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Diet and oral health: probiotics and their use in the periodontal prophylaxis

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Abstract

Maintaining good oral health is essential for overall well-being, and diet plays a significant role in oral health. The oral microbiome made of a diverse community of microorganisms, is influenced by individual factors such as age, gender, environment, as well as dietary choices and its imbalances in the oral microbiota have been associated with dental caries and periodontitis. Periodontitis, a common chronic inflammatory condition of the oral cavity, is a significant public health concern worldwide. It is characterized by the destruction of bone and gum tissues that support the teeth and can lead to tooth loss. The primary cause of periodontal damage is the host-mediated inflammatory and immune responses to the accumulation of microbial plaque. Dietary choices, including the intake of high in acid and sugar foods, can influence the composition of the oral microbiota and contribute to the development of periodontal disease.

Recent studies have focused on the role of probiotics in managing periodontal diseases. Probiotics are beneficial microorganisms that can modify the composition of the sub-gingival microbiota, decrease the concentration of periodontal pathogens, and improve clinical parameters associated with periodontitis. Probiotic species belonging to genera like Lactobacillus, Bifidobacterium, Streptococcus, and Weissella have shown promising results in promoting periodontal health. Clinical trials have demonstrated that probiotics, when used as adjuvant therapy alongside conventional treatments, can lead to significant improvements in periodontal health without any significant side effects. However, the effectiveness and safety of probiotics in managing periodontal diseases remain controversial, and further research is needed. Factors such as probiotic species, dosage, combination of probiotics, and evaluation indices should be carefully considered. Additionally, more systematic studies on the safety profile of probiotics are necessary to ensure their safe application. Consequently, to ensure best dental care, the use of probiotics shows promise in preventing and treating periodontal diseases by modulating the oral microbiota. However, further research is needed to determine the optimal use of probiotics and their long-term effects on oral health.

Introduction

Maintaining good oral health is crucial for overall well-being, and diet plays a significant role in oral health. The oral microbiome, which consists of a diverse community of microorganisms, including bacteria, fungi, and viruses, is influenced by dietary choices. Not surprisingly, dietary choices has been shown to have a significant impact on oral health and therefore composition of the oral microbiota. The oral microbiota is a complex microbial community that resides in the oral cavity composed of over 700 species of bacteria, fungi, viruses, archaea, and protozoa (Peng et al., 2022; Caselli et al., 2020) organized within the distinctive niches including the gingival sulcus, the tongue, the cheek, the hard and soft palates, the floor of the mouth, the throat, the saliva, and the teeth (Deo and Deshmukh, 2019). In particular, the tongue having a numerous papillae is occupied by a diverse microflora which also includes anaerobe; whereas the buccal and palatal mucosae (Deo and Deshmukh, 2019). The oral microbiome, depending on the age, gender, environment, especially diet can undergo large and rapid changes in composition and activity that may impact both oral and general health status (Peng et al., 2022). Studies involving healthy participants are therefore crucial to defining the human oral microbiota in health before trying to confirm any correlation of the oral microbiome with peculiar disease conditions (Caselli et al., 2020). On the other hand, the oral microbiota has been associated with oral disease, including dental caries and periodontitis (Li et al., 2022).

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Periodontitis as a common chronic inflammatory condition of the oral cavity, is a public health problem, affecting about 20–50% of people worldwide, and its global burden is predicted to increase in the future, above all due to the general aging population (Nazir et al., 2020). Gingival inflammation, clinical attachment loss (CAL), radiographic assessed resorption of alveolar bone, presence of periodontal pockets, gingival bleeding upon probing, and teeth mobility are all specific clinical signs of periodontitis that, may lead to premature teeth loss in advanced stages (Papapanou et al., 2018). The primary etiological factor of periodontal damage is the host-mediated inflammatory and immune responses to the accumulation of microbial plaque and its diffusible enzymes, such as lipases, proteases, and nucleases along with important individual causal factors, such as genetic and epigenetic susceptibility (i.e., single nucleotide polymorphism), co-occurring systemic diseases, like osteoporosis, atherosclerosis or diabetes, that may exacerbate the onset and the progression of periodontal disease, as well as lifestyle factors, like tobacco use and diet (Di Stefano et al., 2022). For example, intake of certain foods, such as farmed animal meat, dairy products, refined vegetable oils, and processed cereals, can affect the composition of the oral microbiota. In particularly, a widespread "Westernized" dietary pattern characterized by high-sugary dairy products, farmed animal meats, refined vegetable oils, and processed grains has been associated with pathological changes in the oral microbiota (Santonocito et al., 2022). In addition, low consumption of fruit and vegetables, being a potent source of diet low in vitamin C and D can serve additional risk factors of poor oral health. Similarly, carbohydrate intake has been associated with the abundance and diversity of the subgingival plaque oral microbiome (Millen et al., 2022), and high sugar intake has been found to have an unfavorable effect on the diversity and balance of the oral microbiota (Angarita-Díaz et al., 2022), referred as to dysbiosis; and progressively leading to a shift to a saccharolytic, acidogenic, and aciduric microbiota. Increased abundance of following microbes can increase acid production in mouth that can contribute to tooth decay and erosion. Acidic environments in the mouth can promote the growth of acid-producing and acid-tolerant organisms (Shaalaan et al., 2022). All following changes might over the time lead to peridontitis and development of periodontal disease. Considering the role of diet in maintaining oral health through modulating activity and composition of microbial communities resident in the oral cavity, the main aim of the following article is to assess the effect of microbial-targeted interventions, with specific focus on probiotic in reducing risk of peridontitis.

Probiotics implicated in oral health

Probiotics, defined as living microorganisms that when administered in the adequate amounts can have a beneficial effect on the host (Hill et al., 2014). Despite that supplementation with probiotics is widely used in terms of gastrointestinal health to control intestinal infections, relieve constipation and diarrhea, improve lactose intolerance, etc.; nevertheless, the growing body of evidence supporting the role of human microbiota in human health, now has shown that probiotics can also benefit other body systems, including oral health.

Recently, extensive studies also explored the application of probiotics in oral disease treatment and oral healthcare. Currently, it is found that probiotics contributing to oral health are concentrated in the genera Lactobacillus, Bifidobacterium, Streptococcus, and Weissella, as well as certain scattered species like Bacillus subtilis and Saccharomyces cerevisiae. Several strains of Lactobacillus reuteri, Lactobacillus brevis, Streptococcus salivarius, etc., have been commercially produced as oral health-promoting probiotics, with effects showing improvements in the oral health in common oral diseases such as dental caries, periodontal diseases, oral candida infection, and halitosis (Zhang et al., 2022).

Probiotics implicated in oral health: focus on periodontal disease

Periodontal diseases as chronic inflammatory condition resultant in the destruction of bone and gum tissues that support the teeth, can be classified into (1) gingivitis and (2) periodontitis. Briefly, gingivitis is a mild form of periodontal disease, but the progression of untreated gingivitis can lead to more serious periodontitis by creating deep periodontal pockets that could cause teeth to loosen or lead to tooth loss, which has a marked impact on patients' life.

*** Interesting fact ***
It is reported that as of 2019, there are 1.1 billion patients with severe periodontitis worldwide, and the prevalence of severe periodontitis has increased by 8.44% from 1990 to 2019 (Chen et al., 2021).

The main initial factor of periodontal diseases is creation of dental plaque, which is a microbial biofilm that forms on the teeth and gingiva. If the dental plaques are not removed regularly, the biofilm undergoes maturation, and may lead to formation of pathogenic bacterial complex progressing over time to dental caries, gingivitis, and periodontitis. The bacteria in the biofilm produce toxins that cause inflammation of the gingiva (gingivitis), which can progress to periodontitis if left untreated (Zhang et al., 2022).

Although oral microbiota is diverse as it contains more than 700 bacterial species (Kumar et al., 2005), only a few bacteria are proved to initiate and advance periodontal diseases, with examples such as P. gingivalis, Aggregatibacter actinomycetemcomitans, Tannerella forsythia, Prevotella intermedia, and Fusobacterium nucleatum (Hajishengallis et al., 2012).

Probiotics for periodontal health

Recent evidence from the studies focusing on the role of probiotics in managing periodontal diseases, is often focused on the four periodontopathogens, namely, P. gingivalis (chronic periodontitis), A. actinomycetemcomitans (aggressive periodontitis), P. intermedia (pregnancy gingivitis, moderate and severe gingivitis, acute necrotizing gingivitis,

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and chronic periodontitis), and F. nucleatum (chronic periodontitis and acute necrotizing ulcerative gingivitis).

Although the exact mechanisms of probiotics promoting periodontal health have not been fully elucidated, a considerable amount of research including human trials have revealed that probiotics confer periodontal-health benefits. These benefits were attributed to various probiotic species, especially those belonging to genera Lactobacillus, Bifidobacterium, Streptococcus, and Weissella.

The proposed species along with their properties are listed in Table 1. below.

Table 1. Known probiotic species promoting periodontal health along with their effect on oral health. Adopted from Zhang et al. (2022).

Genus	Species	Implicated effect in oral health
Lactobacillus	Lactobacillus acidophilus	Reduce Fusobacterium nucleatum-induced and Porphyromonas gingivalis-induced inflammation. Inhibit the growth of P. gingivalis. Co-aggregate with F. nucleatum to interfere with adhesion and invasion. Downregulate the virulence-associated factors of P. gingivalis, F. nucleatum (in vitro experiment) and Aggregatibacter actinomycetemcomitans. Degrade A. actinomycetemcomitans biofilms by producing enzymes such as lipase.
	Lactobacillus brevis	Produce arginine deiminase to reduce the level of pro-inflammatory factors (TNF-α, IL-1β, IL-6, and IL-17). Promote a higher ratio between aerobic and anaerobic bacteria. Inhibit A. actinomycetemcomitans in saliva. Inhibit the growth and biofilm formation of Prevotella melaninogenica.
	Lactobacillus casei	Reduce the F. nucleatum-induced pro-inflammatory IL-6 production in oral epithelial cells. Reduce the abundance of P. gingivalis, A. actinomycetemcomitans, and P. intermedia in subgingival plaque. Degrade A. actinomycetemcomitans biofilms by producing enzymes such as lipase.
	Lactobacillus fermentum	Reduce the F. nucleatum-induced pro-inflammatory IL-6 production in oral epithelial cells. Degrade A. actinomycetemcomitans biofilms by producing enzymes such as lipase. Inhibit the growth of P. gingivalis, P. intermedia, and A. actinomycetemcomitans.
	Lactobacillus gasseri	Decrease expression of pro-inflammatory cytokines, such as IL-6 and TNF-α in gingiva infected by P. gingivalis. Reduce exotoxins prouced by A. actinomycetemcomitans. Inhibit the growth of P. gingivalis and P. intermedia. Decrease the colonization of P. gingivalis in gingiva.
	Lactobacillus reuteri	Reduce the F. nucleatum-induced pro-inflammatory cytokine IL-6 production. Inhibit the expression of pro-inflammatory factors (TNF-α, IL-1β, and IL-17). Inhibit P. gingivalis in saliva, supragingival plaque and subgingival plaque, and P. intermedia in saliva. Reduce the load of P. gingivalis in peri-implant mucositis.
	Lactobacillus rhamnosus	Reduce immune cell infiltration. Inhibit the growth of P. gingivalis, A. actinomycetemcomitans, and F. nucleatum. Reduce the biofilm of A. actinomycetemcomitans by releasing postbiotics.

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		Downregulate the virulence-associated factors of A. actinomycetemcomitans.
	Lactobacillus salivarius	Inhibit A. actinomycetemcomitans in saliva. Reduce the expression of A. actinomycetemcomitans exotoxins.
	Lactobacillus johnsonii, Lactobacillus fructosum, Lactobacillus delbrueckii subsp. casei	Degrade A. actinomycetemcomitans biofilms by producing enzymes such as lipase.
Bifidobacterium	Bifidobacterium animalis subsp. lactis	Increase the expression of anti-inflammatory factors (IL-10, TGF-β1, and β-defensins) and reduce the expression of pro-inflammatory factors (TNF-α, IL-1β, IL-6, CINC) in gingival cells in periodontitis. Inhibit the growth of P. gingivalis, P. intermedia, A. actinomycetemcomitans, and F. nucleatum. Reduce the adhesion of P. gingivalis to buccal epithelial cells. Reduce biofilm formation of F. nucleatum and P. gingivalis. Change the ratio between aerobic and anaerobic bacteria and the proportion of subgingival community. Reduce the level of P. gingivalis, Treponema denticola, Fusobacterium nucleatum vincentii, and A. actinomycetemcomitans in deep periodontal pockets, saliva, and dental plaque.
Streptococcus	Streptococcus salivarius	Inhibit the expression of IL-6 and IL-8 induced by P. gingivalis, A. actinomycetemcomitans, and F. nucleatum in gingival fibroblasts. Inhibit the growth of P. gingivalis, P. intermedia, A. actinomycetemcomitans, and F. nucleatum. Inhibit the adhesion of A. actinomycetemcomitans, P. gingivalis, and P. intermedia.
	Streptococcus dentisani	Increase the secretion of IL-10 and decline the level of IFN-γ induced by F. nucleatum in HGF-1. Change cell wall structure of P. intermedia and induce cell lysis of F. nucleatum. Suppress F. nucleatum and P. gingivalis growth and attachment to HGF-1.
	Streptococcus cristatus	Reduce the F. nucleatum-induced pro-inflammatory IL-8 production in oral epithelial cells. Inhibit adhesion and colonization of A. actinomycetemcomitans.
	Streptococcus gordonii, Streptococcus sanguinis, Streptococcus mitis	Inhibit adhesion and colonization of A. actinomycetemcomitans, P. gingivalis, and P. intermedia on hard surfaces or epithelial cells.
Weissella	Weissella cibaria	Reduce the F. nucleatum-induced pro-inflammatory cytokine (IL-6 and IL-8) production in KB cells. Inhibit NF-κB activation and NO production in response to periodontopathogen stimulation in macrophages. Reduce both the production of pro-inflammatory (TNF-α, IL-1β, IL-6) and anti-inflammatory (IL-10) cytokines. Co-aggregate with F. nucleatum, T. denticola, and P. gingivalis and inhibit the growth of F. nucleatum and P. gingivalis. Interfere with the adhesion of F. nucleatum. Produce acid, H2O2, and N-acetylmuramidase to inhibit F. nucleatum, P. gingivalis, and P. intermedia.

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		Reduce the amount of plaque and F. nucleatum, P. gingivalis, P. intermedia, and T. forsythia levels in the oral cavity and P. gingivalis level in gingival cells.

According to several human clinical trials, probiotics have the potential to modify the composition of the sub-gingival microbiota, lowering considerably the concentration of the major periodontal pathogens, and can be used as adjuvant agents to reinforce the clinical improvements provided by mechanical debridement, all without any kind of evidence of short- and long-term side effects in the patients (Di Stefano et et al., 2022).

The recent systematic review assessing the clinical effect of probiotics as an adjuvant treatment to scaling and root planning in patients with periodontitis have shown that administration of probiotics as an adjuvant treatment to periodontal treatment can help improve the clinical parameters, demonstrated as significant decrease of the concentration in the main periodontal pathogens; and importantly this effect is not accompanied by the any side effects (Canut-Delgado et al., 2021). Similarly, assessment of clinical trials investigating use of use of probiotics as adjuvant therapy of periodontal disease have shown that probiotics led to an improvement in periodontal pocket depth, clinical attachment loss, and bleeding on probing parameters; nevertheless, with no improvement in the index plaque parameter (Hardan et al., 2022).

Supplementation with the probiotic lozenges containing Bifidobacterium animalis subsp. lactis (B. lactis) HN019 added as adjuvant to scaling and root planing (SRP) over 30 days significantly reduced number of periodontal pathogens of red and orange complexes, as well as lower proinflammatory cytokine levels in patients with generalized chronic periodontitis, compared to control receiving placebo. Interestingly, patients who obtained probiotic also showed an increase in the number of B. lactis HN019 DNA copies on subgingival biofilm at 30 and 90 days, suggesting additional clinical, microbiological, and immunological benefits in the treatment of chronic periodontitis (Invernici et al., 2018).

Daily intake for 90 days of probiotic lozenge containing the oral probiotic, Lactobacillus reuteri Prodentis, as adjuvant to non-surgical mechanical therapy in implants with mucositis or peri-implantitis, prescribed to patients with a history of periodontal disease has been shown to produce an additional benefits when combined with mechanical treatment, leading to the improvement in the general clinical parameters of patients with mucositis (bleeding on probing) and at the level of implants with mucositis (probing pocket depth) or peri-implantitis (bleeding on probing and probing pocket depth), when compared to treatment alone. However, L. reuteri seem to have a very limited effect on the peri-implant microbiota because the only parameter in which a significant decrease was found was the bacterial load of P. gingivalis in implants with mucositis. Consequently, use of this probiotic may provide an alternative therapeutic approach to consider in the prevention and treatment of peri-implant diseases, but further long-term prospective studies with standardized variables are needed (Galofré et al., 2018).

Use of mouthwash containing L. salivarius NK02 was tested at a dose level of 10^8 CFU/ml over period of 4 weeks was effective in inhibiting the bacterial growth on both saliva and sub-gingival crevice and exhibited antibacterial activity against A. actinomycetemcomitans. In addition, individuals receiving probiotic also demonstarted a significant decrease of gingival index and bleeding on probing compared to those receiving placebo. The rate of decrease in pocket depth was also noticeable in the probiotic group through reduction of probing pocket depth value thereby explaining the decrease in inflammation in gingiva. Overall, this study may suggest that adding probiotic to daily oral care routine in the mouthwash can be used as an alternative for maintaining dental and periodontal health (Sajedinejad et al., 2018).

Considering following evidence, it might be difficult to conclude whether probiotics offer any clinical benefit in the treatment of periodontal disease based on the available evidence; nevertheless the use of probiotics is a promising approach to prevent and treat periodontal diseases, but their practical use for periodontal health needs further research and exploration.

Issues in Current Application of Periodontal Health-Related Probiotics

The current application of probiotics for periodontal health faces several issues, including effectiveness and safety concerns. The effectiveness of probiotics in managing periodontal disease remains controversial, with inconsistent results observed across studies. Factors such as probiotic species or strains, dosage, combination of probiotics, and reaction time may contribute to the variability in outcomes. Additionally, the selection of evaluation indices and the impact on periodontal microbiota and inflammatory factors should be considered. Safety is another crucial aspect to address, as probiotics may have potential risks and side effects. Although classical probiotics are generally recognized as safe, more systematic safety studies are needed, particularly regarding antibiotic resistance, toxin production, and metabolic activities. Probiotic use may also influence host immune responses and disrupt microecology. Therefore, a thorough understanding of the safety profile of probiotics and careful assessment of probiotic products are essential for their safe application (Zhang et al., 2022)).

Conclusions

Probiotics have been explored for their potential role in preventing and managing periodontal diseases, specifically gingivitis and periodontitis. These conditions are characterized by inflammation of the gums and damage to the supporting tissues of the teeth. Pathogenic bacteria, such as P. gingivalis, T. denticola, T. forsythus, and A. actinomycetemcomitans, are associated with periodontitis and

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can evade the host's defense mechanisms. Probiotics, particularly Lactobacilli like L. gasseri and L. fermentum, have been found to be more abundant in the oral cavity of healthy individuals compared to those with chronic periodontitis. Experimental studies have shown that probiotic interventions can enhance microbiota normalization and help prevent the recurrence of periodontal pathogens after mechanical plaque removal. They can also protect the epithelial barrier and maintain periodontal health by preserving tight junction integrity. Addition of probiotics to treatment protocols has resulted in significant reductions in major periodontopathogens like P. gingivalis, A. actinomycetemcomitans, and T. forsythia in subgingival plaque. However, some studies have shown that the benefits of probiotics on periodontal health may diminish over time, with the resurgence of certain pathogens. Long-term use and specific combinations of probiotic strains need to be further explored to optimize their effectiveness. Furthermore, the reduction in anaerobic bacteria in subgingival plaque suggests a potential role for probiotics in modulating the oral microbiota and preventing the progression of periodontitis.

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