

Review Article

Probiotics and Periodontal Disease- An Update

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ABSTRACT:

Probiotics are live microbial feed, which provide benefits to the host. They are a heterogeneous group of nonpathogenic bacteria that are functionally defined by their ability to allay inflammation when introduced into the inflamed intestine. They have been used to improve gastrointestinal health and their popularity has prompted increased interest for their role in promotion of oral health also. The purpose of this review was to discuss recent data bearing on the possible ways of reducing signs of gingivitis and periodontitis by probiotics.

Key words: Probiotics, Periodontitis, Inflammation.

Received: 29-07-2014

Revised: 21-08-2014

Accepted: 02-09-2014

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This article may be cited as: Bhatia V, Kaur GS. Probiotics and Periodontal Disease- An Update. J Adv Med Dent Scie Res 2014;2(3):91-96.

Introduction

Periodontitis is a multifactorial disease that encompasses the hard and soft tissue, microbial colonization (with or without invasion), inflammatory responses and adaptive immune responses. The complexity of the local tissue components, including bacteria and/or their products and virtually all aspects of host response mechanisms, has complicated our ability to elucidate the critical protective functions in the tissues and has continually provided evidence for the potential of host destructive factors as the ultimate causative parameters in the disease.¹ Treatment of periodontal diseases in recent years has moved towards an antibiotic/antimicrobial model of disease

management. Probiotics might be a promising area of research in the treatment of periodontitis.² The term probiotics, the antonym of the term antibiotics, was introduced in 1965 by Lilly and Stillwell as substances produced by microorganisms which promote the growth of other microorganisms. The word probiotic means 'for life' and it is currently used when referring to bacteria associated with beneficial effects on humans and animals. The belief in the beneficial effects of probiotics is based on the knowledge that the intestinal flora can protect humans against infection and that disturbance of this flora can increase susceptibility to infection. The bacteria in yogurt and fermented milk

products constitute the most important source of probiotics for humans.³

Common strains used in Oral Probiotics:

The most commonly-used probiotic strains belong to the genera, *Lactobacillus*, *Bifidobacterium*^{4,5,6} and *Streptococcus*. *Streptococcus salivarius*, *Streptococcus mitis*, and *Streptococcus sanguinis* showed a significantly more pronounced reduction in total anaerobic bacteria, black-pigmented bacteria, and *Campylobacter rectus*. They also retarded a bacterial recolonization of pockets. Probiotic strains of *Lactobacillus* species include *Lactobacillus salivarius*, *Lactobacillus reuteri*, *Lactobacillus acidophilus*, *Lactobacillus fermentum*, *Lactobacillus lactis*, *Lactobacillus helveticus*, and *Lactobacillus rhamnosus*. *Lactobacilli* produce different antimicrobial components, such as organic acids, hydrogen peroxide, low molecular weight antimicrobial substances, bacteriocins, and adhesion inhibitors. Similarly, *Bifidobacterium* strains include *Bifidobacterium bifidum*, *Bifidobacterium longum*, and *Bifidobacterium infantis*.²

Affect of Probiotics on Periodontal Health

Periodontal disease is classified into 2 types: gingivitis and periodontitis. Gingivitis is characterized by inflammation limited to the unattached gingiva, whereas periodontitis is a progressive, destructive disease that affects all supporting tissues of the teeth, including the alveolar bone.⁷ The main pathogenic agents associated with periodontitis are *P. gingivalis*, *Treponema denticola*, *Tannerella forsythia* and *Aggregatibacter actinomycetemcomitans*. These bacteria have a variety of virulent characteristics allowing them to colonize the subgingival sites, escape the host's defence system and cause tissue damage. The persistence of the host's immune response also constitutes a determining factor in progression of the disease.^{7,8}

The primary etiological factors for the development of periodontal disease are bacteria in supra- and subgingival biofilm, efforts for disease prevention and treatment are mainly focused on pathogen reduction and strengthening of the epithelial barrier, thus contributing to decreased susceptibility to infection.⁹ Probiotic bacteria, generally regarded as safe, may favor periodontal health if able to establish themselves in oral biofilm and inhibit pathogen growth and metabolism. From the periodontal perspective it should be noted that the composition of *lactobacilli* species differs in healthy and periodontitis patients and obligately homofermentatives are less prevalent in chronic periodontitis.¹⁰

Probiotics lower the pH so that plaque bacteria cannot form dental plaque and calculus that causes the periodontal disease. They make an excellent maintenance product because they produce antioxidants. Antioxidants prevent plaque formation by neutralizing the free electrons that are needed for the mineral formation. Probiotics are able to breakdown putrescence odours by fixating on the toxic gases (volatile sulphur compounds) and changing them to gases needed for metabolism.² The recent research has shown that taking tablets containing *L. salivarius* WB21 significantly reduced the periodontal pathogens in subgingival plaque¹¹ and improved the periodontal health in volunteers.¹² Also *L. reuteri* reduced the gingival index and bacterial plaque in the treated subjects.¹³ When this bacteria was incorporated in chewing gum it also resulted in improvement of the gingival conditions manifested in reduction of the crevicular fluid volume and gingival bleeding, as well as the inflammatory mediators TNF- α and interleukin-8 level.¹⁴ The probiotic tablets (Wakamate D®; Wakamoto Pharmaceutical Co., Tokyo, Japan) contained 6.7x10⁸ colony forming units (CFU)/tablet of *L. salivarius* WB21 and xylitol (280 mg/tablet)

were originally prepared to contribute for the intestinal microbial balance by providing acid tolerant *L. salivarius* WB21. Using these tablets, it was found that orally administered *L. salivarius* WB21 significantly decreased the plaque index and probing pocket depth of subjects who were smokers, suggesting clinical improvement of the periodontal condition by probiotic intervention. A significant reduction in salivary lactoferrin (Lf) levels was also observed for smokers at eight weeks. Another finding in this clinical trial was the ability of *L. salivarius* WB21 to successfully reduce the prevalence of periodontal pathogens.

This study stresses that a probiotic intervention could be a useful tool for the treatment of inflammation and the clinical symptoms of periodontitis.¹²

L. acidophilus contained in a tablet named Acilact was first clinically tested by pozharitskaia et al in 1994 and they found improved clinical parameters in periodontitis patients and shifts in local microflora towards gram positive cocci and lactobacilli. Later in the year 2002 Grudianov et al also carried out a clinical study where they obtained a probiotic mix in the tablet forms, viz Acilact and Bifidumbacterin and found normalization of micro flora and reduction of signs of gingivitis and periodontitis.¹⁵

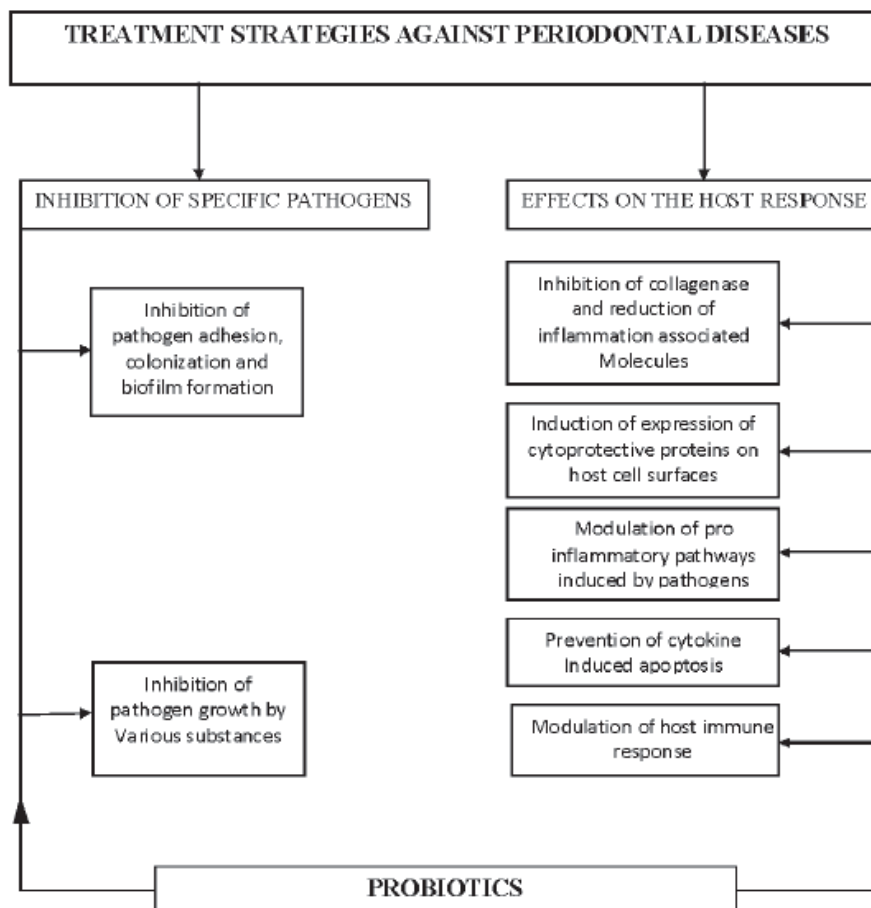


Figure 1: Theoretical Possibilities for Probiotics to affect Periodontal Health.¹⁵

Sunstar (Etoy, Switzerland) 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.¹⁶

A study done by Klais et al 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.¹⁷

Krasse and colleagues 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.¹³

Riccia and colleagues 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.¹⁸

Teughels et al. reported that the subgingival application of a mixture including *S. sanguis*, *S. salivarius* and *S. mitis* after scaling and root planing significantly suppressed the recolonization 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.¹⁹

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).²⁰

Recently Shimazaki and colleagues used epidemiological data to assess the relationship between periodontal health and the consumption of dairy products such as cheese, milk, and yoghurt. The authors found that individuals, particularly nonsmokers, who regularly consumed yoghurt or beverages containing lactic acid exhibited lower probing depths and less loss of clinical attachment than individuals who consumed few of these dairy products. By controlling the growth of the pathogens responsible for periodontitis, the lactic acid bacteria present in yoghurt would be in part responsible for the beneficial effects observed.²¹

Various studies have reported the capacity of lactobacilli to inhibit the growth of periodontopathogens, including *P. gingivalis*, *Prevotella intermedia* and *A. actinomycetemcomitans*.²² Together, these

observations suggest that lactobacilli residing in the oral cavity could play a role in the oral ecological balance.

A particular concern when evaluating probiotic effects on periodontal disease relates to the means of administration of these bacteria. Generally probiotics are delivered in dairy products (mainly fermented milks), as food supplements in tablet forms or in soft drinks. However these routes of administration cannot provide prolonged contact with oral tissues, facilitating probiotic adhesion to saliva coated surfaces.¹² To have a beneficial effect in oral cavity, a probiotic should have a tendency to form a biofilm that acts as a protective lining for oral tissues against oral diseases. Probiotics strains have been shown to vary broadly in their adhesiveness to saliva-coated HA and so in biofilm formation ability. Among probiotics strains *L. rhamnosus* GG exhibited the maximum values of adhesion, comparable to those of the early tooth colonizer *S. sanguinis*. Dairy starter *L. bulgaricus* strains adhered poorly to sHA.²³ A lozenge form or chewing gum tablet or gum might better serve the needs for periodontal health prophylaxis. Controlled clinical trials and long term studies are required to investigate the concentration of probiotic bacteria in the specific means of administration.¹²

Conclusion

Probiotics represent a new area of research in oral medicine, the examination of the close relationships between food and oral health. Only few clinical studies outlining probiotic effectiveness in periodontal disease have been published. Preliminary data obtained by various research laboratories have been encouraging, but numerous randomized clinical studies will be required to clearly establish the potential of probiotics in preventing and treating oral infections.

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Source of support: Nil

Conflict of interest: None declared