

Probiotics – Promotes Periodontal Health? - An Insight

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Abstract Probiotics are live microorganisms which are dietary supplements that when administered in adequate amounts confer wide range of health benefits. Since, probiotics are now widely used in both medical (such as cancer risk reduction, gastrointestinal tract health, and urinary tract health) and dental specialties (reduction in caries development, in achieving periodontal health, reducing oral malodor, etc.), a thorough knowledge of their risks and benefits are mandatory. Evidence now suggests that probiotics may function not only by direct inhibition of pathogenic micro-organisms, but also by more subtle mechanisms including modulation of the mucosal immune system. Little attention has been paid to the identification of beneficial oral bacterial species. Probiotic technology represents a breakthrough approach to maintaining oral health by using natural beneficial bacteria to provide a natural defense against the pathogenic bacterial species. This review endeavors to introduce the concepts of probiotics in periodontics.

Keywords: *probiotics, periodontal therapy, beneficial bacteria, novel therapy*

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1. 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. It results from extension of the inflammatory process initiated in the gingiva to the supporting periodontal tissues. The main pathogenic agents associated with periodontitis are *P. gingivalis*, *T. denticola*, *T. forsythia* and *A. actinomycetemcomitans*. These bacteria have a variety of virulent characteristics allowing them to colonize the subgingival sites, escape the host defence system and cause tissue damage. Advances in periodontal science and treatment approaches over the last decade have radically changed the understanding of periodontal diseases and have opened new, exciting prospects for both non-surgical and surgical therapy of periodontal diseases. Mechanical methods of subgingival debridement accomplished by thorough scaling and root planing, accompanied by oral hygiene procedures, have served as the gold standard of periodontal therapy for decades. In recent years, there have been tremendous changes with regard to the effectiveness of, and attitudes towards, conventional antimicrobial therapy to combat disease. Development of antibiotic resistance has rendered many antibiotics useless against important diseases thereby implementing the necessity to minimise antibiotic use and also develop novel non-antibiotic-based treatments. Hence the use of “Probiotics” in the treatment of periodontal disease has emerged. The term “probiotic” was initially proposed by Lilley and Stillwell in 1965. The first probiotic species to

be introduced in research was *Lactobacillus acidophilus* by Hull et al. in 1984 followed by *Bifidobacterium bifidum* by Holcomb et al. in 1991 [1]. WHO defined that probiotics are live micro-organisms that when administered in adequate amounts confer health benefits upon the host. Oral administration of probiotics may also benefit oral health by preventing the growth of harmful microbiota or by modulating mucosal immunity in the oral cavity [2]. It can be used for plaque modification, altering anaerobic organism colonization, altering pocket depth and improving clinical attachment. The application of selected beneficial bacteria, as an adjunct to scaling and root planing, would also inhibit the periodonto-pathogen recolonization of periodontal pockets and thus achieve and maintain periodontal health [3].

Probiotics are broadly classified into two genus- *Lactobacillus* and *Bifidobacterium*. *Lactobacillus* species from which several probiotic strains have been isolated which include *L. acidophilus*, *L. johnsonii*, *L. casei*, *L. rhamnosus*, *L. gasseri*, and *L. reuteri*. Similarly, the *bifidobacterium* strains include *B. bifidum*, *B. longum*, and *B. infantis*. A probiotic may be made out of a single bacterial strain or it may be a consortium as well. Probiotics can be in powder form, liquid form, gel, paste, granules or available in the form of capsules, sachets, etc [4].

2. Probiotics and Periodontal Health

2.1. Mechanism of Action

The mechanisms of probiotic action in the mouth are expected to be similar to those observed in other parts of

the body. However, oral probiotics should have additional properties than gastrointestinal tract probiotics. For instance, oral probiotic bacteria should adhere to and colonize periodontal tissue including hard non-shedding surfaces and should become part of the biofilm. They should not ferment sugars, which subsequently lower the pH thereby resulting in caries (Caglar et al. 2005a) [5].

Probiotics stimulate dendritic cells resulting in expression of Th1 (T-helper cell 1) or Th2 (T-helper cell 2) response, which modulates immunity. Probiotics enhances innate immunity and modulate pathogen induced inflammation through "Toll-like receptors" on dendritic cell and expressing Th1 or Th2 response. Probiotics can mimic response similar to a pathogen but without periodontal destruction.

Other proposed mechanisms include Glycoprotein – carbohydrate cell surface interaction mediate by inter species interactions. Similarly, *Lactobacillus casei*, *Lactobacillus bulgaricus*, *Lactobacillus rhamnosus*, *Lactobacillus acidophilus* co-aggregate with *Fusobacterium nucleatum*. *Lactobacillus rhamnosus*, and *Lactobacillus paracasei* have strong binding activity to primary pellicle. *Lactobacillus rhamnosus*, *Lactobacillus casei shirota*, *Lactobacillus casei* ATCC 11578 prevent adherence of bacteria to salivary pellicle by altering its composition.

Another mechanism which is postulated is aggregation alteration as *Hetrofermentative Lactobacillus* is the strongest inhibitor of *Aggregatibacter actinomycetem comitans*, *Porphyromonas gingivalis* and *Prevotella intermedia* [6]. *Fusobacterium nucleatum* aggregate with *Weissella ciberia* [7] in preference to *Treponema denticola* and *Porphyromonas gingivalis*. *Lactobacillus rhamnosus* co-aggregates with *Fusobacterium nucleatum*.

Lactobacillus salivarius and *Lactobacillus gasseri* show strong inhibition of periopathogenic bacteria [8]. Secretion of bacteriocins by *Lactobacillus reutri*, e.g., reutrin and reutricyclin inhibits growth of pathogens and has high affinity for host tissue and has antiinflammatory effect by inhibition of proinflammatory mediators [9] similarly *Weissella ceberia* releases catalase.

Apoptosis is yet another proposed mechanism. Probiotics stimulate apoptosis of tumor cells through end product formation. It has also reported to inhibit apoptosis of mucosal cells. Probiotic mixture has also been reported to protect epithelium barrier by maintaining tight junction protein expression and prevent apoptosis of mucous membrane.

2.2. Probiotics in Periodontal Disease

Periodontitis describes a group of related inflammatory diseases resulting in destruction of the tissues that support the tooth. 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 fixing on the toxic gases (volatile sulphur compounds) and changing them to gases needed for metabolism. Lactobacilli can produce different antimicrobial components including organic acids, hydrogen peroxide, low molecular weight

antimicrobial substances, bacteriocins and adhesion inhibitors and have gained prominence as Probiotics. Recently, oral lactobacilli have also been screened for their utility as potential probiotic strains [10,11,12] and strains of oral lactobacilli have been isolated that are inhibitory against *S. mutans*, *Aggregatibacter actinomycetemcomitans*, *Porphyromonas gingivalis* and *Prevotella intermedia*, as well as being tolerant of relevant environmental stresses [13]. A majority of the strains including *L.salivarius* were shown to suppress the growth of *Aggregatibacter actinomycetemcomitans*, *P.gingivalis* and *Prevotella intermedia*. Probiotic strains included in periodontal dressings at optimal concentration of 10⁸ CFU/ml were shown to diminish the number of most frequently isolated periodontal pathogens [14].

2.3. Review of Literature

A study by Koll-Klais et al. showed higher prevalence of lactobacilli, particularly *L. gasseri* and *L. fermentum* in the oral cavity among healthy participants than patients with chronic periodontitis. According to them high levels of *Lactobacillus* in microbiota caused an 82% inhibition in *Porphyromonas gingivalis* and 65% inhibition in *Prevotella intermedia* growth [15]. Patients with periodontal disease who used chewing gum or lozenges containing probiotics saw significant improvement in their periodontal status. Krasse et al. showed a significantly reduced gingival index and bacterial plaque amount in patients treated with *L. reuteri* incorporated in a chewing gum than in a placebo group and concluded that this probiotic was effective to reduce gingivitis and bacterial plaque deposition in patients with moderate-to-severe gingivitis [16]. Riccia et al used lozenges incorporated with *L. brevis* to study its anti-inflammatory effects in a group of patients with chronic periodontitis. The study shows significant improvement not only in the plaque index, gingival index and bleeding on probing for all patients but also a significant reduction in salivary levels of prostaglandin E2 (PGE2) and matrix metalloproteinases (MMPs) [17]. Shimazaki et al in an epidemiological study 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. A similar effect was however not observed with milk or cheese [18]. A study by Teughels et al addressed the hypothesis that the application of selected beneficial bacteria, as an adjunct to scaling and root planing, would inhibit the periodontopathogen recolonization of periodontal pockets. The study confirmed the hypothesis and provides a proof of concept for a Guided Pocket Recolonization (GPR) approach in the treatment of periodontitis [19].

Administration of a tablet containing *L. salivarius* WB21 was able to decrease the probing pocket depth and plaque index significantly, in subjects who were smokers [20]. This clinical trial also proved the ability of *L. salivarius* WB21 to successfully reduce the prevalence of periodontal pathogens. *L. acidophilus* contained in a tablet named Acilact was first clinically tested by Pozharitskaia et al in 1994 [21] and they found improved clinical parameters in periodontitis patients.

3. Discussion

The mouth represents the beginning of the gastrointestinal tract. Since probiotics have been used to successfully treat gastrointestinal diseases [22], an attempt can be made to use the same treatment with regard to oral diseases. Several mechanisms have been proposed to explain how probiotics work:

- Probiotics can create a biofilm, which acts as a protective lining for oral tissues by keeping the bacterial pathogens away by filling the space which pathogens would have invaded in the absence of the biofilm [23].
- Probiotics can also modify the surrounding environment by modulating the pH and/or the oxidation–reduction potential, which may compromise the ability of pathogens to become established.
- These bacteria secrete various antimicrobial substances such as organic acids, hydrogen peroxide and bacteriocins against oral pathogens [24].
- Probiotics may compete for adhesion sites with cariogenic bacteria and periodontal pathogens growth.
- Probiotics may compete for nutrients and growth factors.
- Probiotics may provide beneficial effects by stimulating nonspecific immunity and modulating the humoral and cellular immune response (enhance production of IgA and defensins) [24].
- Probiotics may reduce MMP production.

Few products containing probiotics (such as tablets, lozenges, chewing gums or tooth pastes) are currently available. Gum PerioBalance is the first probiotic marketed by Sunstar (Etoy, Switzerland), specifically formulated to fight periodontal disease. Gum PerioBalance contains a patented combination of 2 strains of *L. reuteri* specially selected for their synergistic properties in fighting both cariogenic bacteria as well as periodontopathogens. Each dose of lozenge contains at least 2×10^8 living cells of *L. reuteri* Prodentis. Users are advised to use a lozenge every day, either after meals or in the evening after brushing their teeth, to allow the probiotics to spread throughout the oral cavity and attach to the various dental surfaces. PerioBiotic™ (Designs for Health, Inc.) tooth paste is an all-natural, fluoride-free oral hygiene supplement containing Dental-Lac™, a functional *Lactobacillus paracasei* probiotic not found in any other toothpaste. Additional studies are however required to evaluate the long-term effects of using these products.

4. Conclusion

Probiotics represent a new area of research in periodontal therapy. The existence of probiotics in the indigenous oral micro flora of humans warrants exploration because these bacteria offer the advantage of being perfectly adapted to the human oral ecosystem. Based on current research data the effects of probiotics on periodontal health and its maintenance are not clear. Preliminary data obtained from research workers have been encouraging but numerous properly controlled,

randomized long term clinical trials will be required to clearly establish the potential of probiotics in preventing and treating periodontal diseases. Much more scientific developments are needed to have a better understanding of these tiny forms of lives in order to broaden their potential applications.

In the recent era of antibiotic usage organisms are fast developing resistance to antibiotics. Probiotics are counterparts of antibiotic which do not develop resistance, further they are body's own resident flora hence are biocompatible. With integration of biophysics with molecular biology, designer probiotics poses huge opportunity to treat diseases in a natural and non invasive way. Periodontitis have established risk of various systemic diseases like diabetes, atherosclerosis, hyperlipidemia, chronic kidney diseases, and spontaneous preterm birth. Thus the need to establish good periodontal health for attaining good systemic health is of utmost importance and probiotics are promising agents which needs in depth research for periodontal application. Although probiotics are in the initial stages of scientific research and application it offers a firm ground for future development.

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