

The Promising Future of Probiotics: A New Era in Periodontal Therapy

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Abstract:

Probiotics are dietary supplements composed of healthy beneficial bacteria, which has only recently been introduced in dentistry after years of successful use in gastrointestinal problems. The development of bacterial resistance to the broad spectrum antibiotics has raised the possibility of a return to the pre-antibiotic dark ages. Time has approached to shift the paradigm of treatment from elimination of specific bacteria to alteration of bacterial ecology by probiotics. The concept of bacteriotherapy to heal diseases or to support immune function was the first introduced in the beginning of 20th century. Its use has been proven in strengthening immune function, to combat allergies, stress and exposure to toxic substances. Commensals delivered in this manner have been found to inhibit pathogenic microflora. Evidence suggests that probiotics not only function by direct inhibition or enhanced competition with pathogenic flora, but also by more delicate mechanisms including modulation of the immune system. The mechanisms of probiotic action are mainly unknown, but inter microbial species interactions are believed to play a key role with their immune stimulatory effects. Less evidence exists on their role in periodontal therapy. A mere change in daily diet by including probiotic enriched food may always halt, retard or even delay the pathophysiology of periodontal diseases, promoting a healthy lifestyle to fight periodontal infections. So far, mainly dairy products have been investigated, but other means like probiotics in chewing gum or lozenges have also been studied. The most suitable vehicles for oral probiotic applications are yet to be found. The introduction of probiotic bacteria in the mouth calls for the ascertainment of their safety considerations. Prebiotics have also been found to promote the growth of beneficial bacterial species. A fulfilled understanding of the broad ecological changes induced in the mouth by probiotics or prebiotics is highly essential to assess their long-term consequences for oral health and disease. Through this review article, we have tried to highlight the impact of probiotics in improving oral health.

Key Words: Antibiotics, commensals, oral health, prebiotics, probiotics

Introduction

The concept of eating bacteria for the goodness of our overall health may sound absolutely incongruent. Many studies have been going on since the late 90's on this subject. There are certain beneficial bacteria that keep the harmful pathogens at bay. In fact, beneficial microbes represent the future of medicine.

Despite the difficulties inherent in characterizing the microbiology of periodontal diseases, a small group of pathogens is recognized because of their close relationship with periodontal disease. The organisms in our oral cavity are a mixture of commensals and pathogens. A commensal microorganism is defined as one that lives on or within the host, but does not cause any apparent disease.¹ Chart 1 describes the role played by commensals in arresting the progression of periodontal disease.

Commensals have been proposed to activate the T-regulatory cells which induce tolerance by the activation of interleukin (IL)-10 and transforming growth factor- β .² Furthermore, they have been found to carry out selective interaction of toll-like receptors which regulates the release of pro-inflammatory cytokines hence down-modulating immune responses. They induce the keratinocytes to release IL-8, which by the phenomenon of chemotaxis ensures a steady increase in the amount of polymorphonuclears in the sulcus (basal inflammatory tone) to fight the periodontal pathogens.³ They also stimulate the keratinocytes to produce antimicrobial peptides which also help in killing the periodontal pathogens.

Probiotics

Probiotics can be defined as "live microorganisms which are administered in adequate amounts with beneficial effects on the

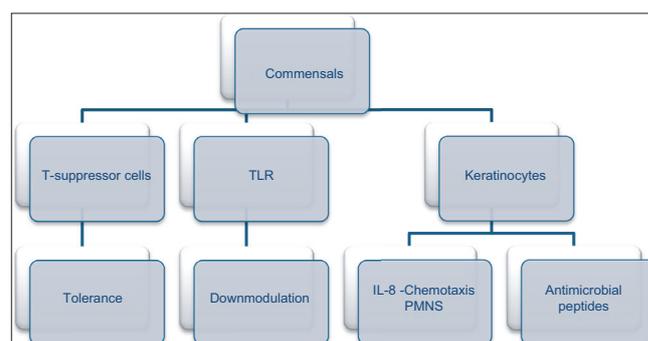


Chart 1: Role of commensals in arresting periodontal disease.¹

host.”⁴ They help to repopulate the beneficial bacteria which in turn would inhibit the proliferation of pathogenic species.

Probiotics unlike antibiotics result in proliferation of beneficial species, which in turn inhibit the growth of pathogenic bacteria. Antibiotics result in reduction of both commensals and pathogens.

Replacement therapy which is similar to probiotics follows the concept of bacterial interference.⁵ The effector strains are not ingested and they colonize the sites where they are introduced. Hence, there is a significant change in the microflora of the site unlike the probiotics.

Lilley and Stillwell (1974) were the first who coined the term “probiotics.” The first scientific foundation of probiotics was laid down by a Ukrainian bacteriologist, Elie Metchnikoff in 1907. He proposed that consumption of fermented milk would act as a source of commensal harmless lactic acid bacteria in the intestine and thereby decrease the intestinal pH and finally suppress the growth of bacteria.^{5,6}

In the year 1984, Hull *et al.* identified the first probiotic species, *Lactobacillus acidophilus*. Later in 1991, Holcomb *et al.* identified *Bifidobacterium bifidum*.^{5,6} In 1954, Kragen *et al.* had reported the usage of lactic acid bacteria in the field of dentistry.⁵

Probiotics have been proposed to act through three important hypothetical mechanisms (Koll Klais *et al.* 2006):⁷

- A. Direct interaction: Probiotics have the capability to interact directly with the disease-causing microbes, making it harder for them to cause the disease.
- B. Competitive exclusion: The beneficial microbes directly compete with the disease by developing microbes for nutrition.
- C. Modulation of host immune response: The interaction of probiotics and strengthening of the immune system.

There are a variety of probiotics, among which bacterial species are predominant.⁸⁻¹⁰ Probiotics have been categorized as lactic acid producing substances, non-lactic acid producing substances, non-pathogenic yeasts and non-spore forming bacteria. Chart 2 describes the classification of probiotics. The majority of probiotic strains belong to the genera, *Lactobacillus* and *Bifidobacterium*. The probiotic strains which have been isolated from *Lactobacilli* species are *L. acidophilus*, *Lactobacillus casei*, *Lactobacillus rhamnosus*, *Lactobacillus jhonsoonii*, *Lactobacillus gasseri*, and *Lactobacillus reuteri*. The strains isolated from *Bifidobacterium* species include *Bifidobacterium bifidum*, *Bifidobacterium longum* and *Bifidobacterium infantis*. There are certain properties which ideally the probiotics should possess which have been enlisted in Table 1.

Vectors of Administration

Probiotics have been incorporated into a variety of mediums such as cheese, yoghurt and chewing gums. The various sources of probiotics have been described in Chart 3.

Applications in Periodontics

Gingivitis

Investigators have been anxious about the effectiveness of probiotics in the treatment of gingivitis. Certain studies have revealed that probiotics not only significantly reduced plaque

Table 1: Ideal properties of probiotics. ^{5,12-14}
Must be non – virulent and non- pathogenic
Must be stable under majority of conditions
Must be capable of survival and metabolism
Must possess a good shelf life
Should act as a replacement as well as a reinstate therapy

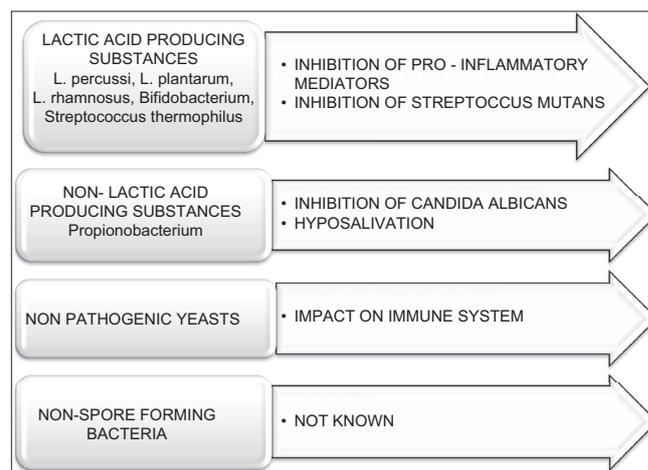


Chart 2: Classification of probiotics.¹¹

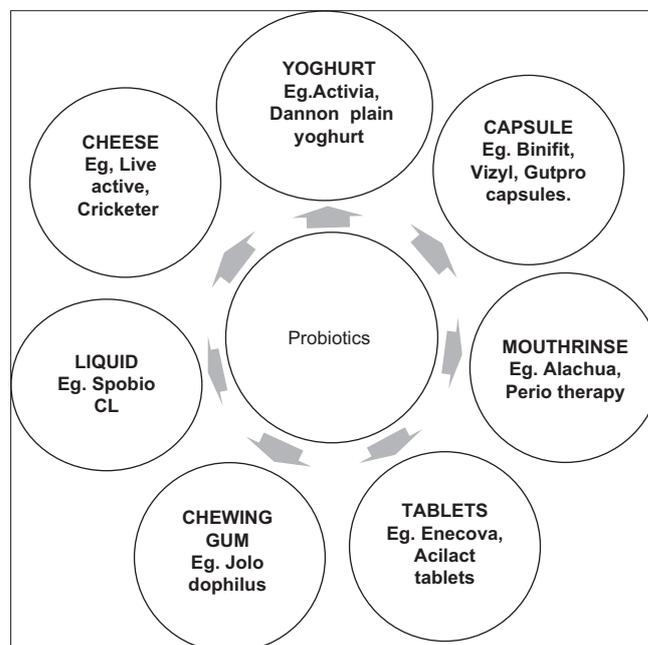


Chart 3: Vectors of administration of probiotics (Farmworth, 2003).¹²

accumulation but also showed a significant reduction in the gingival index scores.

A second study has confirmed that one pair of probiotic strains reduced the presence of cytokines in gingival crevicular fluid also decreased bleeding on probing.⁴

A third study performed by Noel Kelsch and Gregory Kutzman found that the use of dental probiotic had a profound effect on the oral health of patients, showing a 47% reduction in plaque accumulation.

In a randomized controlled double-blind trial, researchers from Finland investigated the effects of orally administered *L. rhamnosus* GG and *Bifidobacterium* subsp. lactis BB-12 on *Streptococcus mutans*. The scientists observed decreased levels of plaque index and a lower incidence of gingivitis.

Previous studies suggested that the probiotic *L. reuteri* prodentis can inhibit plaque and have anti-inflammatory and anti-microbial effects that could make it useful in maintenance of healthy teeth and gums.¹⁵

Probiotic mouthwashes have been demonstrated to cause a significant reduction in plaque formation and gingivitis in 6-8 years old children (Harini and Anegundi 2010).¹⁶

Oral probiotics used in combination with xylitol are highly beneficial after gum treatments. These are of great benefit when used at bedtime by increasing the salivary flow.¹⁷

A team of researchers from the University of Health Sciences conducted a study to test the effect of probiotics in patients with chronic gingivitis. They found that lozenges containing the microbes decreased the oral bacteria 90% more than the traditional treatments.¹⁸

Chronic Periodontitis

The application of specific beneficial bacteria, as an adjunct to scaling and root planning, has also proven to inhibit the recolonization of periodontal pockets by period onto pathogens and thus the maintenance of periodontal health.

In vitro studies have proven that probiotic components can maintain their viability when exposed to saliva and it mediated their adherence to oral surfaces. Strong species dependent and strain dependent activities against periodontal pathogens have been observed.

Teghels *et al.* has conducted a study based on the repeated applications of *Streptococcus sanguinis*, *Streptococcus mitis*, and *Streptococcus salivarius* after root planning and observed a significant reduction of anaerobic species and black pigmented bacteria. It was the first study which assessed the role of

commensal microflora in the modulation of periodontal pocket recolonization.¹⁹

Probiotics act by neutralizing the pH hence preventing the formation of organized dental plaque. The antioxidants produced by the probiotics further prevents plaque accumulation by the neutralization of free electrons which are essential for the mineral formation.²⁰

Acilact, a Russian probiotic preparation has claimed to improve both clinical and microbiological parameters in periodontitis-affected patients. A parallel open-label study conducted by Ishikawa reported results which showed decrease in black-pigmented anaerobic rods and decreased bleeding on probing.²¹

Halitosis

Halitosis is a condition of oral malodor which is ascribed to the disturbed commensal microflora equilibrium (Scully and Greenman 2008). The inhibitory effect of it on the production of volatile sulfur compounds (VSC) by *Fusobacterium nucleatum* has been noticed in a study done by Kang *et al.*²² The most defensible mechanism in VSC production is the formation of hydrogen peroxide engendered by *Weissella cibaria* that dissuades the procreation of *F. nucleatum*.²² *S. salivarius* is well-known to produce VSC. The use of chewable lozenges containing *S. salivarius* K 12 reduced levels of VSC among patients with halitosis. Though probiotics are being marketed for both mouth and gut associated halitosis, their efficacy highly demands more clinical studies.^{19,23}

Studies have proven that adding *S. salivarius* bacteria into the mouth after rinsing with mouthwash can reduce levels of sulfur in one's breath (Burton *et al.*).^{22,23}

A Swedish study has also shown evidence that probiotic *Lactobacillus* bacteria has many benefits for oral health.²⁴ In a recent study published in the Journal of Clinical Microbiology, researchers noted that *S. salivarius* was significantly present in the mouths of volunteers with the best breath. The same bacterium that we use in our specialty oral health probiotics also appeared naturally in the mouths of participants without halitosis - making this species a definite "good breath" microbe.¹⁹

Designer Probiotic

Equipping the probiotics bacteria with the appropriate and necessary genetic element to overcome stress inside and outside host and antagonize invading pathogens. They have been employed in the treatment of HIV and also have been employed as novel vaccine deliver vehicle. By improving the stress tolerance profile of probiotic cultures, the tolerance to processing stress also subsequently improves and thus also helps to prolong the survival during subsequent storage. It finally contributes to a larger proportion of the administered probiotics to reach a desired location.²⁵

Safety Considerations

The safety issues have been a special concern since a few years due to the increased probiotic supplementation of different food products. From the safety point of view, a well-recognized probiotic should not be pathogenic, should not have any growth exhilarating effects on bacteria instigating diarrhea and should not possess the capability to locate antibiotic resistant gene. The probiotics which are being used must satisfactorily be adept to maintain genetic stability in the oral microflora.^{13,25}

Studies based on commercial preparations has shown mismatch of the probiotics on the label while compared with its contents. The presence of active species is not generally found in most of these preparations.

Another important concern regarding probiotics is based on its dose of application.

Certain systemic complications like Lactobacillus endocarditis have also been reported in patients who were on a prolonged therapy of *L. rhamnosus*.^{13,25-27}

Future Prospectives

Due to the various drawbacks of probiotics and their reduced efficiency in rendering commensals to the oral cavity newer agents have been introduced.

Prebiotics are selectively fermented ingredients that allow specific changes, both in the composition and or in the activity of the gastrointestinal microflora that confers health benefits to the host.²⁸ It was first introduced by Gibson *et al.* in 1995.^{29,30} In order to exert its effectiveness, prebiotics must escape digestion in the upper gastrointestinal tract, so that it can be released in the lower tract. Unlike probiotic species, the carbohydrates of prebiotics do not undergo any changes during cooking, a characteristic that makes them unique in the food industry.

With the development of dynamic “functional food markets” worldwide, efforts are being put forward for the improvement of synbiotics. These are generally referred as nutritional supplements combining probiotics and prebiotics in a form of synergism that would bring extra health benefits.³¹ “BION” is the most commercially available synbiotic in India.

Conclusion

The new technological era of the present would be the right time to change the ways bacteria are treated. Further studies are needed to find out the best probiotic strains and means of administration. Basic scientific understanding and research about the minute forms of life and their effect on the treatment of periodontal diseases may further expand the confined field of possible applications of probiotics.

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