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Review Article

Probiotics - A New Horizon in Prevention of Oral Disease

Soni Rajput[1], Manjunath P Puranik[2], Uma S.R.[3]

[1]Post Graduate student, [2]Professor and Head of the Department, [3]Assistant Professor,
Dept of Public Health Dentistry, Government Dental College and Research Institute, Bangalore, Karnataka-560002

Corresponding Author: Soni Rajput

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ABSTRACT

Probiotics are live microbial feed supplement that beneficially affects the host by improving its intestinal microbial balance. Possible mechanisms of action of probiotics in human body are normalisation of the microbiota, modulation of the immune response and metabolic effects. Probiotic bacteria guard the oral health by competing with the oral pathogens for nutrients, growth factors and site of adhesion. Most commonly used oral probiotic strains are *lactobacilli* and *Bifidobacterium*. Lozenges, chewing gums, dairy foods are considered useful vehicles for probiotic bacteria. Hence, the aim of this comprehensive review is to present an update about the current status of probiotics in terms of its application in oral health.

Key words: Bifidobacterium, lactobacilli, oral health, probiotics, review.

INTRODUCTION

The role of diet in health and well-being is universally accredited. Change in food habits has resulted in deterioration of oral health in people of all ages. [1] The increasing global problems with the traditional disease management strategies have prompted for exploration of novel and better alternatives to deal with health issues. The global demand for chemical free, harmless and cost-effective solutions to these issues has increased in last few years. Probiotics have come up as one of the most promising alternate to conventional disease management.

Probiotics have been added to some foods because of their beneficial effects on human health. [1,2] They are also called friendly bacteria or good bacteria. Probiotics being safe for human consumption and resistant to bile and acidic environment survives in the intestine, colonize the human gut and show bacteriocin production to block the invasion of intestine cells by enteroinvasive bacteria. [1] The widespread oral intake of probiotics as preventive and therapeutic products for gastrointestinal health makes it of considerable interest for oral health care.

Probiotics have amazingly come up with the potential for not only preventing the attack of oral pathogens but also the ability to treat various oral diseases, assuring healthy living and increased longevity. This narrative review portrays an update about the current status of probiotics in terms of its application in oral health.

THE BEGINNING OF PROBIOTICS

There is a long history of health claims concerning living microorganisms in food, particularly lactic acid bacteria. In a Persian version of the Old Testament it is stated that "Abraham owed his longevity to the consumption of sour milk". In 76 BC the Roman historian Plinius recommended the administration of fermented milk products

for treating gastroenteritis. [3] Etymologically, the term appears to be a composite of the Latin preposition *pro* (for) and the Greek adjective *biwtikoc* (biotic), the latter deriving from the noun *bioc* (bios, 'life'). However, the term probiotic was coined by Lilley and Stillwell (1965). [1,3-8] Some definitions of probiotics is given in Table 1.

Milestones

1905- Henry Tissier, French paediatrician, observed a low number *Bifidobacteria (*first isolated probiotic bacteria*)* in the stools of the breast-fed infants with diarrhea as compared to the healthy infants. [1,8]

1907- Elie Metchnikoff, Russian scientist and Nobel laureate observed that certain rural populations in Europe (Bulgaria and the Russian steppes) who mainly depended on milk fermented by lactic acid bacteria for their sustenance had comparatively longer lives. By that time, it was known that milk fermented with lactic acid bacteria inhibits the growth of proteolytic bacteria because of its low pH which is caused by the fermentation of lactose. Based on these facts, Metchnikoff proposed that consumption of fermented milk would 'seed' the intestine with harmless lactic acid bacteria, decreases the intestinal pH thereby suppressing the growth of proteolytic bacteria. [1,3,8]

1917- Alfred Nissle, German professor isolated *Escherichia coli* strains from the faeces of an unaffected soldier. *Escherichia coli* strains were used for the treatment of acute gastrointestinal infections when the antibiotics were not yet available. [1,8]

1930s- Witnessed the first clinical trials on probiotics (strains of *E. coli*) for their effect on constipation. [1]

1984-The first probiotic species introduced into research was *Lactobacillus acidophilus* by Hull et al.

1991- Holcombh et al used *Bifidibacterium bifidum*as probiotic in their research. [3]

Table 1: Definitions of probiotics [2]

Author and Year	Definitions
Lilly &Stillwell (1965)	Substances produced by microorganisms that promote the growth of other microorganisms
Parker (1974)	Organisms and substances that contribute to intestinal microbial balance
Fuller (1989)	A live microbial feed supplement that beneficially affects the host animal by improving its intestinal microbial balance
Havenaar&Huis Int Veld (1992)	A viable monoculture or mixed-culture of microorganisms that, when applied to animal or human, beneficially affects the host by improving the properties of the indigenous microflora
Schaafsma (1996)	Living microorganisms that, upon ingestion in certain numbers, exert health benefits beyond inherent basic nutrition
Naidu et al. (1999)	A microbial dietary adjuvant that beneficially affects the host physiology by modulating mucosal and systemic immunity, as well as by improving nutritional and microbial balance in the intestinal tract
Schrezemeir& de Vrese (2001)	A preparation of, or a product containing, viable, defined microorganisms in sufficient numbers, which alter the microflora (by implantation or colonization) in a compartment of the host and as such exert beneficial health effects in this host
2001 (FAO/WHO report)	Live microorganisms that, when administered in adequate amounts, confer a health benefit to the host
2010 [International Life Science Institute (ILSI) Europe] [9]	A live microbial food ingredient that, when ingested in sufficient quantities, exerts health benefits on the consumer

CRITERIA FOR MICRO-ORGANISM TO BE USED AS PROBIOTIC

The idea that probiotics have beneficial effects is based on the knowledge that the intestinal flora can protect humans against infection and interruption of this flora can enhance susceptibility to infection. [10] To be called a probiotic, a bacterial strain must be fully characterized. The genes and species of the micro-organism must be identified according to internationally accepted methods. [8]

Suggested properties and functions of probiotics are as follows: [4,8,11]

- Non-pathogenic
- High cell viability
- Resistance to processing
- Acid resistance and bile tolerance
- Able to interact or to send signals to immune cells
- Must have capacity to influence local metabolic activity
- Ability to persist and adhesion to cancel the flushing effect

METHODS OF ADMINISTRATION

Milk and milk products are the most popular carriers of probiotics. Milk contains calcium, calcium lactate and other organic and inorganic compounds with known anti-cariogenic properties. [1] The most common probiotic strains used orally belong to the genera *lactobacillus* and *Bifidobacteria.* [1,3,4,6,11] Common probiotic vehicles are lozenges, tablets, capsule, mouthrinse, liquid, cheese, yoghurt, ice-creams. [1-3,9] However, for the purposes of prevention or treatment of oral diseases, specifically targeted applications, formulas, devices, or carriers with slow release of probiotics might be needed. [9]

Probiotics are introduced into the products in one of the four basic ways. [2,3]

- A culture concentrate added to a beverage or food (fruit juice).
- Inoculated into prebiotic fibres.
- As Inoculants into a milk dairy products.
- As concentrated and dried cells packaged as dietary supplements (powder, capsule, tablets)

MECHANISMS OF ACTION

Probiotic bacteria guard the oral health by competing with the oral pathogens for nutrients, growth factors and site of adhesion. [2] The suggested mechanisms of probiotic action on oral health are drawn entirely from gastrointestinal studies. Since the mouth represents the first part of the gastrointestinal tract, there is every reason to believe that at least some probiotic mechanisms may also play a role in that part of the system. [3] Hypothetical mechanisms of probiotic action in the oral cavity are given below. [1]

Direct actions

- Direct interaction in dental plaque
- Maintains micro ecological balance in oral cavity
- Competing & intervening with bacterial attachments
- Produces chemicals that inhibit oral pathogenic bacteria

Indirect actions

- Affects local immunity
- Affects non-immunological defence
- Modulates systemic immune function
- Regulation of mucosal immune system
- Produces antioxidants or act as antioxidants
- Prevention of plaque formation by neutralising free electrons
- Upregulation of intestinal barrier integrity & mucin production

PROBIOTICS AND ORAL DISEASES

Probiotics have been tested in prevention of dental caries, periodontal diseases, halitosis and candidiasis and other oral conditions. Table 2 summarises the most commonly strains used in dental diseases.

Table 2: The most commonly used probiotics

Condition	Lactobacillus strains	Bifidobacterium strains	Others
Dental caries and periodontitis	*L. reuteri* DSM 17938 *L. reuteri* ATCC 55730 *L. reuteri* ATCC PTA 5289 *L. paracasei* F19 *L. paracasei* GMNL-33 *L. rhamnosus* GG *L. rhamnosus hct 70* *L. rhamnosus* LB21 *L. salivarius* WB21 *L.casei*	*Bifidobacterium* DN 173010 *Bifidobacterium animalis* subspecies *lactis* BB-12 *Bifidobacterium animalis* subsp. *lactis* DN 173010	S. mutans Ingbritt S. mutans ATCC 25175 S. mutans GS-5 S. sobrinus ATCC 33478
Halitosis	*L. salivarius* WB21 *L. reuteri* DSM 17938 *L.casei* strain *Shirota*		*S.salivaris* K12 *W. Cibaria*
Oral candidiasis	*L. rhamnosus* GG		*Propionibacterium freudenreichii species Shermani JS*

Dental caries

Most studies on the effects of probiotics on caries prevention are aimed at decreasing the number of *Mutans streptococci*. Primarily probiotic *Lactobacillus* and *Bifidobacterium* strains

have been used along with few more strains. Studies have shown a tendency towards decreased number of *Mutans streptococci* in the saliva regardless of the product or strain used. However, this effect is variable. Unfortunately, in most cases, the study groups were relatively small, and the studies were fairly short. [7]

Lactobacilli have been recognized for their antimicrobial activity and ability to interfere with the adhesion of pathogens on epithelial cells and for their anti-biofilm production. It is known for its probiotic potential, acid resistance and bile salt`s tolerance. It is believed to interfere with pathogens by different mechanisms and one of their mechanisms is biosurfactant production which is a structurally diverse group of surface active molecules synthesized by microorganisms. These have several advantages on synthetic surfactants, such as low toxicity, inherent good biodegradability and ecological acceptability. Biosurfactants include unique amphipathic properties derived from their complex structures, which has a hydrophilic moiety and a hydrophobic portion. *L. rhamnosus*, has been shown to produce a substance with potential inhibitory activity against different bacterial species including cariogenic *Streptococcus* species. [11]

Suggested approaches for use of probiotics in prevention of dental caries are as follows-

- Utilizing bacteria that expressed bacteriocins or bacteriocin-like inhibitory substances **(**BLIS**)** that specifically prevented the growth of cariogenic bacteria. [6,7]
- Using recombinant DNA technology to delete the gene encoding lactate dehydrogenase in BCS3-L1 making it unable to produce lactic acid.
- This effector strain is also designed to produce elevated amounts of a novel peptide antibiotic called mutacin 1140 that gives it a strong selective advantage over most other strains of *S. mutans*. [12]
- Utilizing a recombinant strain of *S. mutans* expressing urease, which was shown to reduce the cariogenicity of plaque in an animal model.
- Similarly, genetically modified probiotics with enhanced properties can be developed (‘designer probiotics’) example a recombinant strain of *Lactobacillus.* [6,7]
- Genetically engineered “effector strain” of *S. mutans* that will replace the cariogenic or “wild strain” to prevent or arrest caries and to promote optimal remineralization of tooth surfaces that have been demineralized but that have not become cavitated have been tested example *S. mutans* strain BCS3-L1. [12]

Periodontal disease

Periodontal diseases are among the most prevalent diseases worldwide. They are the major causes of tooth loss in adults. [13] It is generally accepted that in a susceptible host, the presence of pathogenic bacteria and the absence of beneficial bacteria play a role in the development of periodontal disease. However, there has been increased interest in the third etiologic factor through restoring the reduced number of beneficial bacteria by the usage of probiotics. [14]

Probiotics have proved to inhibit plaque formation by lowering the salivary pH and producing antioxidants which utilize the free electrons required for mineralization of plaque. Plaque associated bacteria is unable to form the plaque in the above conditions. Therefore, probiotics indirectly helps to prevent periodontal diseases. [1] Probiotics used in field of periodontitis *are L. reuteri ATC 55730, L. reuteri ATC 5289, L. brevis, L. salivarius, L. casei.* [15] Probiotic strains included in periodontal dressings at optimal concentration of 10^8 CFU/mL were shown to diminish the number of most frequently isolated periodontal pathogens: *Bacteroides sp., Actinomyces sp.* and *S. intermedius*. [3]

Halitosis

Halitosis or Bad Breath is the condition when the breath has unpleasant odor. Halitosis is not only a dental problem but also an embarrassing social problem more than it is an oral health problem. [1] Approximately 80% to 90% of the causes of bad breath originate in the mouth. [12] The rationale for using probiotics is to avoid the re-establishment of volatile sulphur producing bacteria. Probiotics strains included are- *S. salivarius K12***,** *L. salivarius, L. reuteri* DSM 17938. [14]

Candidiasis

Candida albicans is among the most common infectious agents in the oral cavity. The incidence of yeast infections is higher at older age and under the conditions of impaired immunity. *L. rhamnosus* GG, *Propionibacterium freudenreichii, ssp. shermanii* JS has shown to decrease the prevalence of C. albicans in the eldery. [1,2, 14]

Other oral conditions

Mucositis is a painful condition that may lead to dose reduction, treatment delays, or even treatment discontinuation. Intake of probiotic lozenges (*L. Brevis CD2)* reduced the incidence of grade III and IV anticancer therapy-induced oral mucositis and was associated with a lower overall rate of mucositis and a higher rate of anticancer treatment completion. [4,14] Beneficial effect of *L. brevis* CD2 use in an adult hemophilic patient suffering from painful apthous oral ulcerations has been reported. [13] Consumption of 2 kg/day of Turkish yogurt containing *Streptococcus thermophiles* and *Lactobacillus bulgaricus* eliminated pathogenic bacteria in voice prosthetic biofilms. [3]

SAFETY CONSIDERATIONS

The issue of safety is of special concern during the past few years due to the increased probiotic supplementation of different food products. Any viable microorganism is capable of causing bacteremia, especially in patients with severe underlying diseases or in immunocompromised state. In general gas & bloating is one of the side effects of eating probiotic supplement. [8,13]

Probiotic products taken orally as a dietary supplement are manufactured and regulated as foods, not drugs. [13] In the US, probiotics are classified as dietary supplements by the Food and Drug Administration (FDA), thus having less stringent requirements in their demonstration of safety, efficacy, and purity. Specific strains of probiotics fall into the FDA status of generally regarded as safe, while others do not. Generally regarded as safe status (GRAS) only evaluates safety; clinical efficacy is not assessed during this process.

FUTURE PROSPECTS

Probiotic bacteria have been characterized for different oral health purposes, including caries, periodontal diseases, and halitosis. The selection of the best probiotic for oral health and investigation the effect of other probiotics' metabolites on virulence genes and other traits of *S. mutans* are also issues that calls for further studies. In field of oral immunology, probiotics are being used as passive local immunization vehicles against dental caries. [3,11] Understanding the mechanisms whereby probiotic species modulate oral immunity is important, and the role of probiotic therapy in the treatment of oral manifestations of other diseases such as cutaneous diseases should also be investigated. There are no data as to whether probiotics exert any effect on oral manifestations of autoimmune diseases. In this regard it might be interesting to conduct studies on patients with lichen planus, pemphigus vulgaris, cicatricial pemphigoid or aphthous stomatitis. [9] It could be hypothesized that extending research on oral pathology, such as yeast infections, with respect to probiotics, and analysing the molecular mechanisms of probiotic activity, might further broaden the field of their potential applications. [2]

Efforts are needed to advance the scientific knowledge of probiotics and determine their mechanisms of action, as

well as describe when and why they fail in certain situations. Furthermore, the dosage of probiotic administration in each indication should be defined. Finally, safety issues are very important with any kind of bacteriotherapy. [11] Recommendations for future research in probiotics are shown in Table 3.

Table 3: Recommendations for future research in probiotics. [12]

Issue	Comments / Recommendations
Complex microbiology of the oral cavity	Interactions between microorganisms of the mouth are poorly understood /Systematic screening for potential resident probiotic strains.
Different microbial attachment sites	Probably different probiotics are needed for therapy in dental and oral mucosal diseases/Investigating microbial (probiotic) attachment separately on the teeth, and on keratinized and non-keratinized epithelium.
Saliva	Data from gastrointestinal studies are not directly applicable in saliva parameters /Salivary defense mechanisms, both specific and nonspecific, should be investigated in relation to potential probiotics.
Safety	Strains that readily ferment dietary carbohydrates and decrease pH in the mouth are not suitable probiotics for oral health purposes/General safety aspects such as those related to potential invasiveness and antibiotic resistance genes must be screened
Means of administration and dosage	Probiotic therapy in order to be effective needs to be continuously administered /Slow-release approach should be investigated. Optimal dosages of probiotics in oral health indications need to be assessed.
Trials	Randomized controlled trials are needed with patients materials based on proper power calculations/ Probiotic intervention should be tested in the clinical setting using potential strains for specific oral health purposes
Genetically modified microorganisms	Extensive studies on the mechanisms of probiotic action are needed/Whether or not potentially probiotic microbial strains can or should be genetically modified in order to strengthen their beneficial potential or characteristics needs to be investigated.

CONCLUSION

Probiotics represent a new area of research in oral health. As a dental profession, we are slowly moving away from the purely surgical approach of treating dental caries to the use of probiotic strategies that may provide the end of new cavities in treated populations. Probiotics are innovative and revolutionary method in the treatment of dental diseases. Systematic screening and discovery of 'latent' or 'resident' probiotic microorganisms is needed to identify the best candidate probiotics for oral and dental diseases. Although Probiotics are still in "infancy" in terms of health benefits, but surely have opened door for a new paradigm of treating disease on a nano – molecular mode. Hence, Today's new technology era would be the right time to change the way bacteria are treated.

REFERENCES

1. Jain P, Sharma P. Probiotics and their efficacy in improving oral health: a review. J App Pharm Sci. 2012; 2 (11):151-63.
2. Reddy RS, Swapna LA, Ramesh T *et al*. Bacteria in oral health – Probiotics and Prebiotics A Review**.** Int J Bio Med Res. 2011; 2(4):1226-33.
3. Reddy JJ, Sampathkumar N, Aradhya S. Probiotics in dentistry: review of the current status. Rev Clín Pesq Odontol. 2010; 6(3):261-7.
4. Suchetha A, Vinayashree MP, Apoorva SM, Sapna N, Koduru S, Darshan BM. Probiotics-a legacy of good health. J Res Med Den Sci. 2015; 3:1-6.
5. Vijaya KG, Lee EM, Mark AM. Probiotics: mechanisms of action and clinical applications. J Prob Health. 2013; 1:101.
6. Bhardwaj A, Bhardwaj SV. Role of probiotics in dental caries and periodontal disease. Arch Clin Exp Surg. 2012; 1(1):45-49.
7. Bhushan J, Chachra S. Probiotics-their role in prevention of dental caries. J Oral Health Comm Dent. 2010; 4(3):78-82.
8. Zahir S, Bose S, Roychaudhury U. Probiotics and its role in dental caries. Sci Cult. 2011; 77 (11–12): 507-10.
9. Tahmourespour A. Probiotics and the reduction of dental caries risk, contemporary approach to dental caries, Dr. Ming-Yu Li (Ed.). InTech. 2012, pp 271-286. [Internet] [Cited 11 August 2016] Available from: http://probiotics-and-the-reductin-of-dental-caries-risk..
10. Joint FAO/WHO Working Group on Drafting Guidelines for the Evaluation of Probiotics in Food, London, Ontario,

Canada, April 30 and May 1, 2002. [Internet] [Cited 11 August 2016] Available at: www.who.int/foodsafety/publications/fs_management/probiotics2/en/index.html
11. Sanders ME. Probiotics: definition, sources, selection, and uses. Clin. Infect. Dis. 2008;46Suppl 2:S58-61
12. Meurman JH, Stamatova I. Probiotics: contributions to oral health. Oral Dis. 2007; 13(5):443-51.
13. Anderson MH, Shi W. A probiotic approach to caries management. Pediatr Dent. 2006; 28(2):151-3.
14. Anilkumar K, Monisha AL. Role of friendly bacteria in oral health- a short review. Oral Health Prev Dent. 2012; 10(1):3-8.
15. Laleman I, Teughels W. Probiotics in the dental practice: a review. Quintessence Int. 2015; 46(3):255-64.

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