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Probiotics – Their Role in Prevention of Dental Caries

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ABSTRACT

Probiotics have been used to improve gastrointestinal health for quite some time and their popularity has prompted increased interest for their role in promotion of oral health. There also has been a change in understanding of the oral disease process because of better understanding of ecology and microbiology of oral cavity. Very encouraging studies have come up in recent past exploring probiotics in fields of caries, periodontal diseases and few other areas and the results tend to suggest beneficial effects of probiotics on oral health and on whole body in general . Given these recent developments, it was considered timely to review the background and conceptual framework of the use of these agents in reducing dental caries. The evidence for the use of pro or prebiotics for the prevention of caries is reviewed.

KEYWORDS

Probiotics, Dental caries, Prevention

WHAT ARE PROBIOTICS, PREBIOTICS AND SYNBIOTICS

The term probiotic, meaning "for life," is derived from the Greek language. 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). Today two main definitions are used. According to a WHO/FAO report (2002), probiotics are 'Live micro-organisms which, when administered in adequate amounts, confer a health benefit on the host'. International Life Science Institute (ILSI) Europe suggests a definition

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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 term prebiotic was introduced by Gibson and Roberfroid(3). Prebiotic 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 improve the host health. Prebiotics are dietary carbohydrates that escape digestion in the upper gastrointestinal tract, 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.

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(4).

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(5).

ROLE OF PROBIOTICS IN DENTAL CARIES

In caries, there is an increases in acidogenic and acid-tolerating species such as mutans streptococci and lactobacilli, although other bacteria with similar properties can also be found like Bifidobacteria, non-mutans streptococci, Actinomyces spp., Propionibacterium spp., Veillonella spp. and Atopobium spp. 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 utilising 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 ability to colonize teeth and influence the supragingival plaque.
- Also, strains have been screened for suitable antagonistic activity against relevant oral bacteria.
- Another approach utilised 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.

In oral health, possible mechanisms may be

Production of antimicrobial substances

- **Organic acids**
- **Hydrogen peroxide**
- **Bacteriocins**

Binding in 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**

Modify oral conditions

- **Modulating pH**
- **Modification of oxidation reduction potential**

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 Lactcoccus 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, Lactoc. lactis was able to modulate the growth of the oral bacteria, and in particular to diminish the colonization of Streptococcus oralis, Veillonella dispar, Actinomyces naeslundii and of the cariogenic Strep. sobrinus(6).

L. rhamnosus is one of the most extensively studied probiotic and of particular interest 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(7). L. rhamnosus was found to inhibit cariogenic S. mutans but colonization of oral cavity by by L. Rhamnosus seems improbable (8). In seven month kindergarten study by Nase *et al* (2001) children received probiotic L. rhamnosus and subsequently caries risk was 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 probiotic milk group(9). A study aimed at benefit of cheese containing Lactobacillus rhamnosus showed that probiotic intervention helped in reducing the highest level of Streptococcus mutans(10).

In order to assess whether naturally occurring oral lactobacilli have probiotic properties, lactobacilli were isolated from saliva and plaque from children and adolescents, with or without caries lesions. Twenty-three Lactobacillus spp. completely inhibited the growth of all mutans streptococci tested. Species with maximum interference capacity against mutans streptococci included Lactobacillus paracasei, Lactobacillus plantarum, and Lactobacillus rhamnosus(11).

Few studies have reported reduction in mutans streptococci levels in saliva following use of probiotic containing yoghurts but it is not clear whether this decrease is due to the bactericidal activity of yoghurt or other mechanisms. Petti S (2008) investigated the differences in susceptibility of strains of viridans streptococci. In vitro, yoghurt 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(12).Yogurt products containing L.reuteri showed a significant growth inhibitory effect against S. mutans, while yoghurts with lactobaccilli other than L. reuteri did not show such inhibition. Further, double-blind, placebo-

Table 1: Examples of microorganisms that are considered to be probiotics

Lactobacillus spp.	Bifidobacterium spp.	Others
L acidophilus	B. bifidum	Saccharomyces boulardii
L. casei	B. breve	Lactococcus lactis subsp. cremoris
L. crispatus	B. infantis	Enterococcus faecium
L. delbrueckii subsp. bulgaricus	B. longum	Streptococcus salivarius subsp. thermophilus
L. fermentum	B. lactis	S. diaacetylactis
L. gasseri	B. adolescentis	S. intermedius
L. johnsonii		
L. paracasei		
L. plantarum		
L. reuteri		
L. rhamnosus		

Note : i)There is still debate about the probiotic activity of L. delbrueckii subsp. Bulgaricus and Streptococcus thermophilus
ii) Safety concerns remain for Enterococcus faecium because of potential pathogenicity and vancomycin rersistance

controlled trial demonstrated that consuming yogurt with L. reuteri significantly reduced the oral carriage of mutans streptococci, compared with the placebo yogurt(13).

Calgar *et al* (2006) investigated the effect of probiotic bacterium Lactobacillus reuteri on levels of mutans streptococci and lactobacilli which was introduced by two different -straw containing L. reuteri and lozenges containing L. reuteri and 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(14). Calgar *et al* (2007) evaluated the effect of xylitol and probiotic chewing gums on salivary mutans streptococci and lactobacilli and concluded that daily chewing on 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 (15). 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(16).

Lactobacilli have been used to deliver vaccine components for active immunization in vivo. Vectors encoding a single-chain Fv (scFv) antibody fragment, which recognizes the streptococcal antigen I/II (SAI/II) adhesion molecule of Streptococcus mutans, were constructed and expressed in Lactobacillus zeae. After administration of scFv-expressing bacteria to a rat model of dental caries development, S. mutans bacteria counts and caries scores were markedly reduced (17). These studies have suggested that lactobacilli-derived probiotics in dairy products may affect the oral ecology. To study the effect of Bifidobacteria a double-blind, randomized crossover study was performed. A statistically significant reduction of salivary mutans streptococci was recorded after the probiotic yoghurt consumption containing Bifidobacterium, which was in contrast to the controls. A similar trend was seen for lactobacilli, but this decrease failed to reach statistical significance. Investigators concluded that probiotic bifidobacteria in yoghurt may reduce the levels of selected caries-associated microorganisms in saliva(18). In a similar study using Bifidobacterium lactis a statistically significant reduction ($p<0.05$) of salivary mutans streptococci was recorded after consumption of the probiotic ice-cream in adults (19).

Dental caries results from prolonged plaque acidification that leads to the establishment of a cariogenic microflora and demineralization of the tooth. Urease enzymes of oral bacteria hydrolyze urea to ammonia, which can neutralize plaque acids. Clancy KA *et al* (2000) constructed Ureolytic strains of Streptococcus mutans.. In vitro pH drop experiments during metabolism of glucose, urease activity increased. Urease activity appears to influence plaque biochemistry and metabolism in a manner that reduces cariogenicity, suggesting that recombinant, ureolytic bacteria may be useful to promote dental health(20).

Kang MS *et al* (2006) did a study in which they found out that the water-soluble polymers produced from sucrose by the Weissella cibaria isolates inhibited the formation of S. mutans biofilm. In the clinical study, the subjects mouthrinsed with a solution containing W. cibaria CMS1 and exhibited plaque index reduction of approximately 20.7%(21).

CONCLUSION

Most studies on the effects of probiotics on caries prevention are aimed at decreasing the number of mutans streptococci. Primarily probiotic *Lactobacillus* and *Bifidobacterium* strains have been used along with few more strains. Most of the studies have shown a tendency towards decreased number of mutans streptococci in the saliva regardless of the product or strain used. However, this effect is variable Unfortunately, in most cases, the study groups were relatively small, and the studies were fairly short. Preliminary data obtained has been encouraging, but numerous randomized clinical studies will be required to clearly establish the potential of probiotics in prevention of dental caries. Also complete understanding of the broad ecological changes induced in the mouth by probiotics or prebiotics will be essential to assess their long-term consequences for oral health and disease.

REFERENCES

1. Lilly DM, Stillwell RH. Probiotics. Growth promoting factors produced by micro-organisms. Science 1965;**147**:747-748.
2. Schrezenmeir, de Vrese, M. Probiotics, prebiotics, and synbiotics. Adv Biochem Eng Biotechnol 2008;111, 1.
3. Gibson GR, Roberfroid MB. Dietary modulation of the human colonic microbiota: introducing the concept of prebiotics. Journal of Nutrition 1995;**125**:1401-1412.
4. Jürgen Schrezenmeir and Michael de Vrese Probiotics, prebiotics, and synbiotics-approaching a definition. *Am J Clin Nutr* 2001;**73**(suppl):361S–364S.
5. S Parvez, KA Malik, S Ah Kang, HY Kim. Probiotics and their fermented food products are beneficial for health Journal compilation 2006 The Society for Applied Microbiology. *Journal of Applied Microbiology* 2006;**100:**1171-1185.
6. Comelli EM, Guggenheim B, Stingele F, Neeser JR. Selection of dairy bacterial strains as probiotics for oral health. *Eur J Oral Sci* 2002;**110**(3):218-24.
7. Dimitris Charalampopoulos, Robert A. Rastall Prebiotics and Probiotics Science and Technology p 1067-1098.
8. Yli-Knuuttila H, Snäll J, Kari K, Meurman JH Colonization of Lactobacillus rhamnosus GG in the oral cavity. Oral Microbiol Immunol 2006;**21**(2):129-31.
9. 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**(6):412-420.
10. Ahola AJ, Yli-Knuuttila H, Suomalainen T, Poussa T, Ahlstrom 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.
11. Simark-Mattsson C, Emilson CG, Hakansson 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.
12. Petti S, Tarsitani G, Simonetti D'Arca A. Antibacterial activity of yoghurt against viridans streptococci in vitro. *Arch Oral Biol* 2008; **53**(10):985-90.
13. Nikawa H, Makihira S, Fukushima H, *et al*. Lactobacillus reuteri in bovine milk fermented decreases the oral carriage of mutans streptococci. *Int J Food Microbiol* 2004;**95**:219-223.
14. 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.
15. 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.
16. 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.
17. Kruger C, Hu YZ, Pan Q, Marcotte H, Hultberg A, Delwar D, *et al*. In situ delivery of passive immunity by lactobacilli producing single-chain antibodies. *Nature Biotech* 2002;20:702-6.
18. Caglar E, Sandallii N, Twetman S, Kavaloglu S, Ergeneli S, Selvi S. Effect of yogurt with Bifidobacterium DN-173 010 on salivary mutans streptococci and lactobacilli in young adults. *Acta Odontol Scand* 2005;63:317-320.
19. Caglar E, Kuscu OO, Kuvvetli SS, Cildir SK, Sandalli N, Twetman S. Short-term effect of ice-cream containing Bifidobacterium lactis Bb-12 on the number of salivary mutans streptococci and lactobacilli. *Acta Odontol Scand* 2008;**66**:154-158.
20. Clancy KA, Pearson S, Bowen WH, Burne RA. Characterization of recombinant, ureolytic Streptococcus mutans demonstrates an inverse relationship between dental plaque ureolytic capacity and cariogenicity. *Infect Immun* 2000;**68**(5):2621-2629.
21. Kang MS, Chung J, Kim SM, Yang KH, Oh JS. Effect of Weissella cibaria isolates on the formation of Streptococcus mutans biofilm. *Caries Res* 2006;**40**(5):418-425.

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