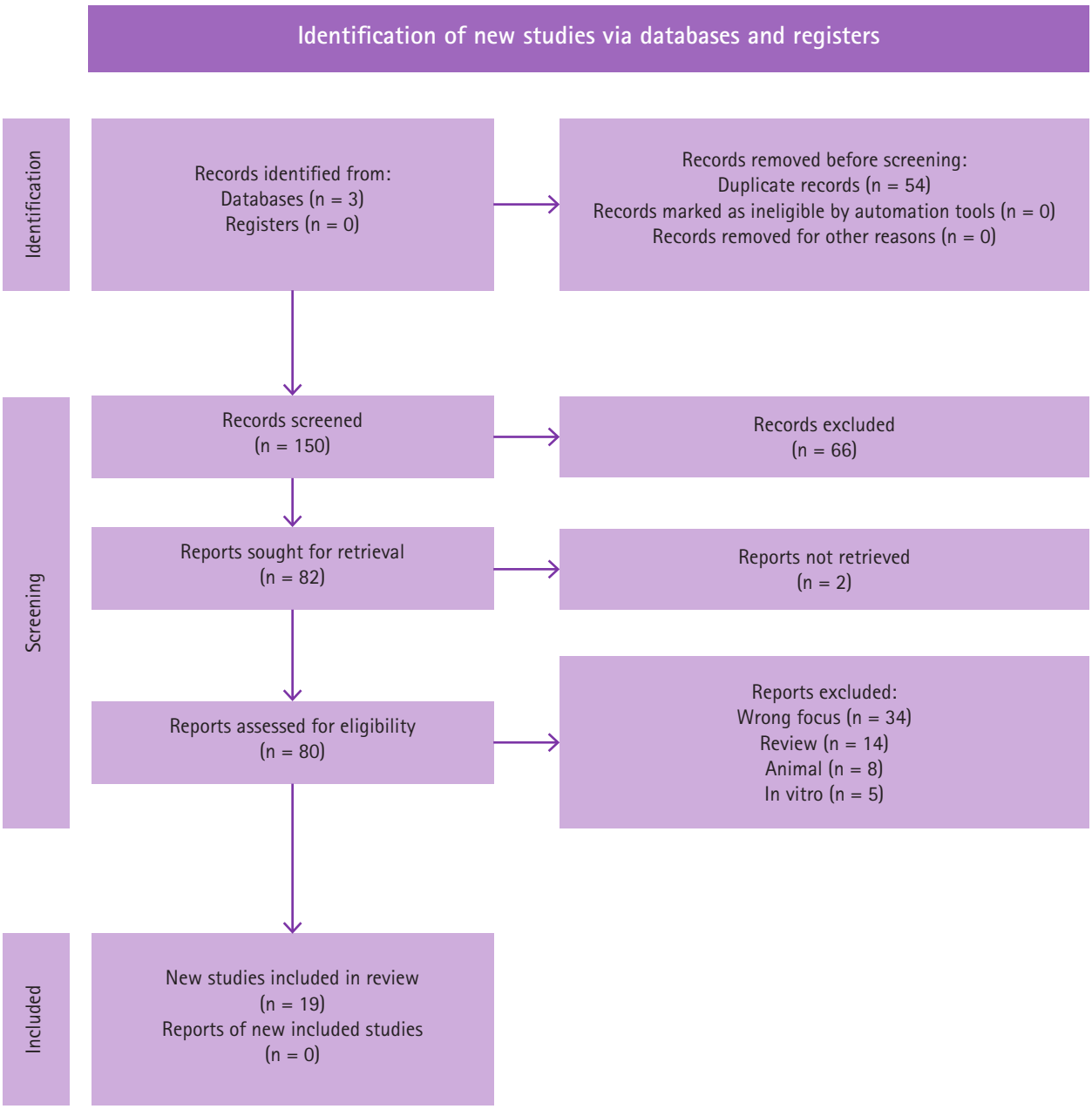
Table 1. Database search strategy

	CINAHL (EBSCOHost) Search Date: 5/12/2022	DOSS Search Date: 5/12/2022	PubMed (NLM) Search Date: 5/12/2022
S1	TI (prebiotics or probiotics) OR AB (prebiotics or probiotics)	TI (prebiotics or probiotics) OR AB (prebiotics or probiotics)	(prebiotics[Title/Abstract] OR probiotics[Title/Abstract] OR "Prebiotics"[Mesh] OR "Probiotics"[Mesh] AND (periodontal[Title/Abstract] OR gingivitis[Title/Abstract] OR gingival[Title/Abstract] OR periodontitis[Title/Abstract] OR "Periodontal Diseases"[Mesh]) AND ("Microbiota"[Mesh] OR microbiome[Title/Abstract] OR microbiota[Title/Abstract])
S2	(MH "Prebiotics+") OR (MH "Probiotics+")	TI (periodontal or gingivitis or gingival or periodontitis) OR AB (periodontal or gingivitis or gingival or periodontitis)	
S3	S1 OR S2	TI (microbiome or microbiota) OR AB (microbiome or microbiota)	
S4	TI (periodontal or gingivitis or gingival or periodontitis) OR AB (periodontal or gingivitis or gingival or periodontitis)	(DE "PREBIOTICS") OR (DE "PROBIOTICS")	
S5	(MH "Periodontal Diseases+")	DE "PERIODONTAL disease" OR DE "CLINICAL attachment loss (Periodontal disease)" OR DE "GINGIVAL diseases" OR DE "PAPILLON Lefevre syndrome" OR DE "PERIODONTITIS" OR DE "TOOTH mobility"	
S6	S4 OR S5	DE "HUMAN microbiota" OR DE "BLOOD microbiology" OR DE "EPITHELIUM microbiology" OR DE "GUT microbiome" OR DE "MYCOBIOME"	
S7	TI (microbiome or microbiota) OR AB (microbiome or microbiota)	S1 OR S4	
S8	(MH "Microbiota+")	S2 OR S5	
S9	S7 OR S8	S3 OR S6	
S10	S3 AND S6 AND S9	S7 AND S8 AND S9	

RESULTS

A total of 204 articles were identified through keyword searches of the 3 databases. After 54 duplicates were removed, 150 articles remained. The titles and abstracts of the 150 articles were then screened. Sixty-six articles were determined to be irrelevant and were therefore discarded. Eighty-two articles were sought for retrieval, 2 of which were inaccessible, resulting in 80 articles remaining. The full text of the remaining 80 articles was reviewed to ensure they met the inclusion criteria. Sixty-one of these articles were then discarded based on the inclusion and exclusion criteria, leaving 19 articles for this scoping review (Figure 1).

Figure 1. Study selection process



In accordance with the inclusion criteria, the 19 articles selected were all human studies. All focussed on the adjunctive use of probiotics in the treatment of periodontal disease. None of the articles explored the use of prebiotics. The 19 articles fell into 1 of 3 categories based on the mode of delivery of the probiotic: 1) lozenge; 2) tablet/capsule; or 3) other (mouthrinse, sachet, and suspension).

Lozenge mode of delivery

Probiotic administration via lozenge was explored in 7 (36.8%) of the 19 articles.[17–23] Four (4) focussed on use of the probiotic *L. reuteri*,[19,20,22,23] 2 on *B. lactis*,[17,18] and 1 study focussed on *L. brevis*.[21] The duration of consumption of the probiotic varied from 14 days[21] to 12 weeks,[19] with

Table 2. Data extraction

Author, year	Methods: Sample size, intervention	Data collected	Probiotic(s) studied	Mode and frequency of delivery	Results	Conclusion
De Oliveira et al. (2022)[13]	Sample size: N = 42 Untreated periodontitis with ≥1 site with probing depth (PD) ≥6 mm and ≥2 sites with PD ≥5 mm in different teeth Probiotics (n = 19) Placebo (n = 23) Intervention: SRP plus placebo or probiotic capsule	PPD, CAL, BOP, suppuration, supragingival plaque, gingival bleeding Subgingival biofilm and stool analysed (checkerboard and 16S rRNA gene sequencing)	*Lactobacillus spp.* (5 strains) *Bifidobacterium spp.* (3 strains)	Mode: capsule Frequency: 1x/day Duration: 30 days	Most subgingival species decreased after intervention; composition/diversity were slightly or not affected by treatments. Significant clinical improvement was similar between groups.	Systemic probiotics in adjunct to subgingival instrumentation did not provide short-term clinical or microbiological benefits in the treatment of periodontitis.
Iwasaki et al. (2016)[24]	Sample size: N = 36 Chronic periodontitis Probiotic (n = 19) Placebo (n = 17) Intervention: NSPT plus placebo or probiotic capsule	PI, GI, BOP, PPD (collected at baseline, week 4, week 8, and week 12)	*Lactobacillus plantarum* heat-killed L-137 (HK L-137)	Mode: capsule Frequency: 1x/day Duration: 12 weeks	PPD sites >4 mm had significant reductions in both test and placebo group with greater in test group when compared to the control group at week 12.	Results suggest that daily intake of HK L-137 can decrease PD in patients undergoing periodontal supportive therapy.
Szkaradkiewicz et al. (2014)[25]	Sample size: N = 38 Moderate chronic periodontitis Probiotics (n = 24) Placebo (n = 14) Intervention: NSPT plus placebo or probiotic tablet	Sulcus bleeding index (SBI), PPD, CAL, gingival crevicular fluid (GCF) from periodontal pockets	*Lactobacillus reuteri*	Mode: tablet Frequency: 2x/day Duration: not stated	Majority receiving probiotics saw significant reduction in pro-inflammatory cytokine response and improvements in clinical indices.	Oral treatment *with L. reuteri* may help control/slow the disease process in patients with chronic periodontitis.
Laleman et al. (2015)[26]	Sample size: N = 48 Untreated moderate to severe adult periodontitis Probiotic (n = 24) Placebo (n = 24) Intervention: SRP and probiotic or placebo tablet	PPD, BOP, CAL, PI, GI, microbiological sampling	*Streptococcus oralis* KJ3, *Streptococcus uberis* KJ2, and *Streptococcus rattus* JH145	Mode: tablet Frequency: 2x/day Duration: 24 weeks	Measures significantly improved in both groups. Salivary *Prevotella intermedia* counts significantly lower in probiotic group at 12-week evaluation.	Results showed no significant differences between placebo and probiotic groups with adjunctive periodontal therapy.

Table 2. *Continued*

Author, year	Methods: Sample size, intervention	Data collected	Probiotic(s) studied	Mode and frequency of delivery	Results	Conclusion
Jebin et al. (2021)[27]	Sample size: N = 30 Stage II/Stage III and Grade A/Grade B periodontitis Probiotic (n = 14) Placebo (n = 13) Intervention: SRP and probiotic or placebo tablet	PI, GI, PPD, CAL, microbiological parameters (*P. gingivalis* and *L. reuteri* levels) evaluated at baseline, 1 month, and 3 months in both groups.	*Lactobacillus reuteri*	Mode: chewable tablets Frequency: 1x/day Duration: 1 month	Results showed statistically significant improvement in clinical and microbiological parameters in Group A (SRP + probiotic) compared to Group B (SRP alone) at all evaluation time points.	A probiotic containing *L. reuteri* may be useful when used in adjunct to initial periodontal therapy in slowing the recolonization process of periodontal pathogens and in improving the clinical outcomes of chronic periodontitis.
Vicario et al. (2013)[28]	Sample size: N = 19 Chronic periodontitis Probiotic (n = 10) Placebo (n = 9) Intervention: Probiotic tablet or placebo. Did not receive SRP	PI, BOP, PPD	*Lactobacillus reuteri*	Mode: tablet Frequency: 1x/day Duration: 30 days	Probiotics resulted in clinically significant short-term improvements in clinical periodontal disease parameters. Percentage of PPD reduction at 1 month for initial pockets of 4 mm to 5 mm was 19% after the probiotic treatment and 38% reduction from initial pockets of ≥6 mm.	Results suggest that a probiotic intervention with *L. reuteri* could be used for treatment of inflammation and clinical symptoms of periodontitis, especially in nonsmoking subjects with initial-to-moderate chronic periodontitis.
Teughels et al. (2013)[19]	Sample size: N = 30 Moderate to severe generalized adult periodontitis Probiotic (n = 15) Placebo (n = 15) Intervention: one-stage full-mouth disinfection plus probiotic lozenge or placebo	PPD, CAL, BOP, REC (recession)	*Lactobacillus reuteri*	Mode: lozenge Frequency: 2x/day Duration: 12 weeks	All clinical parameters were significantly reduced in both groups with no significant statistical differences between groups.	Oral administration of *L. reuteri* lozenges could potentially be a useful adjunctive treatment to SRP for patients with chronic periodontitis.
Shah et al. (2017)[21]	Sample size: N = 18 Probing depth and CAL ≥5 mm and radiographic bone loss Probiotic (n = 6) Probiotic + doxycycline (n = 6) Doxycycline (n = 6) Intervention: SRP then randomized to 1 of 3 groups	PI, GI, PPD, CAL, microbiological parameters (*Lactobacilli* and *A. actinomycetemcomitans* were evaluated)	*Lactobacillus brevis*	Mode: lozenge Frequency: 2x/day Duration: 14-day treatment with probiotic, testing at 5 months.	All clinical parameters were significantly improved when comparing baseline to 5 months.	Fourteen days of treatment with *L. brevis* lozenges had a lasting effect on clinical measures of aggressive periodontitis, notably GI. This effect appears to be similar to results of doxycycline.

Table 2. *Continued*

Author, year	Methods: Sample size, intervention	Data collected	Probiotic(s) studied	Mode and frequency of delivery	Results	Conclusion
Tekce et al. (2015)[20]	Sample size: N = 40 Chronic periodontitis patients with radiographically detected horizontal bone loss Probiotic (n = 20) Placebo (n = 20) Intervention: SRP plus *L. reuteri*-containing lozenges or placebo	PI, GI, BOP, PPD, CAL Microbiological sampling performed at baseline and on days 21, 90, 180, and 360 (analysed by culturing)	*Lactobacillus reuteri*	Mode: lozenge Frequency: 2x/day Duration: 3 weeks	PI, GI, BOP, PPD, and pathogenic bacteria were significantly lower in probiotic group compared with placebo group at all time points. In probiotic group, significantly fewer patients required surgery on ≥3 sites.	*L. reuteri*-containing lozenges may be a useful adjuvant agent to slow recolonization and improve clinical outcomes of chronic periodontitis.
Schlagenhauf et al. (2020)[22]	Sample size: N = 72 BOP on at least one Ramfjord teeth Probiotic (n = 36) Placebo (n = 36) Intervention: Probiotic lozenge. Did not receive SRP	BOP, GI, plaque control record (PCR), PPD, probing attachment level (PAL)	*Lactobacillus reuteri*	Mode: lozenge Frequency: 2x/daily Duration: 42 days	Significant improvements in clinical parameters observed between test and placebo groups.	The regular consumption of lozenges containing *L. reuteri* is an efficacious and easily implementable measure to maintain or improve periodontal health in medically healthy persons independent of the efficacy of personal oral hygiene.
Invernici, et al. (2018)[17]	Sample size: N = 30 Generalized chronic periodontitis Probiotic (n = 15) Placebo (n = 15) Intervention: SRP and probiotic or placebo	PI, bleeding on marginal probing (BOMP), PPD, CAL, gingival recession (GR) Gingival tissues and saliva used to analyse immunologically In vitro assays used to analyse the adhesion of *Bifidobacterium animalis* subsp. *lactis* (HN019)	*Bifidobacterium animalis* subsp. *lactis* HN019	Mode: lozenge Frequency: 1x/day Duration: 30 days Measurements taken at 30 days and 90 days	Test group had a lower plaque index at 30 days and BOMP at 90 days compared to the control group. Higher BD-3, TLR4 and CD-4 expressions in gingival tissues in the test group. HN019 reduced adhesion of *P. gingivalis* and showed antimicrobial potential against periodontopathogens	*B. lactis* HN019 may have potential to improve the effects of NSPT.
Invernici et al. (2020)[18]	Sample size: N = 41 Chronic periodontitis Probiotic (n = 20) Placebo (n = 21) Intervention: SRP and probiotic or placebo	PI, BOP, PPD, CAL, GR Immunological monitoring: GCF Microbiological monitoring: subgingival plaque samples	*Bifidobacterium animalis* subsp. *lactis* (HN019)	Mode: lozenge Frequency: 2x/day Duration: 30 days	The test group showed more of a decrease in PPD and CAL than the control as well as fewer periodontal pathogens, orange complexes, proinflammatory cytokine levels. Test group showed an increase in the number of *B. lactis HN019* DNA copies on subgingival biofilm at 30 and 90 days.	*B. lactis* HN019 in adjunct to SRP promotes additional clinical, microbiological, and immunological benefits in the treatment of chronic periodontitis.

Table 2. *Continued*

Author, year	Methods: Sample size, intervention	Data collected	Probiotic(s) studied	Mode and frequency of delivery	Results	Conclusion
Salinas-Azuceno et al. (2022)[23]	Case Report Sample: 30-year-old female patient with stage IV, grade B periodontitis Intervention: Did not receive SRP. One month of daily consumption of the probiotic lozenge	PPD, CAL, PI, gingival erythema (GE), subgingival microbial identification performed at baseline, immediately after 1 month of oral probiotics consumption, then at 2 months (90 days after baseline)	*Lactobacillus reuteri Prodentis.*	Mode: lozenge Frequency: 2x /day Duration: 30 days	Low values of PPD, CAL, GE, and suppuration were observed at baseline vs. 30 days, with the recovery of tooth 46 fistulation. Decrease in pathogenic bacteria at 30 days.	Under monotherapy with *L. reuteri Prodentis,* periodontal measurements of the patient were maintained, with selective changes in the subgingival microbiota that were proportional to the time of probiotic administration.
Morales et al. (2018)[3]	Sample size: N = 47 Chronic periodontitis Probiotic (n = 16) Antibiotic (n = 16) Placebo (n = 15) Intervention: SRP then probiotic, antibiotic or placebo.	Subgingival plaque samples from 4 periodontal sites. Samples were tested using PCR. Measurements taken at baseline and 3, 6, and 9 months post-therapy.	*Lactobacillus rhamnosus* SP1	Mode: sachet Frequency: 1x/day Duration: 3 months	All test groups had improvements in clinical and microbial parameters at 3, 6, and 9 months post-therapy with no significant differences between groups. Probiotic group showed greater reductions in microbiota. The placebo group showed the greatest reduction in the number of subjects with *P. gingivalis.*	Administration of *L. rhamnosus* SP1 in sachets and azithromycin in pills for the treatment of chronic periodontitis generates clinical and microbiological effects similar to the SRP on its own.
Morales et al. (2016)[32]	Sample size: N = 28 Probing depths (PD) >5 mm and CAL >3 mm, 20% BOP, extensive radiographically determined bone loss Probiotic (n = 14) Placebo (n = 14) Intervention: SRP plus probiotic or placebo. NSPT was performed every 3 months	CAL, PPD, PI, BOP Clinical examination recorded at baseline and 3, 6, 9, and 12 months after therapy.	*Lactobacillus rhamnosus* SP1	Mode: sachet Individuals instructed to dissolve 1 sachet in water (150 mL) Frequency: 1x/day Duration: 3 months	Statistically significant intragroup differences observed in the amount of full-mouth CAL and PI reduction. There was a significant PPD reduction in the test group and BOP reduction in the control group.	The adjunctive use of *L. rhamnosus* SP1 sachets during initial therapy resulted in similar clinical improvements compared with SRP alone.

Table 2. *Continued*

Author, year	Methods: Sample size, intervention	Data collected	Probiotic(s) studied	Mode and frequency of delivery	Results	Conclusion
Penala et al. (2016)[29]	Sample size: N = 32 Intervention: SRP + subgingival delivery of probiotic or placebo and probiotic or placebo mouthrinse for 15 days.	PI, modified gingival index (MGI), BI assessed at baseline, 1, and 3 months; PPD and CAL at baseline and after 3 months Microbial assessment using N-benzoyl-DL-arginine-naphthylamide (BANA) and halitosis assessment using organoleptic scores (ORG) at baseline, 1, and 3 months	*Lactobacillus salivarius* and *Lactobacillus reuteri*	Mode: subgingival delivery of probiotics and probiotic mouthrinse Frequency mouthwash: 1 minute 1x/day Duration: 15 days after SRP Subgingival delivery of probiotic solution at baseline (immediately after SRP), 1 week, 2 weeks, and 4 weeks	All clinical and microbiological parameters were significantly reduced in both groups. Intergroup comparison of PD reduction (PDR) and clinical attachment gain (CAG) revealed no statistical significance except for PDR in moderate pockets for the test group. Test group has shown statistically significant improvement in PI, MGI, BI, BANA, and ORG compared to control group.	The adjunctive use of probiotics offers clinical benefit in terms of pocket depth reduction in moderate pockets and reduced oral malodour parameters.
Sajedinejad et al. (2017)[30]	Sample size: N = 100 Intervention: SRP then instructed to use placebo or test mouthrinse	GI, BOP, PPD	*Lactobacillus salivarious*	Mode: mouthrinse Frequency: 1x/day Duration: 4 weeks	It appeared that the probiotic mouthwash was able to inhibit the bacterial growth on both saliva and sub-gingival crevice and exhibited antibacterial activity against *A. actinomycetemcomitans*. Showed decrease in GI and BOP compared to control.	*L. salivarious* has antibacterial effects against *A. actinomycetemcomitans* and can be used as adjunctive treatment with periodontal therapy.
Ranjith et al. (2022)[31]	Sample size: N = 60 Intervention: SRP then instructed to use probiotic or placebo mouthrinse 2x daily for 30 days.	PI, GI, PPD, CAL, salivary pH	*Lactobacillus acidophilus*, *Lactobacillus rhamnosus*, *Bifidobacterium longum*, and *Saccharomyces boulardii*	Mode: mouthrinse Frequency: 2x/day Duration: 30 days	Results showed a significant improvement in all clinical parameters after 1 and 3 months in the treatment group. Significant elevation of salivary IgA and pH was noticed in the probiotic group in contrast to the placebo group.	This study supports the use of a probiotic-containing mouthrinse in the management and treatment of stage II periodontitis when used in adjunct to mechanical debridement.
Nędzi-Góra et al. (2020)[9]	Sample size: N = 51 Intervention: All patients were in the maintenance phase of periodontitis treatment and had completed the initial treatment phase at least 3 weeks earlier.	PI, BOP, PPD, and the number of colony forming units (CFU) of bacteria in supragingival plaque before and after 30 days	*Lactobacillus salivarius*	Mode: supplement in form of suspension Frequency: 1x/day Duration: 30 days	No changes in the PI scores or PPD between the groups. BOP decreased in both groups. No significant changes in the number of bacteria within the groups. In control, but not study group, positive correlations were observed between the clinical parameters (variables) and the number of bacteria.	The use of the dietary supplement containing *L. salivarius* may reduce pocket depth despite the lack of changes in other clinical parameters and the number of bacteria in supragingival plaque.

the number of participants ranging from 1[23] to 72[22] individuals. Many types of clinical parameters were used within the 7 studies, including periodontal probing depth (PPD), clinical attachment level (CAL), bleeding on probing (BOP), plaque index (PI), gingival index (GI), plaque control record (PCR), probing attachment level (PAL), recession (REC), bleeding on marginal probing (BOMP), and gingival recession (GR). Five (5) of the 7 studies used microbiological parameters.[17,18,20,21,23]

Two (2) of the 7 studies did not complete mechanical debridement in adjunct to receiving a probiotic lozenge.[22,23] One of these studies showed slight clinical improvements in PPD and PAL[22] while the other study, a case report, reported no change in periodontal measurements.[23]

Teughels et al.[19] and Tekce et al.[20] investigated the use of *L. reuteri* lozenges in adjunct to scaling and root planing (SRP) in patients with chronic periodontitis. Tekce et al. found *L. reuteri* may be a useful adjunctive to slow disease progression.[20] Results showed the test groups had improved clinical outcomes and slower recolonization than the control group.[20] Similar findings were reported by Teughels et al., who concluded that *L. reuteri*-containing lozenges may be useful as an adjunctive treatment for patients with chronic periodontitis although no significant difference was found between test and control groups.[19] Both studies by Invernici et al.[17,18] demonstrated a decrease in periodontal parameters in addition to improved microbiological parameters.

The remaining study that utilized a lozenge as the mode of delivery compared the use of the antibiotic doxycycline and probiotics.[21] Shah et al.[21] concluded that a lozenge containing the probiotic *L. brevis* had lasting effects on aggressive periodontitis as evidenced by improvements in the gingival index, but with effects similar to that of doxycycline.

Capsule/tablet mode of delivery

Six (31.6%) of the 19 studies included in this review explored the efficacy of probiotics on periodontal parameters when administered through capsules/tablets.[13,24–28] All measured changes in periodontal parameters including PPD, CAL, BOP, PI, and GI; all but 2[24,28] of the studies also measured microbiological parameters. The duration of the studies ranged from 30 days[13,27,28] to 24 weeks,[26] and the number of participants ranged from 20[28] to 48[26].

Three (3) of the 6 studies focussed on the probiotic strain *L. reuteri*,[25,27,28] 1 on heat-killed *Lactobacillus plantarum*,[24] one on *S. oralis, S. cusberis,* and *S. rattus*,[26] while the remaining study focussed on 5 strains of *Lactobacillus* and 3 *Bifidobacterium* strains.[13]

Both Oliveira et al.[13] and Laleman et al.[26] found that, despite there being some slight decreases in periodontal parameters within the test group, the changes were not significantly different from the group receiving SRP only. Iwasaki et al.[24] found similar results for the majority of periodontal parameters. However, PPDs on teeth with pockets >4 mm had significant reductions in the test group when compared against the control group after 12 weeks.

The 3 studies that explored *L. reuteri*[25,27,28] found that the use of a probiotic containing *L. reuteri* reduced clinical and microbiological parameters for a majority of test subjects when used in adjunct to SRP and helped slow the progression of disease.

Mouthrinse, sachet, and suspension mode of delivery

Of the 19 studies included in this scoping review, 3 (15.8%) administered the probiotic as a mouthrinse,[29–31] 2 (10.5%) administered the probiotic as a sachet,[3,32] and 1 (5.3%) administered the probiotic as a supplement in suspension.[9] Clinical parameters measured, study duration, and number of participants varied between studies.

Indices included subgingival plaque samples,[3,9] CAL,[31,32] PPD,[9,29,32] PI,[9,29,31,32] BOP,[9,30,32] modified gingival index (MGI),[29] BI,[29] microbial and halitosis assessment,[29] GI,[30,31] and salivary pH.[31] The duration of the studies ranged from 30[9,30,31] days to 3 months,[3,29,32] and the number of participants ranged from 28[32] to 100[30]. All of the studies evaluated the effects of the probiotic in adjunct to mechanical debridement. [3,9,29–32]

In addition to different modes of probiotic delivery, the studies also varied in the strain of probiotic used. Three of the studies evaluated the probiotic *L. rhamnosus:* 2 via sachet [3,32] and 1via mouthrinse.[31] Despite a significant reduction in PPD and BOP, the 2 studies that examined administration of *L. rhamnosus* via sachet[3,32] concluded that use of the probiotic had similar clinical and microbiological effects as SRP on its own for the treatment of chronic periodontitis. The results of the study using a mouthrinse containing *L. rhamnosus* in addition to *L. acidophillus, B. longum,* and *S. boulardii* showed a significant improvement in GI, PPD, and CAL, supporting the use of a mouthrinse containing *L. rhamnosus* in adjunct to SRP.[31]

The effects of *L. salivarius* were examined when administered via a mouthrinse,[30] mouthrinse in addition to subgingival delivery,[29] or as a supplement in suspension[9]. The study that explored the use of a mouthrinse containing *L. salivarius* demonstrated a decrease in GI and BOP while exhibiting antibacterial activity against *A.actinomycetemcomitans*.[30] Penala et al.[29] examined the use of a mouthrinse and subgingival delivery of the probiotics *L. salivarius* and *L. reuteri* and concluded that the adjunctive use of probiotics offers clinical benefits in terms of pocket depth reduction in moderate pockets and reduced oral malodour parameters. While the study focusing on *L. salivarius* as a supplement in suspension form showed few differences in clinical and microbiological measures between the test and control group, the authors concluded that the use of the dietary supplement containing *L. salivarius* may reduce pocket depth despite the lack of changes in other clinical parameters and the number of bacteria in supragingival plaque.[9]

DISCUSSION

The aim of this scoping review was to explore the available literature on the use of prebiotics and probiotics as a potential adjunctive therapy for the treatment of periodontal disease, with the intent of identifying gaps in the literature to inform future research and dental hygiene practice. Periodontitis is a multifactorial disease that involves many specific bacteria behaving in a particular manner in conjunction with the host's response to the bacteria.[33] There are many different genera and species of prebiotics and probiotics and several different modes of administration that could be examined to determine their impact on periodontal disease through decreasing pathogenic bacteria, altering the host's immune response, or a combination of both.[34,35] As such, the studies included in this review examined various combinations of these factors, with none of the included studies exploring prebiotics. While the authors chose to develop categories based on the mode of delivery of the probiotic, other categories identified were 1) inclusion of mechanical debridement in the study protocol; 2) use of periodontal indices with or without microbiological testing; and 3) use of specific probiotic strains.

Periodontal disease is an inflammatory disease mainly influenced by the presence of pathogenic bacteria[1,2] embedded in dental biofilm[8]. Home oral hygiene practices, including brushing and interdental care, are important in combatting dysbiosis and maintaining a healthy microflora.[36] When home oral hygiene is inadequate, biofilm accumulates and the presence of pathogenic bacteria increases.[36] As previously mentioned, the traditional treatment of mechanical debridement to remove calculus, biofilm, and toxins is not always effective at halting the progression of periodontal disease.[4] In addition to mechanical debridement, oral health professionals may prescribe antibiotics as an adjunctive treatment, as research has demonstrated that the administration of adjunctive systemic antibiotics increases the effectiveness of mechanical therapy.[37] However, the risk of microbial resistance and the influence on the entire human microbiome linked to systemic antibiotic administration has called the use of antibiotics into question.[38]

Recently, there has been a move towards exploring other treatment modalities to help in the treatment and management of periodontal disease. The use of prebiotics and probiotics is of particular interest as prebiotics and probiotics have the potential to not only decrease pathogenic oral bacteria and reduce the occurrence of dysbiosis, but also to decrease systemic inflammation which can impact the initiation and progression of periodontal disease.[39] To better understand this potential, it is important that, in addition to measuring changes in traditional clinical periodontal indices such as PPD and CAL, the effect on microbiological and immunological parameters also be examined. In addition to measuring changes in clinical indices, 13 of the 19 articles included in this review also measured changes in microbiological parameters,[3,9,13,17–21,23,26,27,29,30] with all but 2[13,25] showing improvements. Additionally, 4 of the 19 studies measured immunological parameters with all finding favourable results.[17,18,25,31] Favourable changes in the oral microbiota or in the immunological markers with the use of probiotics could indicate their potential to manage the dysbiosis that initiates or causes the progression of periodontal disease.

In addition to including measurements of microbiological and immunological parameters, the studies compared many other periodontal indices. To accurately provide a periodontal diagnosis and to monitor the progression of the disease, oral health professionals use several indices. However, it is widely accepted that the most reliable indication of periodontal disease progression is an increase in CAL. All but 5[3,9,22,24,28] of the studies measured CAL. Although CAL is a useful measurement for indicating disease progression, the relatively short duration of most of the studies may not have allowed adequate time for a significant change to be observed.

All but 4[22,23,25,28] of the studies included mechanical debridement in conjunction with the use of probiotics. However, there was wide variation in study protocol. These variations included the interval of mechanical debridement and the use of different periodontal disease classification systems. Of the studies that included mechanical debridement, all but 1[24] did so at the beginning of the study prior to the administration of the probiotic. Depending on the length of the study, performing mechanical debridement throughout the study could be considered more consistent with traditional treatment protocol for periodontal disease where debridement would be completed at 3-month intervals. Longer duration studies with regular periodontal maintenance (SRP) appointments in conjunction with the use of a probiotic may be more useful in identifying the potential role that probiotics could play in slowing or halting the progression of periodontal disease when compared to scaling and root planing alone. Additionally, none of the included studies measured the effects of the probiotics at time points after their final administration. In other words, the studies that found an oral health benefit from probiotic use did not determine how long those benefits remained.

Fourteen of the studies utilized the American Academy of Periodontology (AAP) periodontal classification system that existed prior to 2017,[3,17–21,24–30,32] while 2 of the studies did not specify the periodontal diagnosis of the participants.[13,23] Only 2 of the included studies used the current AAP classification system.[9,31] The use of different classification systems may have affected participant recruitment in addition to the interpretation and understanding of the findings, as it may be easier to see improvements in periodontal indices when periodontal disease is less advanced.

Lactobacillus and *Bifidobacteria* have been the most-studied probiotics in relation to oral health and have been deemed to be effective and safe.[40] It has been proposed that the probiotic *Lactobacillus* could be beneficial in

controlling dental caries.[41] In keeping with this theory, both *Lactobacillus*[3,6,9,13,27,31,42–46] and *Bifidobacterium*[31,42,47–49] were selected as the probiotics in the studies included in this review. None of the studies indicated any adverse events in relation to the use of these probiotics, thereby supporting the safety of using probiotics to help manage periodontal disease.

Probiotics have been studied extensively in the treatment of inflammatory diseases such as inflammatory bowel disease, with *L. reuteri* in particular, demonstrating a positive effect by reducing pathogenic bacteria and promoting absorption of nutrients.[50] Of the studies that examined *L. reuteri*,[19,20,22,23,25,27–29], 5[20,23,25,27,29] measured microbiological parameters with favourable results while the remaining 3[19,22,28] utilized a combination of periodontal indices including PPD, BOP, BI, GI, and CAL, also with favourable results. These results could support the theory that *L. reuteri* could be effective in reducing periodontal pathogens and oral microbiota dysbiosis with the goal of improving periodontal parameters.

Similarly, *Bifidobacterium* probiotics have been reported to support changes in the gut microflora conducive to managing and preventing many diseases involving the gut.[51] *Bifidobacterium* is a genus included in many oral health studies as it has been shown to produce antimicrobial compounds and prevent pathogen adherence.[17] The study conducted by Invernici et al.[17] showed lower counts of *P. gingivalis* and other periodontal pathogens with the use of *Bifidobacterium*, indicating its potential to promote better clinical and microbiological outcomes for patients with chronic periodontitis.

Studies utilized different administration routes for *Lactobacillus* and *Bifidobacterium* including a mouthrinse,[31] chewable tablet,[6] lozenges,[42,43] and a capsule.[13] Results of these studies were mixed. While the capsule containing *Lactobacillus* and *Bifidobacterium* did not show short-term microbiological benefits,[13] the tablets containing 2 *Lactobacillus* strains and *P. acidilacti* showed significant reduction in severe inflammation sites and reduction of *Tannerella forsythia,* a periodontal pathogen that initiates periodontal disease.[6,52] Lozenges containing both *Bifidobacterium* and *Lactobacillus* strains showed improved clinical parameters through decreased GI and PI, although no microbial salivary changes were reported.[42] These results point to the potential systemic use of both *Lactobacillus* and *Bifidobacterium* to minimize the inflammatory response and decrease the initiation and progression of periodontal disease.

Future research

This scoping review identified gaps in the literature that could inform future research. While prebiotics may play a role in positively influencing the microbiome, none of the 19 studies included in this review examined prebiotics. Further research is required to better identify the effectiveness of prebiotics on their own or in conjunction with probiotics.

The protocol of the studies varied widely, with the most notable differences being in the type and administration route of the probiotic, duration of the study, and parameters measured. Future research should focus on developing a standardized study protocol to allow for comparison of the results of different probiotics via different routes of administration. Longer term studies to measure the extended effects of probiotics are also indicated.

Limitations

While the research team conducted a robust review of the available literature, this review does have limitations. The research team chose to limit the search to 3 databases. While those databases were selected due to their foci and size, there may have been articles in other databases that were not identified. Only articles written in English could be reviewed for this study as all members of the research team are English speaking. It is possible that some valuable studies that met the inclusion criteria but were written in languages other than English were excluded. Additionally, researchers only screened articles that were published within the last 10 years. It may be possible that relevant studies published prior to 2013 were missed in the search. In accordance with Stage 2 of the Arksey and O'Malley framework[12] for scoping reviews, only the title and abstracts of the initial 150 collated articles were screened for relevance to the topic. Due to the involvement of multiple researchers in the screening and a limited context for each screened study, it is possible that studies may have been missed in this process.

CONCLUSION

Most of the literature identified in this review indicated that the use of probiotics may have a positive impact on periodontal health by decreasing periodontal pathogens, reducing the number of inflammatory markers, and/or restoring homeostasis of the microbiome in periodontally involved subjects. To better inform dental hygiene practice and treatment modalities for periodontal disease, more research is required to determine the most effective probiotics, administration routes, duration of consumption of the probiotic, and extended effects of the probiotics.

CONFLICTS OF INTEREST

The authors declare no known conflicts of interest.

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