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Probiotics in Periodontics. Good for Bad!!! : A Review

Deepak H Dave, Sujal C Shah*, Monali Shah, and Neeraj Deshpande

Department of Periodontics, Sumandeep vidyapeeth, KM Shah Dental College & Hospital, At. & Po. Piparia, Ta. Waghodia, Dist. Vadodara-391760, India

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***For Correspondence:**

Department of Periodontics, Sumandeep vidyapeeth, KM Shah Dental College & Hospital, At. & Po. Piparia, Ta. Waghodia, Dist. Vadodara-391760, India
Phone: +919727974087

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ABSTRACT

The concept of probiotics i.e. health beneficial microorganisms dates back as early as in the 20th century. It has become an area of interest to researchers in recent times. There has been a paradigm shift of treatment from specific bacterial elimination to altering bacterial ecology by probiotics. With the increase in the incidence of resistance to antibiotics, probiotics may be a promising area of research in periodontal therapy. There exists enough evidence to support the role of probiotics in dental caries but less evidence exists for their role in periodontal disease. Probiotics provide an effective and economic means to combat periodontal disease. Thus, a mere change in diet by including probiotic foods may halt, retard, or even significantly delay the pathogenesis of periodontal diseases, promoting a healthy lifestyle to fight periodontal infections. Many questions have been raised pertaining to the benefits of probiotic administration, as their role in periodontics is still in infancy. A complete understanding of the broad ecologic changes they induce in the mouth is essential to assess their long term consequences for oral health and disease. This paper reviews the evidences for the use of probiotics and prebiotics for maintenance of oral health and for the prevention of periodontal disease.

INTRODUCTION

With the emergence of multiresistant strains, antibiotic resistance has become a booming problem that has led scientists to develop novel means for fighting infectious diseases. Also there has been a major shift in treatment options from non specific to specific approach. Now treatment options propose altering ecology of niches, in order to modify pathological plaque to a biofilm of commensalisms. The concept of probiotics dates back to the first decade of 1900 when Ukrainian bacteriologist Elie Metchnikoff found that bacteria in fermented products could compete with microbes injurious to host and hence injurious to health. The term probiotics, antonym of antibiotics was introduced in 1965 by Lilly & Stillwell as substances produced by microorganisms which promote the growth of other microorganisms [1]. The definition of probiotics as it is known today is the one adopted by the International Scientific Association for Probiotics and Prebiotics term: 'Live microorganisms which when administered in adequate amounts, confer a health benefit on the host' [2].

Probiotic species mostly belong to the genera Lactobacillus and Bifidobacterium. Others belong to *Enterococcus, Streptococcus*, *Escherichia* group. *Dello vibrio* bacteriovorous is a newer probiotic strain introduced few years back. These bacteria are generally regarded as safe (GRAS) because they can reside in the human body causing no harm and, on the other hand, are also important for promoting health. They play a crucial role in halting, altering, or delaying periodontal diseases and have great potential in arena of periodontics in terms of plaque modification, altering anaerobic bacteria colonization, improvement of pocket depth and clinical attachment loss.

The oral cavity has been suggested as a relevant target for probiotic application. To be able to exert its properties in the oral cavity, it is essential for the probiotic organism to resist the oral environmental conditions and defense mechanisms, to be able to adhere

to saliva coated surfaces, to colonize and grow in the mouth and to inhibit oral pathogens. Generally, there is scarce evidence that probiotics permanently resides in the human body and in the mouth, in particular [3,4].

Mechanism of Action:

Taking into account the two major strategies against periodontal diseases, namely the elimination of specific pathogens and suppression of destructive host response, the probiotic approach might add value in achieving these treatment goals. Fig 1 outlines the plausible mechanisms whereby probiotic species might positively affect periodontal health.

- Adherence and binding to oral surface [5,6]
- Co-aggregation capacity with *F. nucleatum* [7]
- Inhibition of pathogens by various substances [8,9]
- Altering the balance of pro-inflammatory and anti-inflammatory cytokines and regulation of immune response[10]

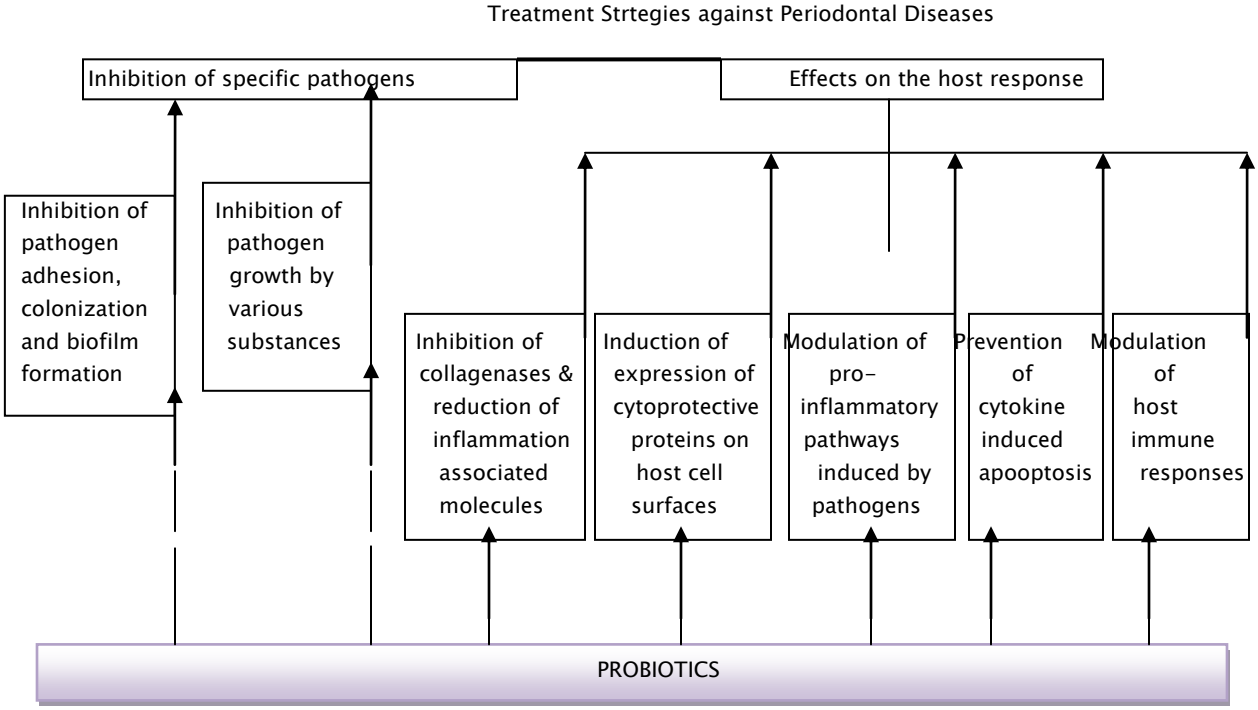

Figure 1: Mechanism of action of probiotics in periodontal disease

Replacement Therapy

The term replacement therapy (bacteriotherapy or bacterial interference) has been sometimes used interchangeably with probiotics [11]. This term has been coined by Teughels et al [12]. It refers to the basic idea of replacing pathogenic bacteria by supplying commensalisms, which have same characteristics for oral adherence. Table 1 illustrates the difference between probiotic therapy and replacement therapy [13].

Table 1: Difference between probiotic therapy and replacement therapy [13]

Replacement Therapy	Probiotic Therapy
Effector strain is not ingested and is applied directly on the site of infection by clinician	Probiotics are generally used as dietary supplements .Can be used by individual
Colonization of the site by the effect or strain is essential	Probiotics are able to exert a beneficial effect without permanently colonizing the site
Involves dramatic and long-term change in the indigenous microbiota	Involves transient microbiological change
Directed at displacing or preventing colonization of a pathogen	
Has a minimal immunological impact	Exerts beneficial effects by influencing the immune system

P. gingivalis, A. actinomycetemcomitans, T. forsythia and *T. denticola* are the main periopathogens of the Socransky's red and green complex. *S. oralis* and *S. uberis* have been reported to inhibit growth of pathogens both in laboratory and animal models. In the absence of these bacteria, tissues become more prone to periodontal disease [14].

Chewing gum "PERIO BALANCE" is the first probiotic gum, specifically formulated to fight periodontal disease. It's a combination of two strains of *L. reuteri* specially selected for their synergetic properties in fighting cariogenic bacteria and periodontopathogens. Each dose of lozenge contains at least 2×10^8 living cells of *L. reuteri* prodentis. Lozenge has to be used daily after meal or in the evening after brushing teeth, to allow probiotics to spread and adhere to various oral surfaces.

Krasse et al [5] evaluated *L. reuteri* in a recurrent gingivitis case. A parallel, double blind, randomized, placebo controlled study with 59 patients having moderate to severe gingivitis were selected. *L. reuteri* strains were administered via chewing gums twice a day for 2 weeks at a concentration of 1×10^8 CFU along with scaling and root planing. After 2 weeks, the clinical parameters were improved in the group consuming probiotic chewing gums.

Staab B, Eick S, et al [15] observed the reduction of MMP-3, Elastase activity on 50 students with plaque induced gingivitis after having probiotic milk drink for 8 weeks containing *L. casei* species.

Kang et al [16] in a cross over, open label placebo controlled study including 72 subjects evaluated the efficacy of a probiotic *W. cibaria* CMS1 rinse. Subjects were instructed to rinse in the morning, afternoon and evening with a 15 ml rinse after brushing. There was a significant reduction in plaque scores in the probiotic rinse group. Hence, *W. cibaria* isolates possess the ability to inhibit biofilm formation.

Hillman et al [17] carried out a parallel open label placebo controlled study on 24 gnotobiotic rats including a single baseline application and showed significant decreased levels of *A. actinomycetemcomitans* when compared with placebo group.

Grudianov et al[12] using a mixture of probiotics, reported improvements in clinical signs of gingivitis. Probiotics have also been employed as antimutagenic and anticariogenic agents.

Matsuoka et al [18] did a parallel open label study on 84 subjects consuming *L. salivarius* T1 2711 tablets 5 times a day for 8 weeks and showed decrease in bleeding on probing and *P.gingivlis* counts.

Teughels et al [19] conducted a split mouth study on beagle dogs with artificially created pockets. Bacterial pellets of *S. sanguis* KTH-4, *S. salivarius* TOVE and *S. mitis* BMS were applied locally in pockets at 1,2 and 4 weeks. They showed decreased counts of anaerobic bacteria and C. rectus with decreased pocket recolonization and bleeding on probing when compared with controls.

Acilact, a probiotic complex of five live lyophilized lactic acid bacteria, has been claimed to improve both clinical and microbiologic parameters in gingivitis and mild periodontitis patients [20].

Mayanagi et al[21] studied the effect of *L. salivarius* WB21 tablets on periodontopathic bacteria in a double blind, placebo controlled, randomized clinical trial on 66 healthy subjects. The results showed significant reduction in the sum total of five periodontopathic bacteria: *A. actinomycetemcomitans, P. intermedia, P. gingivalis, T. denticola* and *T. forsythia* in the probiotic group compared to the placebo group.

Probiotics in Halitosis Management

Breath malodor is a considerable social problem and most of its etiologic factors are present in the orpharynx (tongue coating, gingivitis, periodontitis, tonsillitis). Volatile sulphur compounds (VSC's) produced by *F. nucleatum, P. gingivalis, P. intermedia* and *T. denticola* are responsible for halitosis. *W. cibaria* possesses the ability to inhibit VSC production. Co-aggregation of F. nucleatum with other periopathogens results in secondary colonization of biofilm and contributes substantially to VSC production in oral cavity [22].

Hydrogen peroxide has been implicated in maintenance of a stable ecological system and protection against invading pathogens. It reduces the concentration of sulphur gas significantly.

Kang et al [23] reported that *W. cibaria* has the capacity to coaggregate with *F. nucleatum*, adhere to epithelial cells and produce hydrogen peroxide as well as bacteriocin which inhibits the proliferation of *F. nucleatum*. Gargling with a solution containing *W. cibaria* was associated with a net reduction in hydrogen sulphide production and consequently reduction in bad breath.

Tomoyuki et al [24] did a randomized controlled trial to evaluate the efficacy of *L. salivarius* WB21 tablets in halitosis management and showed that oral malodor parameters significantly reduced at the end of 2 weeks of administration of the probiotic tablet compared to placebo tablets.

Burton et al [25] conducted a randomized placebo controlled trial on 23 subjects to assess the efficacy of *S. salivarius* K12 lozenge for oral malodor correction. The results showed significantly reduced VSC levels in the *S. salivarius* lozenge group at 1 week compared to placebo.

Prebiotics

Prebiotics are non digestible oligosaccharides that affect the proliferation of resident commensal bacteria, which may exert beneficial effects on the host [26]. Examples: insulin-type fructans, maltodextrin, fructo-oligosaccharides and galctosaccharides.

Synbiotics

Combined administration of prebiotics with probiotics to provide definite health benefits by synergistic action.

Natural Supplements

Probiotics: Fermented vegetables like turnips and cabbage in north Europe
Fermented tea (Kombucha) in Russia and China
Water kefir (Tibicos) and water crystals is a probiotic beverage in Japan
Ginger beer (symbiotic culture of bacteria and yeast)
Fermented lemons in Morroco
Coconut kefir is a probiotic beverage made from young coconut water
Sour pickles (alternative to vinegar pickles) encourages the growth of Lactobacillus
Other sources: dairy products

Prebiotics: Soyabean, inulin sources like Jerusalem artichoke, jicama and chicory root, raw oats, unrefined wheat, unrefined barley and yacon.

Probiotic Dosage

No consensus exists regarding the minimum number of microorganisms that must be ingested to obtain a benefcial effect [27]. Typically, a probiotic should contain several billion microorganisms to increase the likelihood of adequate gut colonization [28]. Various studies have reported different values, $1\times10^{8-10}$, $1\times10^{9-10}$, $1\times10^{10-11}$ [27]

Probiotics are supplied along with prebiotic in form of powder sachet, gelatin capsules, or suspension. "BION" commercially available in Indian market (combination of pro- and pre-biotic) has 0.48 billion spores of Lactobacillus bifidum, Streptococcus thrmophilus, and 0.10 billion spores of *Saccharomyces boulardi* along with 300 mg of fructo-oligosaccharides, is prescribed as single dose daily before meals in the morning.

Safety Issues

Probiotics organisms are classified by FDA as generally regarded as safe (GRAS).

Criteria of an ideal microorganism used as probiotics[29]

- Ability to persist
- High cell viability, resistant to low pH and acids
- Able to interact or to send signals to immune cells
- Adhesion to cancel the flushing effect
- Should be of human origin

- Resistance to processing
- Influence local metabolic activity

Some cases of bacteraemia and fungenaemia have been reported in immunocompromised individuals in gut syndrome and chronic diseases

Lactobacillus endocarditis was reported after dental treatment in a patient taking *L. rhamnosus* [30]

Liver abscess was reported in an individual on *L. rhamnosus* GG[31]

Stimulation of immune system by probiotics showed degradation in autoimmune diseases, and transferred antibiotic resistance to pathogens [29].

Hence, it is clear that careful selection of the strain to be ingested for a particular disease is important, and the mode and time of the administration as well as the age of the subject taking probiotics is crucial.

CONCLUSION

The oral cavity with a well maintained balance of different species may be a potential source for health-promoting probiotic bacteria. The use of probiotics in oral care applications is gaining momentum. In today's world, it would be the right time to change the way bacteria are treated. There is increasing evidence that the use of probiotic strains can deliver oral health benefits. Probiotics, counterparts of antibiotics are free from issues of developing resistance and being body's own resident flora are most easily accepted by the host.

Periodontitis has been established as a risk factor for various systemic diseases like diabetes, atherosclerosis, hyperlipidemia, chronic kidney diseases, and spontaneous preterm birth. Thus, a need to establish good periodontal health for attaining good systemic health is of utmost importance and probiotics are promising and safe options, which are required to be explored in depth for periodontal application. Extensive work is needed to fully optimize and quantify the extent of this benefit. Systematic studies and randomized controlled trials are needed to come up with the best probiotic/prebiotic strains and means of their administration in various oral health conditions. Hence probiotics, though in its juvenile stage of research in terms of periodontal health benefits is a promising modality for treating periodontal diseases.

List of Abbreviations

- *L- lactobacillus*
- *S- Steptococcus*
- *F- Fusobacterium*
- *W- Weissella*
- *A.a- Aggregatibacter actinomycetemcomitans*
- *P. gingivalis- Porphyromonas gingivalis*
- *P. intermedia- Prevotella intermedia*
- *T. denticola- Treponema denticola*
- *T. forsythia- Tenerella forsythis*
- *S. oralis- Streptococcus oralis*
- *S. uberis- Streptococcus uberis*
- *C. rectus- Campylobacter rectus*
- FDA- Food and drug administration
- GRAS- Generally regarded as safe
- VSC- Volatile sulphur compounds

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