

PERIODONTAL HEALTH AND PROBIOTICS : A REVIEW

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ABSTRACT

Probiotics are living non pathogenic micro organisms that are involved in improving the health of the Gastrointestinal tract of the host body. In recent times, prebiotics and probiotics have shown to effectively alter the host microbial interface by achieving homeostasis and develop a natural balance of the microbial flora in the respiratory tract and the oral cavity. Prebiotics are non digestible food ingredients which help in increasing population of probiotic bacteria. Studies have suggested reduction of dental caries, gingivitis, periodontitis, halitosis bacteria linked to the use of probiotics. They act by reducing the amount of harmful oral bacteria by means of utilizing abundant health associated oral microbial species. Additionally, nitrate reducing bacteria have shown promising effect in improving efficacy of probiotic strains to accentuate oral health benefits. The aim of this review is to collate the existing information available on use of probiotics and prebiotic in oral cavity.

KEY WORDS

probiotics, prebiotics, periodontitis, halitosis, synbiotics, guided pocket recolonization.

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INTRODUCTION

Some of the most prevalent oral health diseases are gingivitis and periodontitis.¹ Specifically, periodontitis which consists of gingival inflammation, loss of connective tissue attachment, leading to resorption of alveolar bone and subsequent tooth loss.² A variety of treatment modalities are being tried on in adjunct to scaling and root planning to manage the ongoing inflammation and restore the lost periodontium. *Porphyromonas gingivalis*, *Treponema denticola*, *Tannerella forsythus*, and *Aggregatibacter actinomycetemcomitans* are the primary organisms connected to periodontitis.

Scaling and root planing is a non-surgical treatment that removes the plaque and calculus from the crown and the root surfaces of the teeth and thus leads the reduction of the microorganisms load. Scaling and root planning is the treatment considered as the gold standard, and this type of treatment has been shown to reduce the bacterial load and eliminate the etiology. Supportive treatments for scaling and root planning include systemic and local antibiotics, local drug delivery, host modulation therapy, lasers, are some of the other novel methods.³

For many years, probiotics have been used in general medicine for the treatment of inflammatory bowel diseases and for the prevention of allergies and respiratory infections.⁴ In dentistry, the probiotics might prevent or treat oral diseases such as caries, gingivitis, or periodontitis.⁵ Commonly used probiotics in dentistry are *Bifidobacterium* and *Lactobacillus*.⁶ There is evidence that the use of a probiotic yogurt supplemented with *Bifidobacterium animalis* subsp. *lactis* (*B. lactis*) could have a positive effect on plaque buildup and gingival inflammation.

In their joint report on probiotics published in 2001, the Food and Agriculture Organization of the United Nations and the World Health Organization (FAO/WHO) defined Probiotics as “live microorganisms, which when administered in adequate amounts, confer a health benefit on the host”. The most frequently used genera are lactobacilli and bifidobacteria. In 1907, Russian

scientist the Nobel laureate Elie Metchnikoff realized that consumption of Bulgarian yoghurt (which contains lactic acid bacteria) was good for health. He devoted the last decade of his life to the study of lactic acid-producing bacteria as a means of increasing human longevity. From his work, the concept of probiotics was born and a new field of microbiology was opened. The term probiotic, as an antonym to the term antibiotic, was originally proposed in 1965 by Lilley and Stillwell. The first probiotic species introduced into research were *Lactobacillus acidophilus* by Hull et al in 1984.

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

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.

PROBIOTICS, PREBIOTICS AND SYMBIOTICS

Probiotics:

Probiotics are bacterial cultures or living microorganisms which upon ingestion in certain numbers, exert health benefits beyond inherent, general nutrition and support a good and healthy intestinal flora.

Prebiotic:

The human gastrointestinal tract constitutes a greatly complex ecosystem of bacterial population. Some are beneficial organisms such as e.g. *Lactobacillus* and *Bifidobacterium*, some are harmful e.g. *Helicobacter pylori*, *Clostridium perfringens*. Dietary incorporation of the prebiotics can favor the growth of these beneficial good bacteria over that of harmful pathogenic ones.

A prebiotic is defined as “a nonabsorbable food component that beneficially stimulates one or more of the gut-beneficial microbe groups and thus has a positive effect on human health. The most commonly used prebiotics are carbohydrate substrates (eg dietary fiber)

Inulin, fructo-oligosaccharides (FOS), Galacto-oligosaccharide lactulose Malto-oligosaccharides, and resistant starch (Gibson et al, 1995) are some of the examples of prebiotics.

Synbiotics:

Synbiotics is the word coined for the combined

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

ESSENTIAL QUALIFICATIONS FOR PROBIOTICS

1. It should not be harmful or toxic
2. It should be human-made.
3. It should have good cell viability rate.
4. It should have the ability to improve the host's condition, through promoting growth or disease resistance.
5. It should have the ability to communicate with other immune cells.
6. It should be able to affect the regional metabolic activity.
7. It should be clinically validated and documented health effect
8. It must be reliable and durable enough to withstand prolonged field and storage circumstances.⁸
9. It must be able to survive and function under the conditions of the gut, such as resistance to organic acids and low pH(acidic environments), adherence capability to human intestinal cells.
10. Production of antimicrobial substances

MECHANISM OF ACTION

Probiotics create antimicrobial agents such as lactic acid, hydrogen peroxide, which has an antiseptic effect, and compete with pathogens that lead to increase the immune response of the host. 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 environment and its intestinal lining, improves food digestion, helps in production of amino acids, proteins, and various vitamins, as a result of improved gut health, it also improves absorption of calcium, iron, and vitamin D.

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 described as following.

Direct mechanism

Probiotics have a very essential quality of its ability to adhere to various surfaces in the oral cavity. These bacteria can colonize the biofilm on the tooth surfaces and in the gingival sulcus. It prevents the formation colonies by the pathogenic microbes. Probiotics help maintain a balance within the microbial communities.

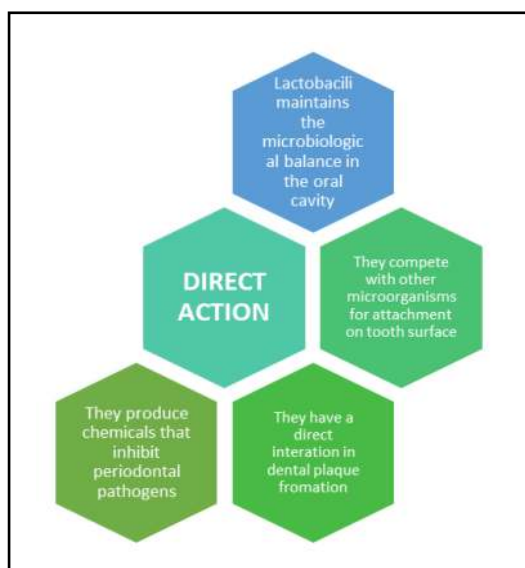


FIG. 1(a) MECHANISM OF ACTION



FIG. 1(b) MECHANISM OF ACTION

Competitive exclusion

By altering the environmental pH, probiotics restrict the adhering capabilities of various pathogenic microbes thus proving its ability to compete with those pathogenic bacterial species in colonizing various niches within the oral cavity. They compete not only for adherence but also for their growth factors and nutrients. Due to this competitive inhibition, the overall bacterial count of the pathogenic bacterial species is greatly reduced in the oral cavity.

Modulation of Host Immune Response

Probiotic bacteria have been shown to influence immunoglobulin production such as IgA, which plays a vital role in mucosal immunity as it acts as a barrier against pathogenic bacteria and other harmful foreign substances. As per Ciorba and Stenson (2009), probiotics can help improve 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).⁹

Thus, the probiotic bacteria work for the host, firstly, by competing with harmful pathogens for adhesion site and then colonizes the oral surface. After colonization of probiotic organism, they start competing with other harmful oral pathogens for nutrients and growth factors. Then, they produce certain antimicrobial compounds for inhibition of growth of pathogenic organisms, including organic acids, hydrogen peroxide, carbon peroxide, diacetyl, low molecular weight antimicrobial substances, bacteriocins, and adhesion inhibitors etc.

PROBIOTICS IN MEDICINE

Probiotics have historically been employed in gastroenterology. Evidence-based Research has suggested that, specific probiotic strains help maintain the intestinal tract's microbial balance, which helps the host to make the immune system better and also helps reducing inflammation (Ciorba, 2012). Research is being done on probiotics because of its beneficial effects on certain health conditions such as inflammatory bowel disease, allergies, irritable bowel syndrome, 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 IN DENTISTRY

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

Probiotics cause stimulation of dendritic cells which further leads to expression of T-helper cell 1 or T-helper cell 2 and modifies immunity. Probiotics have the ability to generate a pathogen's reaction without causing periodontal damage that is usually associated with the pathogen.¹⁰ The most effective inhibitor is Lactobacillus, the most potent inhibitor against *P. gingivalis*, and *Prevotella*

intermedia and *A. actinomycetemcomitans*. Both *Lactobacillus salivarius* and *Lactobacillus gasseri* exhibit strong periopathogenic bacterial inhibition. *Lactobacillus reutri* produces Bacteriocins, such as reutrin and reutricyclin, have a high affinity for host tissue, work against adherence of pathogens, and acts by inhibiting the ways of proinflammatory mediators of inflammation.

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.¹¹ 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*. Numerous studies have shown that lactobacilli have the ability to stop the growth of periodontopathogens such *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. Because they produce acid rather than H₂O₂ or bacteriocin, homofermentative lactobacilli have been shown to have an inhibitory effect on periodontal infections.¹²

Probiotics And Halitosis

The foul and unpleasant odour that comes from the mouth and is because of the volatile sulphur compounds (VSC) which results in halitosis or oral malodor. *Fusobacterium nucleatum*, *P. gingivalis*, *P. intermedia*, *T. denticola*, are some of the bacteria associated with production of VSC.¹³ Kang et al. noticed reduced amounts of the volatile sulphide constituents formed by *F. nucleatum* after consuming *W. cibaria*. *W. cibaria* was inhibiting *F. nucleatum* by producing hydrogen peroxide. *Streptococcus salivarius* competes for colonisation sites with pathogenic above mentioned species responsible for increased levels of VSC.¹⁴ Burton et al. investigated the use of *Streptococcus salivarius* K12 (SS K12) tablets and placebo and probiotics chlorhexidine mouth rinses in treating halitosis, showing a definitive substantial decrease in halitosis levels.¹⁵

PROBIOTIC-GUIDED POCKET RECOLONIZATION

Guided periodontal pocket recolonization confers to the idea of replacing the harmful bacteria in the gingival sulcus and periodontal pockets with good microorganisms. The treatment concept of guided pocket recolonization (GPR) is depending on the quality and quantity of microbes present in the subgingival pocket microbiota that result from a dedicated application of probiotics subgingivally

following SRP to prevent re-colonization of periodontal pockets by periodontopathogens.¹⁶

Probiotics are “live bacteria that, when administered in adequate amounts, confer a health benefit to the host”.¹⁷ The rationale for the use of probiotics in periodontal therapy is conversion of the dysbiotic pocket environment to a beneficial, symbiotic microbiome. Guided pocket recolonization works on the principles of competitive exclusion, host immune modulation, and the ability of probiotics to fight for the adherent sites to prevent pathogenic organisms adherence.^{18,19}

Probiotics have actively opposing effects on pathogens, affecting their ability to attach to subgingival tissue surfaces.²⁰

Teughels et al. came to conclusion in a study, that adding certain good bacteria as a supplement to scaling and root planing as an adjunct would prevent the recolonization of periodontal pockets by harmful periodontopathogens. Nackaerts et al. observed improvements in bone level and bone density when *Streptococcus sanguis*, *S. salivarius*, and *S. mitis* were administered subgingivally in dog models.

SOME OF THE COMMERCIALY AVAILABLE PROBIOTICS:

Gum PerioBalance

It is the first probiotic specifically formulated to fight periodontal diseases. It is a chewing gum containing two strains of *L. reuteri*. The two strains of *L. reuteri* are selected specifically due to their synergistic properties of fighting against bacteria causing dental caries and some which are responsible for periodontal destruction. Krause et al. assessed *L. reuteri* in individuals with recurrent gingivitis. Patients with gingivitis ranging from moderate to severe were recruited. The recommended use is to take one lozenge every day.

Acilact

A complex preparation of live lyophilized acidophilic lactobacteria is acilact. first clinically tested by Pozharitskaia et al. in 1994. In a later study, Grudianov et al. (2002) obtained a probiotic mix in the tablet forms, containing Acilact and Bifidumbacterin, and found conversion of pathogenic microflora to commensal microflora and improvement in signs of periodontal diseases.

Bifidumbacterin

Available in vials, it contains probiotic bacteria of strains of *bifidobacterium bifidum*. After scaling and root planing, oral administration of these tablets for 20 days are expected to decrease clinical and microbiological parameters of gingivitis and early stages of periodontitis

ProDentis

Contains a natural occurring lactic acid bacteria found in oral cavity, *Lactobacillus reuteri* Developed by Swedish company BioGaia. Can be available in the form of lozenges and chewing gums in mint flavor.

Other commercial products are Wakamate D and Periobotic.

CONTRAINDICATIONS AND PRECAUTIONS

- Contamination during manufacturing process must be taken care.
- In patients with central venous catheters, usage of probiotics must be advanced with caution.
- There are several case reports of *Saccharomyces cerevisiae* (*Saccharomyces boulardii*) probiotic associated with fungemia.
- Numerous human research must be performed to make sure that the newer strains of organisms are safe to be used so as to qualify as a probiotic.
- Precautions, Instructions and clear labelling is to be advised for strains such as *Saccharomyces boulardii* (*Saccharomyces cerevisiae*), which imposes certain restrictions on its usage, such as for individuals with a leaky gut or at risk of blood-borne infection.
- In persons with hypersensitivity to lactose or milk, *Lactobacillus* preparations are contraindicated.

FUTURE PERSPECTIVES

Genetic engineering on probiotic acidogenic bacteria can be implemented to further improve their caries preventing capability. Various in vitro and in vivo studies can be performed to develop specific strains of the bacteria to produce more bacterocin. Specific mutations can be performed to create specially designed genetic engineered strains of bacteria which can inhibit the growth of pathogenic microorganisms in the oral cavity. Having proper precautions are necessary to ensure these new mutant organisms do not cause any unwanted effect in the oral cavity. Dairy products modified with probiotic lactobacilli and prebiotics are also being currently developed for future use. Many studies have been done evaluating the effects of probiotics in the gastrointestinal tract as well as for treatments of oral infections, specifically periodontitis. Future advancements in molecular biology, nanotechnology, microbiological, Immunological techniques, and tissue engineering procedures can be used in bringing up an ideal or near-ideal probiotic preparation, specially curated for treatment of periodontitis.

CONCLUSION

Maintaining oral hygiene and using different probiotic strains, has resulted in reduction in bacterial translocation through periodontal pockets. The rationale behind the use of probiotics in periodontal therapy is converting the dysbiotic pocket microbiota to a symbiotic microbiome.

Probiotics when used as an adjuvant therapy, has shown improvements in the periodontal pocket depth and clinical attachment level gain. Some reports have explained that a decrease in the levels of TNF- α , IL-1 β , and IL-17 in the periodontal pockets of patients with periodontitis is observed following the treatment with the probiotic strain of *Lactobacillus reuteri*. In a meta-analysis by Harlan L et al. , there has been shown to have found a decrease in the pro inflammatory response in cases of chronic periodontitis on usage of probiotics.

In the above discussion, various aspects of probiotics and their application for the treatment of oral diseases. Probiotics being a recent treatment strategy in periodontics, more research is required in this field. In the near future, it is expected to see various probiotic preparations and their application for the treatment of various oral diseases specifically periodontal diseases.

REFERENCES

1. Nguyen T, Brody H, Radaic A, Kapila Y. Probiotics for periodontal health—Current molecular findings. *Periodontology* 2000. 2021 Oct;87(1):254-67.
2. Mangla C. “Probiotics in Periodontics: A Review”. *Journal of Advanced Medical and Dental Sciences Research* 6.7 (2018):17- 22.
3. Hardan L, Bourgi R, Cuevas-Suárez CE, Flores-Rodríguez M, Omaña-Covarrubias A, Nicastro M, Lazarescu F, Zarow M, Monteiro P, Jakubowicz N, Proc P, Lukomska-Szymanska M. The Use of Probiotics as Adjuvant Therapy of Periodontal Treatment: A Systematic Review and Meta-Analysis of Clinical Trials. *Pharmaceutics*. 2022 May 9;14(5):1017.
4. Minić I, Pejčić A., Bradić-Vasić M. Effect of the Local Probiotics in the Therapy of Periodontitis A Randomized Prospective Study. *Int. J. Dent. Hyg.* 2022;20:401–407. doi: 10.1111/idh.12509
5. Kang M.-S., Lee D.-S., Lee S.-A., Kim M.-S., Nam S.-H. Effects of Probiotic Bacterium *Weissella Cibaria* CMU on Periodontal Health and Microbiota: A Randomised, Double-Blind, Placebo-Controlled Trial. *BMC Oral Health*. 2020;20:243. doi: 10.1186/s12903-020-01231-2.
6. Costacurta M., Sicuro L., Margiotta S., Ingrasciotta I., Docimo R. Clinical Effects of *Lactobacillus reuteri*

- Probiotic in Treatment of Chronic Periodontitis. A Randomized, Controlled Trial. *Oral Implantol.* 2018;11:191–198.
7. Grudianov AI, Dmitrieva NA, Fomenko EV. Use of probiotics Bifidumbacterin and Acilact in tablets in therapy of periodontal inflammations. *Stomatologiia.* 2002 Jan 1;81(1):39-43.
 8. Guarner F, Perdigon G, Coerthier G, Salminen S, Koletzko B, Morelli L. Should yoghurt cultures be considered probiotic? *Br J Nutr.* 2005;93:783-786
 9. Behal R, Mali AM, Gilda SS, Paradkar AR. Evaluation of local drug-delivery system containing 2% whole turmeric gel used as an adjunct to scaling and root planing in chronic periodontitis: A clinical and microbiological study. *Journal of Indian society of Periodontology.* 2011 Jan 1;15(1):35-8.
 10. Bose BB. Probiotics – Promotes periodontal health? – An insight. *Int J Dent Sci Res* 2013;1:6770.
 11. Grudianov AI, Dmitrieva NA, Fomenko EV. Use of probiotics bifidumbacterin and acilact in tablets in therapy of periodontal inflammations. *Stomatologiia (Mosk)* 2002;81:39-43.
 12. Gupta G. Probiotics and periodontal health. *J Med Life* 2011;4:387-94.
 13. Manikandan GR, Janam P. Probiotics in periodontics – A short review. *IOSR J Dent Med Sci* 2015;14:103-6.
 14. Gibson GR, Roberfroid MB. Dietary modulation of the human colonic microbiota: Introducing the concept of prebiotics. *Journal of Nutrition.* 1995;125:1401-1412 Defining the idea of prebiotics. 1995;125:1401–412 in *Journal of Nutrition.*
 15. Burton JP, Chilcott CN, Moore CJ, Speiser G, Tagg JR. A preliminary study of the effect of probiotic *Streptococcus salivarius* K12 on oral malodour parameters. *J Appl Microbiol.* 2006 Apr;100(4):754-64.
 16. Teughels W, Newman MG, Coucke W, Haffajee AD, Van Der Mei HC, Haake SK, et al. Guiding periodontal pocket recolonization: a proof of concept. *J Dent Res* 2007;86:1078-82.
 17. Food and Agriculture Organization of the United Nations; World Health Organization. Probiotics in food: health and nutritional properties and guidelines for evaluation. Rome: Food and Agriculture Organization of the United Nations; 2006.
 18. Boesten RJ, de Vos WM. Interactomics in the human intestine: Lactobacilli and Bifidobacteria make a difference. *J Clin Gastroenterol* 2008;42 Suppl 3 Pt 2:S163-7.
 19. Papadimitriou K, Zoumpopoulou G, Foligné B, Alexandraki V, Kazou M, Pot B, et al. Discovering probiotic microorganisms: in vitro, in vivo, genetic and omics approaches. *Front Microbiol* 2015;6:58.
 20. Singh RK, Chang HW, Yan D, Lee KM, Ucmak D, Wong K, et al. Influence of diet on the gut microbiome and implications for human health. *J Transl Med* 2017;15:73.