

Probiotics and Oral Health

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ABSTRACT

The number of products containing probiotics, viable bacteria with proven health benefits, entering the market is increasing. Traditionally, probiotics have been associated with gut health, and most clinical interest has been focused on their use for prevention or treatment of gastrointestinal infections and diseases; however, during the last decade several investigators have also suggested the use of probiotics for oral health purposes. The aim of this review is to examine potential mechanisms of probiotic bacteria in the oral cavity and summarize observed effects of probiotics with respect to oral health. The review focuses on probiotic lactobacilli and bifidobacteria, genera that are most used in various probiotic products. (Eur J Dent 2010;4:348-355)

Key words: Probiotics; Oral health; *Lactobacillus*; *Bifidobacterium*.

INTRODUCTION

Probiotics can be defined as living microbes, or as food ingredients containing living microbes, that beneficially influence the health of the host when used in adequate numbers.¹ Both definitions have in common the idea that probiotic microorganisms are living. Furthermore, the efficacy and safety of probiotics should be scientifically proven. Probiotic effects are strain specific; thus each individual bacterial strain must be tested separately for the health benefit in question, and the effects described for one strain cannot be directly applied to others.²

Traditionally, probiotics have been associated with gut health, and most clinical interest has fo-

cused on the prevention or treatment of gastrointestinal infections and diseases; however, during the last decade, an increasing number of established and proposed health effects of probiotic bacteria have been reported, including enhancement of the adaptive immune response, treatment or prevention of urogenital and respiratory tract infections, and prevention or alleviation of allergies and atopic diseases in infants.^{2,3} Several investigators have also suggested probiotics for oral health purposes. Interestingly, probiotics are also suggested to increase the lifetime of voice prosthesis by inhibiting the adhesion of unwanted microbes.⁴⁻⁶

The most commonly used probiotic bacterial strains belong to the genera *Lactobacillus* and *Bifidobacterium*.³ These bacterial genera are regarded as a part of the normal human microbiota. In the oral cavity, lactobacilli usually comprise fewer than 1% of the total cultivable microbiota, but no species specific to the oral cavity has been found. In contrast, some species are found in both oral and fecal samples.^{7,8} Species commonly isolated

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from saliva samples include *L. paracasei*, *L. plantarum*, *L. rhamnosus*, and *L. salivarius*.⁷⁻¹⁰ Culture-based studies suggest that bifidobacteria are among the first anaerobes in the oral cavity.¹¹ Indeed, both lactobacilli and bifidobacteria can be found in breast milk, suggesting early exposure of the oral cavity to these bacteria.^{12,13} Bifidobacterial species isolated from oral samples include *B. bifidum*, *B. dentium*, and *B. longum*.^{8,14,15}

Lactobacilli and bifidobacteria are generally regarded as safe, and, since the early writing of Metchnikoff,¹⁶ even more fermented food products have been associated with health benefits. In respect to normal microbiota and oral health, there seem to be differences in the ability of lactobacilli isolated from caries-active or healthy subjects to inhibit *Streptococcus mutans* in vitro.¹⁰ In addition, the species composition of both *Lactobacillus* and *Bifidobacterium* microbiota is different between patients with periodontitis and those who are periodontally healthy.^{17,18} On the other hand, both lactobacilli and bifidobacteria are also associated with dental caries.^{19,20} In addition, caries-associated lactobacilli and bifidobacteria have been characterized as exogenous and opportunistic colonizers possibly acquired from food.^{15,21}

During the last few years, several authors have suggested that probiotic bacteria originally planned for gut health could also be beneficial to oral health. The aim of this review is to examine potential mechanisms of probiotic bacteria in the oral cavity and to summarize observed effects of probiotics with respect to oral health. Finally, some future aspects are briefly discussed. This review focuses on probiotic lactobacilli and bifidobacteria, genera that are most used in various probiotic products.

POTENTIAL MECHANISMS OF PROBIOTIC EFFECTS IN THE ORAL CAVITY

The general mechanisms of probiotics can be divided into three main categories: normalization of the intestinal microbiota, modulation of the immune response, and metabolic effects.²² The mechanisms of probiotic action in the oral cavity could be analogous to those described for the intestine. Possible ways that probiotics might affect oral health are summarized in Figure 1. Thus far oral colonization by probiotic bacteria

has often been considered essential for them to exert oral effects; however, the possibility of systemic effects cannot be excluded, although the total sIgA levels in saliva seem unaffected by probiotic use.^{23,24} Interestingly, maternal use of some probiotic strains seems to influence the composition of breast milk.²⁵

In respect to commensal oral microbes, several aspects support the idea that it may be possible to find bacteria that could be useful in prevention or treatment of oral diseases. In fact, it has been suggested that some observed probiotic effects are not just properties of a few well-studied strains but common to several species.²⁶⁻²⁸ The ecological plaque hypothesis suggests that selective pressure in environmental conditions can change the balance between oral health and disease.²⁹ As bacteria can also influence their environment, and both synergistic and antagonistic interactions are suggested for bacteria in dental plaque, the environmental pressure described in the ecological plaque hypothesis could be introduced partly by bacteria. Second, it is well recognized that the normal microbiota protect the oral cavity from infections. Finally, just as there are bacterial species associated with oral diseases, there are also species that seem to be associated with oral health;^{20,30,31} however, it is questionable whether bacteria administered in food could influence relatively stable oral microbiota, in particular in adults. In addition, it must be kept in mind that all the mechanisms described in this section are based on in vitro results, and the clinical evidence is based mainly on short clinical pilot studies.

OBSERVED EFFECTS ON ORAL HEALTH

Caries and caries-associated microbes

Several studies suggest that consumption of products containing probiotic lactobacilli or bifidobacteria could reduce the number of mutans streptococci in saliva.³²⁻⁴⁰ The tendency toward a decreased number of mutans streptococci in the saliva seems to be independent of the product or strain used; however, such effect has not been observed in all studies.⁴¹ The discrepancies between results cannot be explained by only the use of different probiotic strains, as different results have also been obtained using the same strains. In most of these studies, the levels of salivary lacto-

bacilli have also been measured. With three products, an increase in the number of salivary *Lactobacillus* has been observed.^{33,41} Unfortunately, with respect to dental caries, the study groups have mainly been relatively small, and the studies fairly short. Furthermore, it is important to realize that the salivary level of caries-associated microbes does not equate to dental caries. In fact, the microbiota of unstimulated whole saliva resembles that of the tongue more than of dental plaque.⁴² Thus, no conclusive statement about the effects of probiotic bacteria on dental caries can be made.

Periodontal diseases

The first studies of the use of probiotics for enhancing oral health were for the treatment of periodontal inflammation.⁴³ Patients with various periodontal diseases, gingivitis, periodontitis, and pregnancy gingivitis, were locally treated with a culture supernatant of a *L. acidophilus* strain. Significant recovery was reported for almost every patient. There has been significant interest in using probiotics in treatment of periodontal disease

recently, too. The probiotic strains used in these studies include *L. reuteri* strains, *L. brevis* (CD2), *L. casei* Shirota, *L. salivarius* WB21, and *Bacillus subtilis*. *L. reuteri* and *L. brevis* have improved gingival health, as measured by decreased gum bleeding.⁴⁴⁻⁴⁶ The use of probiotic chewing gum containing *L. reuteri* ATCC 55730 and ATCC PTA 5289 also decreased levels of pro-inflammatory cytokines in GCF,⁴⁶ and the use of *L. brevis* decreased MMP (collagenase) activity and other inflammatory markers in saliva.⁴⁵ With *L. casei* Shirota and *Bacillus subtilis* no difference in test and control groups in gingival bleeding or measured plaque index was observed, but the use of *L. casei* Shirota decreased PMN elastase and MMP-3 activities in GCF, and gingival inflammation was lower in the group consuming the probiotic product, as measured by MPO activity after a four-day period of experimental gingivitis.⁴⁷ *B. subtilis* seemed to reduce the number of periodontal pathogens.⁴⁸ Use of tablets containing *L. salivarius* WB21 has been shown to decrease gingival pocket depth, particularly in high-risk groups such as smokers, and

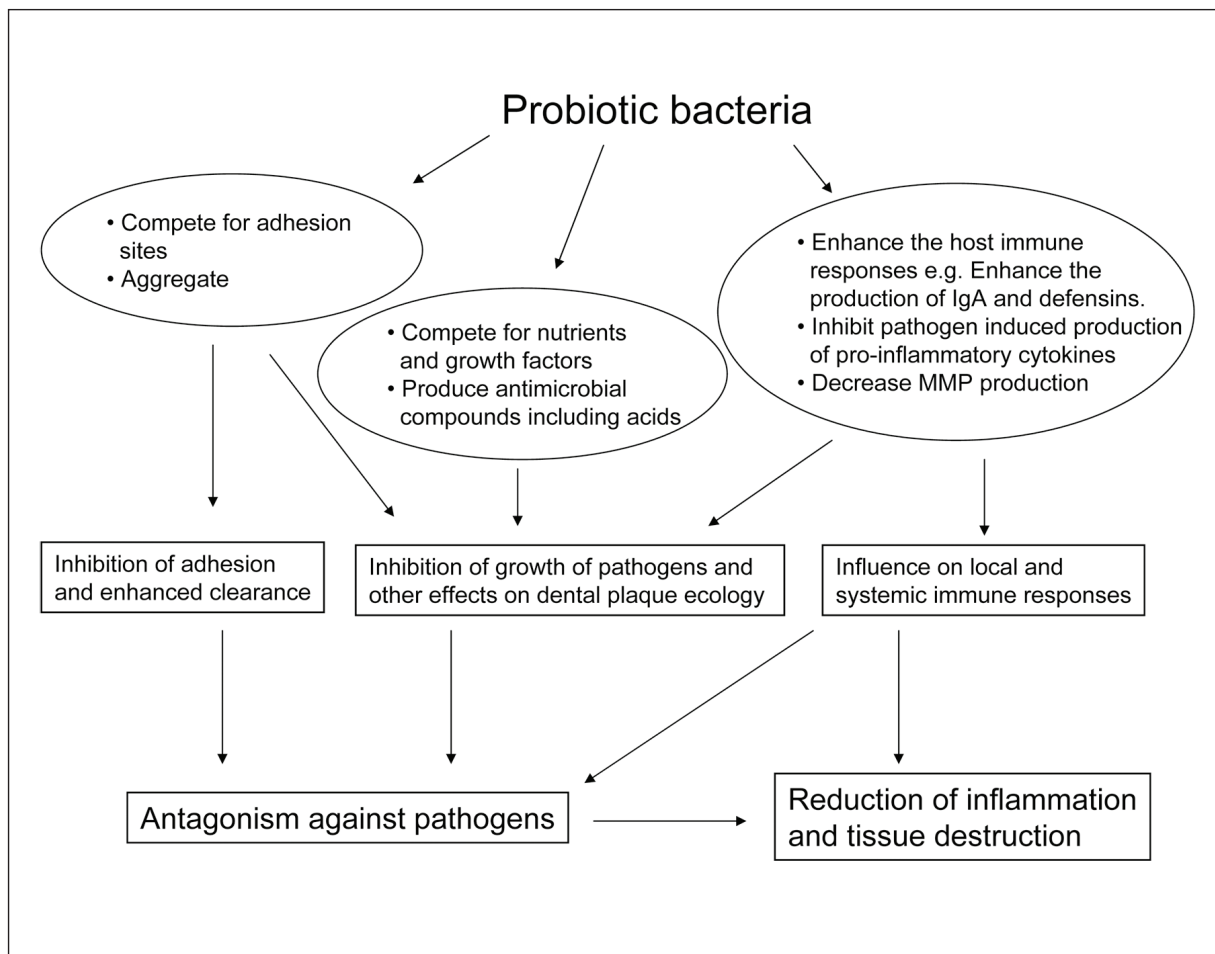


Figure 1. Potential mechanisms by which probiotic bacteria could affect oral health (Modified from⁷⁶, with additional references,^{27,28,45,46,65,74,77-79}).

also affect the number of periodontopathogens in plaque.^{49,50} Again, although encouraging results have been observed, most studies have been fairly short. Furthermore, in some studies the observed differences were quite small, though statistically significant.

Oral candida

To the writer's knowledge, only two studies have investigated the effects of probiotic bacteria on oral *Candida* infection in humans.^{33,51} When a test group of elderly people consumed cheese containing *L. rhamnosus* strains GG and LC705 and *Propionibacterium freudenreichii ssp. shermanii* JS for 16 weeks, the number of high oral yeast counts decreased, but no changes were observed in mucosal lesions.⁵¹ In a shorter study with younger subjects, no significant difference was observed between effects of probiotic and those of control cheese on salivary *Candida* counts.³³

Halitosis

Halitosis is not a disease but a discomfort, although some oral diseases including periodontitis may be the underlying cause; however, in approximately 90% of cases, the origin can be found in the oral cavity,⁵² and probiotics are marketed for the treatment of both mouth- and gut-associated halitosis. Despite that, only a few clinical studies have found different probiotic strains or products to be efficacious. The studied strains include *E. coli* Nisle 1917, *S. salivarius* K12, three *Weissella confusa* isolates, and a lactic acid-forming bacterial mixture, not specified by the authors of that work.⁵³⁻⁵⁶

COLONIZATION AND SAFETY OF PROBIOTICS IN THE ORAL CAVITY

Some probiotic *Lactobacillus* and *Streptococcus* strains seem able to colonize the oral cavity of some people during the time that products containing them are in active use. However, both in vitro and in vivo evidence indicate that the differences between various probiotic strains, products, and also host individuals are obvious.^{26,44,57,58} *L. rhamnosus* GG and two different *L. reuteri* strains have been reported to colonize the oral cavity of 48–100% of volunteers consuming products containing them.^{44,58-60} In addition, *S. salivarius* K12, used for treating oral malodor, temporarily colonizes the oral cavity for a short time after use.⁶¹

Furthermore, consumption of a mixture of seven different *Lactobacillus* strains increased the number of salivary *Lactobacillus* counts, although the identities of the strains in the saliva were not determined.⁴¹ It seems feasible that probiotic bacteria would colonize the oral cavity only when they were used in products in contact with the mouth. Indeed, Maukonen et al⁸ did not detect any of the probiotic bacteria administered in capsules in saliva samples. Surprisingly, consumption of capsules containing a mixture of seven different *Lactobacillus* strains increased the number of salivary *Lactobacillus* counts.⁴¹ *L. reuteri* ATCC 55730 (= *L. reuteri* SD2112) does not seem to influence the total number of salivary lactobacilli,³⁶ but *L. rhamnosus* GG may increase it.³³

Maybe because long-term colonization by probiotic bacteria is unlikely, albeit possible,⁵⁸ potential adverse effects of probiotic bacteria in the oral cavity have not been a subject of much intensive research; however, probiotic products are used widely; therefore, when dental health is considered, the acidogenicity of lactobacilli and bifidobacteria cannot be overlooked. For example, one *L. salivarius* strain is able to induce caries in an animal model,⁶² and another is able to make a biofilm model more cariogenic.⁶³

FUTURE ASPECTS

Recently, oral lactic acid bacteria and bifidobacteria have been isolated and characterized for various oral health purposes, including caries, periodontal diseases, and halitosis.^{10,56,64-68} In addition, dairy strains have been studied with the aim of characterizing potential new oral probiotics;^{69,70} thus, the new probiotic products targeted for oral health purposes do not necessarily comprise the same species as products now in market. Furthermore, the species might not necessarily belong only to genera *Lactobacillus* or *Bifidobacterium*. Indeed, *S. salivarius* K12 is used to treat oral malodor,⁵⁵ and preliminary results have been published on the safety and efficacy of a probiotic mouthwash containing three different oral streptococci for reducing the number of bacteria associated with dental caries and periodontitis.⁷¹

Genetically modified microbes bring a new dimension to the concept of probiotics. One approach is to reduce the harmful properties of pathogenic strains naturally colonizing the oral

cavity. The modified strain could then be used to replace the original pathogen. One ambitious and promising example is the generation of an *S. mutans* strain with a complete deletion of the open reading frame of lactate hydrogenase and thus significantly reduced cariogenicity.⁷² Another option could be to enhance the properties of a potentially beneficial strain. One example is the construction of an *L. paracasei* strain with a functional scFV (single-chain variable fragment) antibody binding to the surface of *Porphyromonas gingivalis*.⁷³

Probiotics are by definition viable, and until recently the viability of probiotic bacteria was usually ascertained by culture; however, both in the intestine and in the oral cavity, a significant proportion of bacteria are not yet cultivable. In addition, bacteria in biofilms can enter a dormant state; therefore, it can be speculated that bacteria with the ability to influence the microbiota in these sites need not necessarily be culturable. There has also been debate on the definition of “viable,” and even whether the definition of probiotic should be changed. Indeed, heat-killed beneficial oral *Streptococcus* strains have been shown to exert effects similar to those of a living bacterium.⁷⁴ Furthermore, viable but nonculturable probiotic bacteria maintain properties of viable bacteria.⁷⁵

SUMMARY AND CONCLUSIONS

The interest in oral probiotics has been growing during the last decades. Most of the studies have been conducted with probiotic strains originally suggested for gut health; however, it is important to realize that each of the suggested health benefits should be studied for each bacterial strain individually. Thus, a probiotic bacterium in the mouth is not necessarily an oral probiotic. Furthermore, it is quite possible that the same species are not optimal for all oral health purposes; e.g., different properties might be desired in respect to dental and gingival health.

At least some of the probiotic bacteria used in various probiotic products may colonize the oral cavity during the time they are in use; thus, the effects of probiotic bacteria in the oral cavity are important to understand. Probiotic bacteria seem to affect both oral microbiota and immune responses. On the other hand, the extent to which bacteria in food or in food ingredients can influence rela-

tively stable oral microbiota is difficult to predict. Thus, both research to unravel the mechanisms of possible probiotic action and long-term clinical trials are needed if probiotics are to provide a new scientifically proven means of preventing or treating oral diseases.

Several health-promoting effects of probiotic bacteria are well documented,^{2,3} and there is no reason to restrict the use of probiotic products because their effects on oral health are not yet well understood; however, their recommendation for dental health purposes is not yet justified.

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