

Role of Probiotics in Dental Caries and Periodontal Disease

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Abstract

Probiotics have been found to be beneficial to host health. In medicine, probiotics are used mainly in support therapy for gastro-intestinal diseases. In recent years, probiotics have been used as a treatment to promote oral health. There has also been a change in understanding of the oral disease process because of better understanding of the ecology and microbiology of the oral cavity. Very encouraging studies exploring probiotics in the fields of caries, periodontal diseases and few other areas have come up in the recent past and the results tend to suggest beneficial effects of probiotics on oral health and on the whole body in general. Extensive research to create a probiotic product intended to maintain dental and periodontal health is needed. This article reviews the role of probiotics in dental caries and periodontal disease.

Keywords: Dental caries, periodontal disease, probiotics

Introduction

In the early 1900's, Dr. Metnikoff of Russia found that certain Bulgarians lived longer, pain-free and disease-free lives. He attributed their healthy longevity to their diet. The diet consisted of yogurt, sour dough, bread and buttermilk. Dr. Metnikoff discovered that these fermented foods contained friendly beneficial bacteria that were able to take rotten putrescence food and digest them to release by-products that were full of nutrients and which destroyed the foul odor. These friendly bacteria that kept the potential pathogens from causing disease were termed Probiotics. The term 'probiotic', meaning "for life", is derived from the Greek lan-

guage. It was first used by Lilly and Stillwell in 1965 to describe, "substances secreted by one microorganism which stimulates the growth of another" and thus was contrasted with the term 'antibiotic' [1]. According to a WHO/FAO report (2002), probiotics are 'Live micro-organisms which, when administered in adequate amount, confer a health benefit on the host'. International Life Science Institute (ILSI) Europe suggests a definition according to which a probiotic is 'a live microbial food ingredient that, when ingested in sufficient quantities, exerts health benefits on the consumer'. Both definitions have in common the idea that probiotic micro-organisms are living and exert proven health effects [2]. The first probiotic species to be intro-

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duced in research was *Lactobacillus acidophilus* by Hull et al. in 1984 [3], followed by *Bifidobacterium bifidum* by Holcomb et al. in 1991 [4].

Prebiotic

The term 'prebiotic' was introduced by Gibson and Roberfroid [5]. It is a non-digestible food ingredient that confers benefits on the host by selectively stimulating the growth and/or activity of one bacterium or a group of bacteria in the colon, and thus improves the host health. Prebiotics are dietary carbohydrates that escape digestion in the upper gastrointestinal tract and alter the bacterial composition of the gut by changing the type of the substrate provided to the existing microbial population in the gut, e.g. fructo oligosaccharides, gluco oligosaccharides and inulin.

Synbiotic

The term 'synbiotic' is used when a product contains both probiotics and prebiotics. Because the word alludes to synergism, this term should be reserved for products in which the prebiotic compound selectively favors the probiotic compound [6].

Several clinical studies have already demonstrated the effectiveness of certain probiotics in the treatment of systemic and infectious diseases, such as acute diarrhea and Crohn disease. Other studies have suggested potential applications in the treatment of cardiovascular disease, urogenital infections and cancers. Probiotics also proved useful in treating problems arising from the excessive use of antibiotics, specifically the appearance of bacteria. The oral cavity has only recently been suggested as a relevant target for probiotic applications. So far, oral probiotics have been evaluated primarily in the management of dental caries. However, there are very few studies on probiotics from the periodontal health perspective. The following review explores the role of probiotics in dental caries and periodontal diseases.

Mechanisms of action of probiotics in general and specifically on oral health

The mechanisms by which probiotics exert their effects are largely unknown, but may involve modifying gut pH, antagonizing pathogens through production of antimicrobial compounds, competing for pathogen binding and receptor sites as well as for available nutrients and growth factors, stimulating immunomodulatory cells, and producing lactase.

Probiotic bacteria have been shown to influence the immune system through several molecular mechanisms [7].

In oral health, possible mechanisms may be:

Production of antimicrobial substances

- Organic acids
- Hydrogen peroxide
- Bacteriocins
- Binding in the Oral Cavity
- Compete with pathogens for adhesion sites
- Involvement in metabolism of substrates (competing with oral micro-organisms for substrates available)
- Immuno modulatory
- Stimulate non-specific immunity
- Modulate humoral and cellular immune response
- Modifying oral conditions
- Modulating pH
- Modification of oxidation reduction potential

Role of probiotics in dental caries

In caries, there is an increase in acidogenic and acid-tolerating species, such as mutans streptococci and lactobacilli, although other bacteria, like *Bifidobacteria*, nonmutans streptococci, *Actinomyces* spp., *Propionibacterium* spp., *Veillonella* spp. and *Atopobium* spp., with similar properties can also be found. The use of probiotics and molecular genetics to replace and displace cariogenic bacteria with noncariogenic bacteria has shown promising results. These studies have employed different approaches:

- Early studies concentrated on utilizing bacteria that expressed bacteriocins or bacteriocin-like inhibitory substances (BLIS) that specifically prevented the growth of cariogenic bacteria.
- One approach has been to identify food grade and probiotic bacteria, which have the ability to colonize teeth and influence the supragingival plaque.
- Also, strains have been screened for suitable antagonistic activity against relevant oral bacteria.
- Another approach utilized a recombinant strain of *S. mutans* expressing urease, which was shown to reduce the cariogenicity of plaque in an animal model.

- Similarly, genetically modified probiotics with enhanced properties can be developed ('designer probiotics'). For example, a recombinant strain of *Lactobacillus* that expressed antibodies targeting one of the major adhesions of *S. mutans* (antigen I/ II) was able to reduce both the viable counts of *S. mutans* and the caries score in a rat model.

Review of the studies involving probiotics for decreasing dental caries

Comelli EM et al. (2002) studied 23 dairy bacterial strains for the prevention of dental caries and reported that only two strains, namely *Streptococcus thermophilus* and *Lactococcus lactis*, were able to adhere to saliva-coated hydroxyapatite and were further successfully incorporated into a biofilm similar to the dental plaque. Furthermore, they could grow together with five strains of oral bacterial species commonly found in supragingival plaque. In this system, *Lactococcus lactis* was able to modulate the growth of the oral bacteria, and was particularly able to diminish the colonization of *Streptococcus oralis*, *Veillonella dispar*, *Actinomyces naeslundii* and *Streptococcus sobrinus* [8]. *L. rhamnosus* is one of the most extensively studied probiotics in oral biology, since it does not readily ferment sucrose and is safer for teeth than lactic acid-producing bacteria. Controlled studies have shown the effectiveness of *L. rhamnosus* in reducing caries [9].

L. rhamnosus was found to inhibit cariogenic *S. mutans*, but colonization of the oral cavity by *L. rhamnosus* seems improbable [10]. In a seven-month study on a kindergarten by Nase et al. (2001), children received the probiotic *L. rhamnosus* and the caries risk was subsequently calculated according to clinical and microbiological data (*S. mutans* level in saliva and plaque). Results showed less dental caries and lower levels of *S. mutans* in the probiotic milk-consuming group [11]. A study aimed at showing the benefit of cheese-containing *Lactobacillus rhamnosus* showed that probiotic intervention helped in reducing the highest level of *Streptococcus mutans* [12].

In order to assess whether naturally occurring oral lactobacilli have probiotic properties, lactobacilli were isolated from saliva and plaque in children and adolescents, with or without caries lesions. Twenty-three *Lactobacillus* spp. completely inhibited the growth of all mutans streptococci tested. The species with maximum interference capacity against mutans streptococci included *Lactobacillus paracasei*, *Lactobacillus plantarum*, and *Lactobacillus rhamnosus* [13].

Few studies have reported a reduction in mutans streptococci levels in saliva following the use of probiotic-containing yogurts, but it is not clear whether this decrease is due to the

bactericidal activity of yogurt or other mechanisms. Petti S (2008) investigated the differences in susceptibility of strains of viridians streptococci. In vitro, yogurt with live bacteria showed selective anti-mutans activity, suggesting that the overall decrease in mutans streptococci in vivo could be due to a bactericidal effect on *S. mutans* [14]. Yogurt products containing *L. reuteri* showed a significant growth inhibitory effect against *S. mutans*, while yogurts with lactobacilli other than *L. reuteri* did not show such inhibition. Moreover, a double-blind, placebo-controlled trial demonstrated that consuming yogurt with *L. reuteri* significantly reduced the oral carriage of mutans streptococci, compared to the placebo yogurt [15].

Calgar et al. (2006) investigated the effect of the probiotic bacterium *Lactobacillus reuteri* on levels of mutans streptococci and lactobacilli, which was introduced by two different straws containing *L. reuteri* and lozenges containing *L. reuteri*; they concluded that short-term daily ingestion of lactobacilli-derived probiotics delivered by prepared straws or lozenges reduced the levels of salivary mutans streptococci in young adults [16]. Calgar et al. (2007) evaluated the effect of xylitol and probiotic chewing gums on salivary mutans streptococci and lactobacilli and concluded that daily chewing of gums containing probiotic bacteria or xylitol reduced the levels of salivary mutans streptococci in a significant way. However, a combination of probiotic and xylitol gums did not seem to enhance this effect [17]. In a similar study they showed that sucking a medical device containing the probiotic lozenge with *L. reuteri* once daily for 10 days reduced the levels of salivary mutans [18].

Probiotics and periodontal disease

Periodontal diseases are a group of diseases that affect the tissues that support and anchor the teeth. Treatment of periodontal diseases in recent years has moved toward an antibiotic /antimicrobial model of disease management. Probiotics might be a promising area of research in the treatment of periodontitis. Narva and associates [19] have shown that, during the fermentation process in milk, *L. helveticus* produces short peptides that act on osteoblasts and increases their activity in bone formation. These bioactive peptides could thereby contribute to reducing the bone resorption associated with periodontitis. A study done by Klais et al. [20] showed that the prevalence of Lactobacilli, particularly *Lactobacillus gasseri* and *L. fermentum*, in the oral cavity was greater among healthy participants than among patients with chronic periodontitis. Various studies have reported the capacity of lactobacilli to

inhibit the growth of periodontopathogens, including *P. gingivalis*, *Prevotella intermedia* and *A. actinomycetemcomitans*. These observations suggest that lactobacilli residing in the oral cavity could play a role in the oral ecological balance. Krasse and colleagues [21] assessed the beneficial effect of *L. reuteri* against gingivitis. After 14 days of ingesting the probiotic incorporated into the chewing gum, the oral cavity of patients with a moderate to severe form of gingivitis had been colonized to be *L. reuteri*, and the plaque index had been reduced.

Riccia and colleagues [22] recently studied the anti-inflammatory effects of *L. brevis* in a group of patients with chronic periodontitis. This study showed a significant reduction in salivary levels of PGE2 and MMPs. The authors suggested that the beneficial anti-inflammatory effects of *L. brevis* could be attributed to its capacity to prevent the production of nitric oxide and, consequently, the release of PGE2 and the activation of MMPs induced by nitric oxide.

However, *L. brevis* may also be antagonistic, leading to a reduction in the quantity of plaque and therefore an improvement in the gingival index. Teughels et al. [23] reported that the subgingival application of a mixture including *S. sanguis*, *S. salivarius* and *S. mitis* after scaling and root planing significantly suppressed the re-colonization of *P. gingivalis* and *P. intermedia* in the beagle dog model. This guided pocket recolonization approach may provide a valuable addition or alternative to the armamentarium of treatment options for periodontitis. Sunstar (Etoy, Switzerland) [24] recently began marketing the first probiotic specifically formulated to fight periodontal disease. Gum Perio Balance contains a patented combination of two strains of *L. reuteri*, specially selected for their synergistic properties in fighting cariogenic bacteria and periodontal pathogens. Each dose of lozenge contains at least 2×10^8 living cells of *reuteri*. Users are advised to use a lozenge every day, either after a meal or in the evening after brushing their teeth, to allow the probiotics to spread throughout the oral cavity and to attach to the various dental surfaces. Additional studies are required to evaluate the long-term effects of using these products. Yakult's *L. casei* strain Shirota is one of the most studied probiotic strains. Fifty volunteer students were recruited to participate in the study. One group was required to drink 65 ml of Yakult daily, giving a daily probiotic dose of 100 billion bacteria per 100 ml. The other group was given no product to consume at all. After eight weeks of drinking the probiotic milk, the researcher showed that the probiotic was associated with reduction in elastase activity and matrix metalloproteinases-3 (MMP-3) [25].

Conclusion

The oral cavity with a well-maintained balance of species and species interactions may be a potential source for health-promoting probiotic bacteria. There is limited evidence supporting some uses of probiotics. Much more scientific knowledge is needed about probiotics, including their safety and appropriate use. Effects found from one species or strain of probiotics do not necessarily hold true for others, or even for different preparations of the same species or strain. The full potential of probiotics can be realized when their benefits can be established scientifically.

Conflict of interest statement

The authors do not declare any conflict of interest or financial support in this study.

References

1. Lilly DM, Stillwell RH. Probiotics. Growth promoting factors produced by microorganisms. *Science* 1965; 147:747-748.
2. de Vrese M, Schrezenmeir J. Probiotics, prebiotics, and synbiotics. *Adv Biochem Eng Biotechnol* 2008; 111: 1-66.
3. Hull RR, Roberts AV, Mayes JJ. Survival of *Lactobacillus acidophilus* in yogurt. *Aust J Dairy Technol* 1984; 39:164-166.
4. Holcomb JE, Frank JF, McGregor JU. Viability of *Lactobacillus acidophilus* and *Bifidobacterium bifidum* in soft-serve frozen yogurt. *Cult Dairy Prod J* 1991; 26: 4-5.
5. Gibson GR, Roberfroid MB. Dietary modulation of the human colonic microbiota: introducing the concept of prebiotics. *J Nutr* 1995; 125:1401-1412.
6. Schrezenmeir J, de Vrese M. Probiotics, prebiotics, and synbiotics—approaching a definition. *Am J Clin Nutr* 2001; 73(suppl):361S-364S.
7. Parvez S, Malik KA, Ah Kang S, Kim HY. Probiotics and their fermented food products are beneficial for health. *J Appl Microbiol* 2006; 100: 1171-1185.
8. Comelli EM, Guggenheim B, Stingle F, Neeser JR. Selection of dairy bacterial strains as probiotics for oral health. *Eur J Oral Sci* 2002; 110:218-224.
9. Meurman JH. Prebiotics and Probiotics and Oral Health. In: Charalampopoulos D, Rastall RA (eds). *Prebiotics and Probiotics Science and Technology*, Springer, New York, 2009; 1067-1098.

10. Yli-Knuuttila H, Snäll J, Kari K, Meurman JH. Colonization of *Lactobacillus rhamnosus* GG in the oral cavity. *Oral Microbiol Immunol* 2006;21:129-131.
11. Näse L, Hatakka K, Savilahti E, Saxelin M, Pönkä A, Poussa T, et al. Effect of long-term consumption of a probiotic bacterium, *Lactobacillus rhamnosus* GG, in milk on dental caries and caries risk in children. *Caries Res* 2001;35:412-420.
12. Ahola AJ, Yli-Knuuttila H, Suomalainen T, Poussa T, Ahlström A, Meurman JH, et al. Short-term consumption of probiotic-containing cheese and its effect on dental caries risk factors. *Arch Oral Biol* 2002;47:799-804.
13. Simark-Mattsson C, Emilson CG, Håkansson EG, Jacobsson C, Roos K, Holm S. *Lactobacillus*-mediated interference of mutans streptococci in caries-free vs. caries-active subjects. *Eur J Oral Sci* 2007;115:308-314.
14. Petti S, Tarsitani G, Simonetti D'Arca A. Antibacterial activity of yoghurt against viridans streptococci in vitro. *Arch Oral Biol* 2008;53:985-990.
15. Nikawa H, Makihira S, Fukushima H, Nishimura H, Ozaki Y, Ishida K, et al. *Lactobacillus reuteri* in bovine milk fermented decreases the oral carriage of mutans streptococci. *Int J Food Microbiol* 2004;95:219-223.
16. Caglar E, Cildir SK, Ergeneli S, Sandalli N, Twetman S. Salivary mutans streptococci and lactobacilli levels after ingestion of the probiotic bacterium *Lactobacillus reuteri* ATCC 55730 by straws or tablets. *Acta Odontol Scand* 2006;64:314-318.
17. Caglar E, Kavaloglu SC, Kuscu OO, Sandalli N, Holgerson PL, Twetman S. Effect of chewing gums containing xylitol or probiotic bacteria on salivary mutans streptococci and lactobacilli. *Clin Oral Investig* 2007;11:425-429.
18. Caglar E, Kuscu OO, Cildir SK, Kuvvetli SS, Sandalli N. A probiotic lozenge administered medical device and its effect on salivary mutans streptococci and lactobacilli. *Int J Paediatr Dent* 2008;18:35-39.
19. Narva M, Halleen J, Väänänen K, Korpela R. Effects of *Lactobacillus helveticus* fermented milk on bone cells in vitro. *Life Sci* 2004;75:1727-1734.
20. Köll-Klais P, Mändar R, Leibur E, Marcotte H, Hammarström L, Mikelsaar M. Oral lactobacilli in chronic periodontitis and periodontal health: species composition and antimicrobial activity. *Oral Microbiol Immunol* 2005;20:354-361.
21. Krasse P, Carlsson B, Dahl C, Paulsson A, Nilsson A, Sinkiewicz G. Decreased gum bleeding and reduced gingivitis by the probiotic *Lactobacillus reuteri*. *Swed Dent J* 2006;30:55-60.
22. Riccia DN, Bizzini F, Perilli MG, Polimeni A, Trinchieri V, Amicosante G, Cifone MG. Anti-inflammatory effects of *Lactobacillus brevis* (CD2) on periodontal disease. *Oral Dis* 2007;13:376-385.
23. Teughels W, Newman MG, Coucke W, Haffajee AD, Van Der Mei HC, Haake SK, et al. Guiding periodontal pocket recolonization: a proof of concept. *J Dent Res* 2007;86:1078-1082.
24. Bresson JL, Flynn A, Heinonen M, Hulshof K, Korhonen H, Lagiou P, et al. Gum Periobalance™ tablets and chewing gum and oral health. *The EFSA Journal* 2009;1178:1-8.
25. Staab B, Eick S, Knöfler G, Jentsch H. The influence of a probiotic milk drink on the development of gingivitis: a pilot study. *J Clin Periodontol* 2009;36:850-856.