

Probiotics in Periodontics – A review

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Abstract

This review article aims in discussing the benefits of probiotics and its role in periodontics. To find relevant randomised controlled studies comparing human and animal probiotic therapies in periodontitis, PubMed and reference from prior reviews were searched.

Symbiotic have been created by combining probiotics and prebiotics. Probiotics have been successfully employed in the medical community to treat a wide range of illnesses. By changing the host defence system and preventing the release of proinflammatory cytokines that can mediate tissue destruction, probiotics have been demonstrated to be effective in preventing periodontal tissue destruction. It has been shown that probiotics

increase ecological pH and have an inhibitory effect on volatile sulphur compounds, which aid in the management of halitosis. The rising use of probiotics in periodontal therapy has been highlighted by the notion of guided tissue recolonization.

Future studies conducted independently are required to look into particular probiotic strains, dosages, delivery techniques, treatment schedules, mechanisms of action, safety, and ways to maintain the effects of probiotic therapies.

Keywords: Probiotics, Periodontitis, Alveolar Bone Loss, Gingivitis, Periodontal Diseases

Introduction

According to Petersen (2003), periodontitis is a common chronic inflammatory illness that affects the adult population's dentition. To restore the lost periodontium and manage the ongoing inflammation brought on by the periodontopathic organism, numerous interventions have been tried. Porphyromonas gingivalis, Treponema denticola, Tannerella forsythus, and Aggregatibacter actinomycetemcomitans are the primary organisms connected to periodontitis. Current methods used to minimise the pathogenic germs include subgingival debridement, surgical interventions, and in some situations, selective use of antibiotics and antiseptics. Although the bacterial load and related inflammation are temporarily reduced by these treatments, they frequently are insufficient to control the condition (Quirynen et al., 2002; Teughels et al., 2007a). Therefore, it's necessary to look for other adjunctive tactics. One of the many novel ways being examined as an adjuvant treatment for the management of periodontitis is the administration of beneficial bacteria, or probiotics, with antibacterial and anti-inflammatory qualities. This strategy may provide a low-risk, affordable, and simple-to-use treatment alternative.

Probiotics are defined as living microorganisms, principally bacteria, that are safe for human consumption and when ingested in sufficient quantities, have beneficial effects on human health, beyond basic nutrition.^[1] Through the development of bacterial replacement treatment, probiotics, which are often utilised in the medical area, are now used to manage and treat periodontal disease. Due to the development of antimicrobial resistance and the recurrent recolonization of treated locations with harmful bacteria, probiotics are now routinely employed in the context of oral health.

The term "probiotics" was originally used in 1965 by Lilly and Stillwell, who defined it as "Living microbes that deliver beneficial effects to the host's health when administered in adequate amounts".^[2] According to Gibson and Roberfroid^[3], a "prebiotic" is a non-digestible food element that has a positive impact on the host by selectively promoting the development and/or activity of one or a small number of microorganisms in the colon, improving host health.

The definition of probiotics has changed over time, and they are now defined as "living microorganisms, mostly bacteria, non-pathogenic, used as nutritional supplement, which, after being consumed in an appropriate quantity, boost the gastrointestinal microbial equilibrium and cause beneficial effects on the health of those who ingest them".^[3] For human health, they are regarded as secure^[4]. The consumption of probiotics for treating oral infections such dental caries and periodontal disorders has recently drawn a lot of attention. The amount of knowledge on probiotics' effects on periodontal health, however, is currently somewhat limited.^[5]

Several studies such as Gorbach and Goldin (1985), Näse et al. (2001), Grudianov et al. (2002), Wei et al., Von Bultzingslowen et al., Hatakka et al. (2007) have spoken about the relation between bacterial strains like Lactobacillus rhamnosus, Bifidobacterium spp, and Lactobacillus plantarum, which have a positive effect on tooth adhesion and their action against diseases such as dental cavities (caries) and yeast infection.^[7-10]

Periodontal diseases are being treated with antibiotics or other antimicrobials in recent years. Probiotic research in periodontal care, however, may hold promise given the rising prevalence of antibiotic resistance^[11]. An oral probiotic is currently available that uses a proprietary combination containing two types of Lactobacillus reuteri to fight dental plaque, gingivitis, and cariogenic

bacteria. Because of the presence of it in the person's gastrointestinal system and creation of the broad-spectrum antibiotic chemical "reuterina," which, when administered in the proper quantity, gives the required antibacterial action to maintain the intestinal microbiota, this is 100% natural ^[12].

A more recent probiotic strain, *Dello vibrio bacteriovorus*, was introduced a few years ago. These bacteria are crucial for supporting health and are usually thought of as safe (GRAS) since they can live in the human system without harming it. They offer considerable promise in the field of periodontics with respect to plaque modification, modifying anaerobic bacteria colonisation, improving pocket depth, and preventing clinical attachment loss. They play a crucial role in stopping, changing, or delaying periodontal disorders.^[13] Hence this review article was designed to explore the basics of probiotics and its use in treatment and prevention of periodontal diseases.

History

Since the middle of the nineteenth century, when Lactic Acid Bacteria (LAB) were discovered, many individuals have come to the conclusion that dairy products fermented by lactobacillales have many positive effects on our health ^[2].

Communities of bacteria coexist with the host in a state of periodontal health, influencing the host's immune system and overall health. Dysbiosis, a term for a disruption in the microbial equilibrium, has been linked to a number of illnesses (Goulet, 2015). In part, an increase in harmful bacteria and a decrease in beneficial bacteria have been linked to obesity, metabolic disorders, gastrointestinal disorders, autoimmune disorders, allergies, and cancer (Logan et al., 2003).

All kinds of pickled foods and drinks, including Korean kimchi, Indonesian tempeh, Indian chutney, Japanese

miso, sauerkraut, kefir, yoghurt, and cheese, include healthy bacteria. Lactic acid bacteria, primarily lactobacilli, transform carbohydrates to lactic acid during the preservation process known as "lacto fermentation," which is an anaerobic process (Turpin et al., 2010). Consumption of fermented foods is a long-standing tradition that dates back to 5400 BC, while suggestions for treating digestive disorders first appeared in 76 AD (Rawlings, 2013).

The idea that probiotics may have health benefits and that fermented dairy goods have these capabilities was initially put forth by Elie Metchnikoff. ^[1,4,12,14]

Henry Tissier, a French paediatrician, independently discovered that infants with diarrhoea had a low quantity of bacteria in their stools that had an odd, Y-shaped morphology during Metchnikoff's scientific presentation of the benefits of lactic acid bacteria. On the contrary, healthy children had a lot of these bifid bacteria.^[4] He therefore proposed that these bacteria might be given to patients with diarrhoea in order to aid in re-establishment of healthy gut flora.

In 1907, the Nobel laureate and biologist of Ukrainian descent, researching at the Pasteur Institute in Paris, identified *Lactobacillus bulgaricus* and came up with the hypothesis that lactic acid bacteria, which are found in Bulgarian yoghurt, could extend life by avoiding putrefaction in the gastrointestinal tract. He based this on the fact that he had noticed that Bulgarians survived longer than the average person.^[15,16] As a result, the idea of probiotics was created, and a new branch of microbiology was established.

The term "probiotics," as it is now used, "was initially coined by Lilly and Stillwell^[17] in an alternate context in 1965 to represent 'substances' released by a single microbe which promotes the growth of another." Later in 2001, the World Health Organisation gave probiotics the

definition "Live microorganisms that, when given in sufficient quantities, provide a health benefit to the host."^[18]

Mechanism of Action

Probiotics perform a wide range of beneficial tasks, significantly influencing one's health. They create lactic acid, which has an antibacterial impact, hydrogen peroxide, which has an antiseptic effect, and substances that fight pathogens like viruses and fungi. According to Ciorba (2012), LeBlanc et al. (2012), Jonathan and David (2013), probiotics are crucial for the growth and regulation of the immune system, preservation of a healthy gastrointestinal tract lining, food digestion, synthesis of amino acids, proteins, and various vitamins, as well as the absorption of calcium, iron, and vitamin D.

Probiotics' exact methods of action are yet unknown and may vary depending on a number of variables, including the condition being addressed, the strain and concentration of probiotics employed, the stage at which they are delivered, the presence of prebiotics, and enteric bacteria. (Geier et al., 2007).

According to Gueimonde and Salminen (2006), Shira and Gorbach (2006), and Devine and Marsh (2009), probiotic benefits might result from three basic local or systemic mechanisms of action:

1. Pathogens and probiotics indirectly compete for important nutrients, and probiotics can also reduce pathogen adherence by altering the pH of the surrounding environment.
2. Probiotics play a direct role in the lactic acid, hydrogen peroxide, and bacteriocin synthesis, which are all antimicrobial compounds that can either kill or hinder the growth of periodontal infections.
3. According to Ciorba and Stenson (2009), probiotics can affect the host by improving the integrity of the

intestinal barrier and modulating the host's innate and adaptive immune response (reducing production of pro-inflammatory cytokines like IL-6, IL-1, and TNF and increasing production of anti-inflammatory cytokines like IL-10).

The probiotic method might be useful in reaching these therapy objectives when considering the two main tactics against periodontal disorders, namely the eradication of particular microorganisms and suppression of damaging host reaction. According to the following mechanisms, it functions:

- Binding and adhesion to the oral surface
- Possibility of co-aggregation with *F. nucleatum*
- Pathogen inhibition by a variety of chemicals
- adjusting the ratio of cytokines that promote and inhibit inflammation as well as the control of immune response.^[10]

Criteria For Probiotics

1. It should be able to improve the host animal's condition, for as through promoting growth or disease resistance.
2. It must be human-made.
3. It ought to have a good cell viability rate.
4. It should not be harmful or pathogenic.
5. It need to be able to communicate with or alert immune cells.
6. It should be able to affect the regional metabolic activity.
7. It must be able to survive and function under the conditions of the gut, such as resistance to organic acids and low pH.
8. It must be reliable and durable enough to withstand prolonged field and storage circumstances.^[13]

Rationale For the Use of Probiotics

When using conventional antibiotic therapy, a disease cannot be completely cured and it becomes more severe.

In conventional antibiotic therapy, more multidrug-resistant bacteria emerge and disease prevention is prioritised over disease management. Probiotics may prevent colonisation resistance, the introduction of new types of bacteria, shifting paradigms in our knowledge of disease causation, and the prevention of prospective pathogens' colonisation, overgrowth, and translocation.

Probiotics In Medicine

Probiotics have historically been employed in gastroenterology. According to evidence-based evaluations, specific probiotic strains help maintain the intestinal tract's microbial balance, which strengthens the immune system and lowers inflammation (Ciorba, 2012). Probiotics have been the subject of clinical research that looked at how they affected conditions like allergies, irritable bowel syndrome, inflammatory bowel disease, Crohn's disease, and antibiotic-associated diarrhoea (Meurman, 2005; Vaghef-Mehrabany et al., 2014). Additionally, laboratory research has produced encouraging outcomes for the treatment of colon cancer and childhood autism (Rafter, 2003; Critchfield et al., 2011).

Probiotics And Oral Health

Studies on the possible health advantages of probiotics for overall health have been extensively published, but there have been far fewer studies on their potential benefits for dental health. In terms of probiotic strains, dosages, and application methods, these vary greatly (Teughels et al., 2011). Examples include cheese, lozenges, milk, kefir, ice cream, gum, drops, powder, and mouthwash.

Streptococcus mutans concentrations in saliva can be decreased by probiotics, according to research on their effectiveness in preventing dental caries (Näse et al., 2001). Probiotics may help prevent dental caries, according to a new meta-analysis (Laleman et al., 2014).

Additionally, probiotics have been studied in relation to oral disorders such as halitosis, mucositis brought on by chemotherapy, and candidiasis (Stamatova and Meurman, 2009; Laleman and Teughels, 2015).

Probiotics And Periodontal Disease

The expression of T-helper cell 1 or T-helper cell 2 in response to probiotic stimulation of dendritic cells modifies immunity. Probiotics have the ability to replicate a pathogen's reaction without causing periodontal damage.^[19] Aggregation modification by heterofermentative processes is another way. The most effective inhibitor of *A. actinomycetemcomitans*, *P. gingivalis*, and *Prevotella intermedia* is *Lactobacillus*. Both *Lactobacillus salivarius* and *Lactobacillus gasseri* exhibit strong periopathogenic bacterial inhibition. Bacteriocins secreted by *Lactobacillus reutri*, such as reutrin and reutricyclin, have a high affinity for host tissue, limit the growth of pathogens, and have anti-inflammatory effects by blocking proinflammatory mediators. The same mechanism is used and catalase is released by *Weissella cibaria*.^[19]

Another route by which probiotics influence tumour cell death is through the production of end products. Periodontitis is mostly caused by the pathogenic organisms *P. gingivalis*, *T. denticola*, *T. forsythus*, and *A. actinomycetemcomitans*. These bacteria possess a variety of pathogenic traits that enable them to colonise subgingival locations, get past the host's defences, and harm tissue as a result. The disease's progression is also aided by the host's immune response's persistence.^[1,20] In periodontal disorders, there is an increase in plaque mass and a switch to obligatory anaerobic and proteolytic bacteria, majority of which are Gram-negative. Probiotic medication produced better microbiota normalisation than the control group, according to Grudianov et al.'s analysis of the impact of probiotic tablets on gingivitis

and various grades of periodontitis.^[21] In a recent study, individuals who had chronic periodontitis had a lower prevalence of lactobacilli in their oral cavity than healthy participants did. This was especially true of *L. gasseri* and *L. fermentum*.^[1] Numerous studies have shown that lactobacilli have the ability to stop the growth of periodontopathogens such as *P. gingivalis*, *P. intermedia*, and *A. actinomycetemcomitans*. Thus, it has been proven that lactobacilli found in oral cavities contribute to the ecological balance of the mouth.^[1]

Because they produce acid rather than H₂O₂ or bacteriocin, homofermentative lactobacilli have been shown to have an inhibitory effect on periodontal infections.^[1] Although there was no correlation between greater bifidobacterial counts and reduced black-pigmented anaerobe counts, Hojo et al.'s study demonstrated that bifidobacteria suppress some black-pigmented anaerobes by fighting for a crucial growth nutrient, vitamin K. Thus, probiotics contribute to the creation of a great maintenance product by releasing antioxidants that stop the development of plaque.

Probiotics And Halitosis

The foul and disagreeable odour that comes from the mouth and is brought on by volatile sulphur compounds (VSC) is known as halitosis or oral malodor. *P. gingivalis*, *P. intermedia*, *T. denticola*, and *Fusobacterium nucleatum* are the bacteria in charge of producing VSC.^[22] Regular probiotic use aids in halitosis management. The ecological pH of the *W. cibaria* strains was higher than what would typically be seen in association with lactobacilli, which is positive in terms of the usefulness of this species in the circumstances of probiotic use.^[23] Kang et al. noticed reduced amounts of the volatile sulphide constituents formed by *F. nucleatum* after consuming *W. cibaria*, and he hypothesised that this was because *W. cibaria* was

producing hydrogen peroxide, which was inhibiting *F. nucleatum*.^[24] By competing for colonisation sites with species that raise the levels of VSC, the oral probiotic candidate *Streptococcus salivarius* has shown that it has an inhibitory effect on VSC.^[3]

Commercially Available Probiotics

Commercially, probiotics can be purchased as lozenges, toothpaste, chewing gum, or mouthwash.

Gum Perio Balance

This is perhaps the first probiotic that has been created expressly to combat periodontal disease. It includes a patented mixture of two *L. reuteri* strains that were chosen for their complementary abilities to combat cariogenic microbes and periodontopathogens.

PeriBiotic

This toothpaste is a fluoride-free, all-natural dental hygiene aid that contains DentalLac, a unique functional probiotic strain of *Lactobacillus paracasei* not present in any other toothpaste.^[13]

Bifidum bacterin, Acilact, Vitanar

In individuals with gingivitis and moderate periodontitis, this probiotics preparation containing a mixture of five active lyophilized lactic acid-producing bacteria is said to enhance several clinical and microbiologic markers.^[13]

Wakamate D

This probiotic pill provides 6.5 10⁸ CFU of *L. salivarius* WB21 per tablet together with 280 mg of xylitol, which was created to support the gut microbial balance by supplying acid-tolerant *L. salivarius* WB21.^[13]

Prodentis

This probiotic lozenge contains a combination of two strains of *Lactobacillus reuteri*, each of which has a minimum of 1 10⁸ CFU: DSM 17938 and ATCC PTA 5289.

Probiotics As Guided Tissue Recolonization

Guided periodontal pocket recolonization refers to the idea of replacing the harmful bacteria in the gingival sulcus with good microorganisms. In a study on directing periodontal pockets, Teughels et al. made the hypothesis that adding certain helpful bacteria as a supplement during scaling and root planing would prevent the recolonization of periodontal pockets by periodontopathogens. However, the growing issue of resistance to antibiotics has rekindled interest in the use of alternative microbes.^[4] Nackaerts observed improvements in bone level and bone density when *Streptococcus sanguis*, *S. salivarius*, and *S. mitis* were administered subgingivally in dog models. This resulted in a delay in the recolonization of periodontal pathogens, a decrease in inflammation, and an improvement in bone density.^[24]

Risks And Side Effects

Before using a strain as a probiotic, it is crucial to thoroughly research and pick it because different strains of the same species do not all have the same characteristics. Probiotics have few digestive side effects.

L. bulgaricus was shown to be unable to break down particular parts of host tissue.^[1] Patients with impaired immune systems should not use probiotics.^[25] In immunocompromised people, babies, patients with chronic diseases, people with short gut syndrome, and those who have previously undergone lengthy hospitalisation and surgical intervention, bacteremia and fungemia have been documented after probiotic administration.^[24] After receiving dental work, an individual with mitral regurgitation who was taking a probiotic supplement containing *Lactobacillus rhamnosus* developed *Lactobacillus* endocarditis. Following the administration of probiotic-containing *L.*

rhamnosus GG, the liver abscess was described. In a rat model, it has been demonstrated that a probiotic strain of *L. salivarius* is cariogenic. Several probiotic lactobacilli and bifidobacteria ferment dietary carbohydrates in vitro to generate acid.

Probiotic Dosage

Regarding the bare minimum of microorganisms that must be consumed to have a beneficial effect, there is no general agreement^[26]. For an effective gut colonisation, a probiotic typically has to include several billion bacteria^[27]. Several investigations have reported a range of values, including 1108-10, 1109-10, and 11010-11^[27]. Prebiotics and probiotics are provided together in powder sachets, gelatin capsules, or suspension form. "BION" is a commercially available pro- and pre-biotic that is sold in India. It contains 300 mg of fructo-oligosaccharides, 0.48 billion spores of *Lactobacillus bifidum*, 0.10 billion spores of *Streptococcus thermophilus*, and 0.10 billion spores of *Saccharomyces boulardii*. It is recommended as a single dose every morning before meals.

Safety of probiotics

The safety aspect of probiotics must be thoroughly examined before they are marketed.

1. Probiotic strains that have been thoroughly examined and prepared are generally very safe to be used by humans orally and vaginally.
2. To qualify as probiotics, newer strains and products must demonstrate their safety in human research.
3. When a strain, such as *Saccharomyces boulardii* (*Saccharomyces cerevisiae*), imposes certain restrictions on its usage, such as for individuals with a leaky gut or at risk of blood-borne infection, clear labelling is advised.^[5]

Conclusion

Reduced probing pocket depth, increased attachment level, and decreased bleeding on probing suppuration are the objectives of periodontal therapy. To accomplish the therapeutic results, a new microbial population is required. Other protocols, such as the combination of mechanical debridement alongside systemic antibiotics, have therefore been successfully used in the management of periodontal disorders with the aim of amplifying the impact of periodontal therapy. The use of antibiotics temporarily, either locally or systemically, does not significantly improve the long-term effects of periodontal therapy. The problems with antibiotics are associated with the eradication of the entire microflora, regardless of their pathogenicity, and the development of antibiotic resistance.

Given the advantages of probiotics, this therapy may be a good complement to or replacement for periodontal treatments. Probiotic use in dental care applications is on the rise. There is mounting evidence that using probiotic strains now available can improve oral health. Therefore, suggesting a treatment that combines non-surgical therapy and probiotic consumption may lead to improved regulation of bacterial plaque and thereby support a successful periodontal treatment. They may also have an impact on immunological markers. To completely optimise and quantify the magnitude of this advantage, more study is required. To identify the optimum probiotic/prebiotic strains and methods of delivery in a variety of oral health issues, systematic investigations and randomised controlled trials are required. Probiotics are a viable treatment option for periodontal problems even if research into their potential advantages for periodontal health is still in its early stages.

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