Review Article

Bacteriotherapy: Harnessing the Healing Power of Bacteria in Endodontics – A Narrative Review

Dr.Abhishek Badade[1], Dr.Ajay Kabra[2], Dr.Madhuri Agrawal[3], Dr.Praveen Dhore[4], Dr.Pooja Nakate[5]

[1]Reader and PG Guide, Department of Conservative dentistry and Endodontics, MIDSR Dental College, Vishwanathpuram, Ambajogai Road, Latur
[2]PG Student, Department of Conservative dentistry and Endodontics, MIDSR Dental College, Vishwanathpuram, Ambajogai Road, Latur
[3]Reader and PG Guide, Department of Conservative dentistry and Endodontics, MIDSR Dental College, Vishwanathpuram, Ambajogai Road, Latur
[4]Reader and PG Guide, Department of Conservative dentistry and Endodontics, MIDSR Dental College, Vishwanathpuram, Ambajogai Road, Latur
[5]Lecturer, Department of Conservative dentistry and Endodontics, MIDSR Dental College, Vishwanathpuram, Ambajogai Road, Latur

Abstract:

The oral microbiome is a complex ecosystem made up of bacteria, fungi, archaea, and viruses that play a crucial role in maintaining oral health. Factors such as diet, smoking, alcohol use, lifestyle habits, and medical conditions can disrupt the balance of the oral microbiome, leading to dysbiosis. This imbalance can contribute to various oral health problems, including dental caries, pulpitis, gingivitis, periodontitis, oral candidiasis, and halitosis. Probiotics have become a potential alternative treatment to solve problem of dysbiosis. As stated by the World Health Organization (WHO).“Probiotics are live microorganisms that when administered in adequate amounts confer health benefit on the host.” These microorganisms compete with pathogenic microorganisms for nutrition and to boost their population by inhibiting the growth of harmful microorganisms. There is documented evidence supporting the use of probiotics in preventing dental caries, as an intracanal medicament, as a root canal irrigant, and in managing periodontal diseases. This poster presents a review of various scientific literature and research on the potential applications of probiotics in conservative dentistry and endodontics, focusing on their role in managing endodontic infections and promoting a healthy ecological balance and healing.

Keywords: Probiotic, Dysbiosis

Corresponding Author: Dr.Abhishek Badade, Department of Conservative dentistry and Endodontics, MIDSR Dental College, Vishwanathpuram, Ambajogai Road, Latur

INTRODUCTION:

We all at certain point of time had pleasure of enjoying our grandmother’s homemade fermented foods and drinks weather it was her pickles, fresh yoghurt, kefir, kimchi or our favourite dosas and idlis, these all fermented foods contain beneficial bacteria which breakdown starch and sugar producing antimicrobial substances which contribute to growth of good bacteria.

Our oral cavity harbors a complex ecosystem of microorganisms, encompassing a wide variety of

bacteria, fungi, archaea, and viruses. These microorganisms play a crucial role in maintaining our oral heath ultimately achieving homeostasis. The oral microbiome, with its natural defense mechanisms, serves as a protective barrier that prevents the colonization of harmful bacteria. But various factors like diet rich in sugars and carbohydrates, smoking and tobacco use, alcohol consumption, lifestyle habits like irregularly brushing, medical conditions can disrupt this balanced environment leading to dysbiosis, this imbalance leads to various oral health problems, such as dental caries, gingivitis, periodontitis, oral candidiasis, and halitosis. Our aim is to convert this dysbiosis (unbalanced environment) into eubiosis (balanced environment).1

In today's era of widespread antimicrobial resistance, there is need of finding effective alternative to traditional antibiotics among them the most promising alternatives are probiotics and prebiotics, which maintain the balance between host and microbiome is essential for maintaining health.2

Year	Author	Discoveries/Findings
1857	Louis Pasteur	Discovered Lactic acid bacteria.
1878	Lister	Isolated Lactic acid bacteria from rancid milk.
1890	Ernst Monro	Discovered Lactobacillus acidophilus.
1899	Henry Tissier	Discovered Bifidobacterium.
1907	Ellie Metchnikoff	Stated that consumption of fermented Bulgarian yoghurt can promote a good and better health these drinks were rich in Lactobacillus bulgaris. He is considered as the father of modern probiotics.
1965	D.M. Lilley and L.H. Stillwell	Coined the term probiotics.
2001	Nase et al	Stated that use of probiotics reduced risk of dental caries.
2010	Gibson and Roberfroid	Gave definition of prebiotic.

The term probiotics which is derived from Latin word "Pro" meaning "for" and Greek word "Bios" meaning "life". According to FAO/WHO (The Food Agricultural Organization/World Health Organization) probiotics are live microorganisms which when administered in adequate amounts confer a health benefit on the host. Prebiotics on the other hand are nondigestible food supplements that promote the growth and survival of intestinal microbes selectively. Prebiotics and probiotics together constitute symbiotic, also referred as conbiotics.3 Examples of prebiotics include inulin, lactulose, fucto-oligosaccharides, galacto-oligosaccharides etc.2

History: 3

General Properties:3

- Probiotics should have positive effect on the host, either by directly inhibiting pathogens or by enhancing host's immune defense.
- It must maintain high cell viability.
- It should be non-toxic and non-pathogenic.
- It should be able to interact with immune cells.
- The bacteria should influence local metabolic processes.
- Probiotics need to survive and function in challenging conditions like low pH and organic acids.
- They must be stable and remain viable during both storage and use.
- The bacteria should be capable of adhering to the intended environment.
- The microbe should not possess the ability to transfer antibiotic resistance genes.
- It should contain a high number of viable cells.
- It must be genetically stable.
- It should exhibit anti-genotoxic properties.
- It should have a short generation time.

MECHANISM OF ACTION

Probiotics produce many antimicrobial compounds like lactic acid, acetic acid, diacetyl, hydrogen peroxide, bacteriocins, and biosurfactants. Lactic acid, for instance, is able to cross the cell membrane in its undissociated form, lowering the intracellular

pH and disrupting essential cellular functions, which harms pathogens. Hydrogen peroxide, on the other hand, can damage epithelial cells and kill other bacteria, while also help in maintaining homeostasis through its accumulation. Bacteriocins inhibit microorganisms by creating pores in the cytoplasmic membrane, interfering with enzymatic reactions, or through nuclease activity.4 Lantibiotics, a class of bacteriocins, which are ribosomally synthesized and posttranslationally modified peptides (RiPPs) produced by bacteria.5 Biosurfactants work by preventing pathogen adhesion to epithelial cells, thus inhibiting their growth. Lactobacillus reuteri is capable of producing antimicrobial substances such as organic acids, ethanol, reutericyclin, and reuterin. Additionally, certain strains of Lactobacillus reuteri can produce vitamins B12 (cobalamin) and B9 (folate).4

Probiotic bacteria increase Ph of oral cavity creating alkaline environment, they compete for nutrients and adhesion sites and stimulates hosts immune system. Probiotics can inhibit streptococcus mutans by coaggregating with them hence preventing formation of dental plaque. The preferred carbohydrate source of streptococcus mutans is sucrose and its metabolism leads to acid production causing tooth decay probiotic bacteria can consume sucrose which is beneficial for streptococcus mutans inhibition, probiotic bacteria have also been shown to produce nitric oxide an antimicrobial and anti-inflammatory molecule, they show antioxidant activity potentially useful to limit periodontal disease associated with inflammation.6

PROBIOTICS ROLE IN ORAL CAVITY

Direct Interaction

- Prevention of pathogen attachment to surfaces.
- Prevention of colonization and biofilm formation.
- Synthesis of protective proteins on host cell surfaces.
- Facilitation of oral microorganism attachment to proteins and the creation of dental biofilms.

Competitive Exclusion

- Synthesis of chemical compounds.
- Competition and interference with bacterial adhesions.
- Involvement in the metabolism of substrates.

Indirect Interaction

- Impact on local immunity.
- Regulation of mucosal barrier function.
- Modulation of systemic immune response.
- Influence on non-immunological defense mechanisms

COMMONLY STUDIED PROBIOTICS

- Lactobacillus – L. acidophilusa, L.amylovorusa, L.caseia, L.cebollobiosus, L.crispatus, L. curvatus, L. delbrueckii subsp. bulgaricus, L.fermentum, L.gasseria, L.helveticus, L. johnsoniia, L.lactis, L.paracasei, L.penstosusa, L.plantaruma, L.reuteria, L.rhamnosusa, L. salivarius.
- Bifidobacterium – B. adolescentis, B. animalisa , B. bifidum, B. breve, B. infantis, B. lactis, B. longuma , B. thermophiles.
- Lactic acid bacteria – Enterococcus faecium, Lactococcus lactisa, L. lactis subsp. cremoris, Leuconstoc mesenteroides, Pediococcus acidilactici, Streptococcus salivarius subsp. thermophilus, Streptococcus thermophilusa , S. intermedius, S. diaacetylactis, Sporolactobacillus inulinus.
- Non-lactic acid bacteria –Bacillus cereus var. toyoi, Bacillus coagulans, Bacillus clausiia .

Strains Used In Oral Probiotics[7]:

- Streptococcus – S.oralis strain KJ3, S.uberis strain KJ, Streptococcus rattus strain JH145, Streptococcus salivarius strains K12 and M18.
- Lactobacillus – Lactiplantibacillus plantarum (formerly Lactobacillus plantarum) strain 299 (or DSM 6595) and strain 299v (or DSM 9843), HEAL19 (or DSM 15313), L-137, DSM 32131, NC8, and 44048, Lacticaseibacillus paracasei strains including 8,700:2 (or DSM 13434), Lpc-37, ET-22, SD1, adp-1, ET-22 and SD1, Limosilactobacillus reuteri strains, especially DSM 17938 and ATCC PTA 5289.
- Bifidobacterium – B. breve strain Bb-03 (or B-3) and B. lactis Bl-04.

- Bacillus – Bacillus coagulans strain Unique IS2.

Vehicles

- Chewing gums4
- Tablets4
- Capsules4
- Sachet4
- Lozenges4
- Milk4,8
- Cheese4,9
- Curd4,10

PROBIOTICS AND CARIES MANAGEMENT

Dental caries is caused by cariogenic bacteria that ferment carbohydrates, producing organic acids. These acids then dissolve the minerals in the tooth, causing them to diffuse out and leading to the formation of cavities. The prevalence of dental caries has risen in developing countries due to increased consumption of refined sugars, limited exposure to fluoride, and high costs of oral health care. Several studies have investigated the role of probiotics in preventing the development of dental caries. According to Nase et al., consuming milk supplemented with L. rhamnosus GG reduced the development of dental caries by 6% and lowered the concentration of S. mutans in children. Ahola et al. studied the short-term effects of consuming cheese containing L. rhamnosus GG and L. rhamnosus LC 705 on the oral cariogenic microbial flora of young adults, comparing it to the consumption of regular cheese.4,8,9

Montalto et al. compared the effects of oral probiotics, administered both in capsule and liquid form, with a placebo on S. mutans count.11,12 Nikawa et al. investigated the impact of yogurt containing L. reuteri on the oral carriage of mutans streptococci, finding that it reduced their presence. It was also reported that L. reuteri produces compounds like reuterin and reutericyclin, which are water-soluble, broad-spectrum antimicrobials effective across a wide pH range and resistant to proteolytic and lipolytic enzymes.13 Caglar et al. explored whether short-term consumption of yogurt containing bifidobacterium influenced the levels of salivary mutans streptococci and lactobacilli in young adults.14 Additionally, eight probiotic strains were tested in vitro for their ability to inhibit the growth and biofilm formation of S. mutans strains (ATCC 20532 and ATCC 25175). Lactobacillus acidophilus La-5 demonstrated significantly higher inhibition of S. mutans growth compared to the other probiotics.

Lactobacillus casei LC-11 was found to inhibit S. mutans biofilm formation similarly to other probiotics but exhibited the highest retention of probiotics in biofilms. Furthermore, mineral loss from S. mutans monospecies biofilms was significantly lower compared to mixed-species biofilms of S. mutans and L. acidophilus La-5, but it was notably higher than in biofilms consisting of S. mutans and L. casei LC-11. These findings suggest that while probiotics can inhibit S. mutans, they do not necessarily reduce the cariogenic potential of S. mutans-probiotic biofilms. In another study, the effectiveness of probiotic tablets in treating early carious lesions in adolescents was assessed using quantitative light-induced fluorescence. Thirty-six healthy adolescents (ages 12–17) were randomly divided into two parallel groups for a placebo-controlled trial. The experimental group received two probiotic tablets daily containing L. reuteri strains (DSM 17938 and ATCC PTA 5289, both at 1 × 10^8 CFU) for 3 months, while the control group received placebo tablets with no live bacteria. Significant signs of enamel demineralization (white spots) appeared on the premolars of the placebo group and on the incisors of the experimental group.

In the test group, fluorescence significantly decreased over time, but no significant differences in fluorescence values were observed between the two groups, and the lesion areas remained unchanged in both. Another study investigated the effects of daily oral supplementation with L. reuteri ATCC 55730 on the oral health of mothers in the final month of pregnancy and their children during their first year. This single-blind, placebo-controlled, multicenter trial involved 113 children. The probiotic group (n = 60) received five oil drops containing a total of 1 × 108 CFU, while the placebo group (n = 53) received

oil drops without probiotics. The results indicated that 49 children in the probiotic group and 31 children in the placebo group were caries-free. The probiotic group also exhibited a significantly lower prevalence of approximal carious lesions and fewer sites of gingivitis compared to the placebo group. Long-term daily supplementation of L. reuteri from birth through the first year was associated with reduced caries prevalence and lower gingivitis scores in primary dentition by age 9. Additionally, a study comparing probiotic-supplemented milk with regular milk in preschool children (aged 2–3 years) found that milk containing L. rhamnosus led to an 11.4% reduction in caries prevalence after 10 months of intervention. The development of cavitated lesions was also significantly lower in the probiotic group (9.7%) compared to the control group (24.3%).4

PROBIOTICS IN ENDODONTICS

The success of root canal treatment depends on three key principles: thorough cleaning of the root canal system, disinfection, and three-dimensional filling with an appropriate seal. However, despite careful execution, factors such as persistent infections within the root and surrounding tissues, foreign body reactions, and retained cysts can lead to treatment failure. Many studies indicate that the main cause of root canal treatment failure is the survival of microorganisms within the root-filled tooth, emphasizing the need for materials that can effectively reduce harmful microorganisms in the apical region. Probiotics are one such innovation that may help address this issue.

Sudha Ravi et al. evaluated the antibacterial efficacy of two commercially available probiotics, BIFILAC and VSL 3, as intracanal medicaments against Enterococcus faecalis, concluding that probiotics can be effectively used to combat this bacteria in root canals.15

Similarly, Hoda El-Sayed et al. investigated the inhibitory effect of Lactobacillus rhamnosus (B-445) as a probiotic irrigant on the growth of Enterococcus faecalis and found that L. rhamnosus has a potential inhibitory effect on its growth, suggesting it could serve as a new, natural, and safe probiotic irrigant.14

COMMERCIALLY AVAILABLE PROBIOTICS:

- ProBiora Health ™
- Blis Technologies
- Oral Complete
- Oral Health Probiotics by NatureWise®.
- Advanced Oral Probiotics
- Hyperbiotics®
- Probiotic Oral Refresh

CONCLUSION

The innovative approach of bacteriotherapy using probiotics offers a challenging yet promising complement to antimicrobial treatment in root canal systems. With the added benefits of being natural and minimally toxic, probiotics not only eliminate pathogens but also prevent their recolonization. This helps in preventing caries, reducing the likelihood of endodontic failure, and enhancing the long-term success of root canal treatments.

REFERENCES

1. Rajasekaran JJ, Krishnamurthy HK, Bosco J, Jayaraman V, Krishna K, Wang T, Bei K. Oral microbiome: a review of its impact on oral and systemic health. Microorganisms. 2024 Sep;12(9):1797.
2. Yu X, Devine DA, Vernon JJ. Manipulating the diseased oral microbiome: the power of probiotics and prebiotics. Journal of Oral Microbiology. 2024 Dec 31;16(1):2307416.
3. Mrinalini, Dr & Hegde, Mithra. (2021). Probiotics in Dental Caries.
4. Bustamante M, Oomah BD, Mosi-Roa Y, Rubilar M, Burgos-Díaz C. Probiotics as an adjunct therapy for the treatment of halitosis, dental caries and periodontitis. Probiotics and antimicrobial proteins. 2020 Jun;12:325-34.
5. Barbour A, Smith L, Oveisi M, Williams M, Huang RC, Marks C, Fine N, Sun C, Younesi F, Zargaran S, Orugunty R. Discovery of phosphorylated lantibiotics with proimmune activity that regulate the oral microbiome.

Proceedings of the National Academy of Sciences. 2023 May 30;120(22):e2219392120.
6. Saha S, Tomaro-Duchesneau C, Rodes L, Malhotra M, Tabrizian M, Prakash S. Investigation of probiotic bacteria as dental caries and periodontal disease biotherapeutics. Beneficial microbes. 2014 Dec 1;5(4):447-60.
7. Beattie RE. Probiotics for oral health: A critical evaluation of bacterial strains. Frontiers in Microbiology. 2024 Jun 24;15:1430810.
8. Näse L, Hatakka K, Savilahti E, Saxelin M, Pönkä A, Poussa T, Korpela R, Meurman JH. Effect of long–term consumption of a probiotic bacterium, Lactobacillus rhamnosus GG, in milk on dental caries and caries risk in children. Caries research. 2001 Dec 14;35(6):412-20.
9. Ahola AJ, Yli-Knuuttila H, Suomalainen T, Poussa T, Ahlström A, Meurman JH, Korpela R. Short-term consumption of probiotic-containing cheese and its effect on dental caries risk factors. Archives of oral biology. 2002 Nov 1;47(11):799-804.
10. Srivastava S, Saha S, Kumari M, Mohd S. Effect of probiotic curd on salivary pH and Streptococcus mutans: a double blind parallel randomized controlled trial. Journal of clinical and diagnostic research: JCDR. 2016 Feb;10(2):ZC13.
11. Teughels W, Van Essche M, Sliepen I, Quirynen M. Probiotics and oral healthcare. Periodontology 2000. 2008 Oct 1;48(1).
12. Montalto M, Vastola M, Marigo L, Covino M, Graziosetto R, Curigliano V, Santoro L, Cuoco L, Manna R, Gasbarrini G. Probiotic treatment increases salivary counts of lactobacilli: a double-blind, randomized, controlled study. Digestion. 2004 Jul 1;69(1):53-6.
13. Nikawa H, Makihira S, Fukushima H, Nishimura H, Ozaki Y, Ishida K, Darmawan S, Hamada T, Hara K, Matsumoto A, Takemoto T. Lactobacillus reuteri in bovine milk fermented decreases the oral carriage of mutans streptococci. International journal of food microbiology. 2004 Sep 1;95(2):219-23.
14. Çaglar E, Sandalli N, Twetman S, Kavaloglu S, Ergeneli S, Selvi S. Effect of yogurt with Bifidobacterium DN-173 010 on salivary mutans streptococci and lactobacilli in young adults. Acta Odontologica Scandinavica. 2005 Jan 1;63(6):317-20.
15. Ravi S, Ananthan HB, Reddy BN, Sankar S, Natarajan SN, Sankar S. Evaluation of Antibacterial Efficacy of Two Commercially Available Probiotics as Intracanal Medicament against Enterococcus faecalis: An In Vitro Study. The Journal of Contemporary Dental Practice. 2023 May 25;24(3):157-61.
16. El-Sayed H, Aly Y, Elgamily H, Nagy MM. A promising probiotic irrigant: an in vitro study. Open Access Macedonian Journal of Medical Sciences. 2019 Feb 2;7(3):407.