

# REVIEW ARTICLE

## PROBIOTICS: BEING HEALTHY IN A NATURAL WAY

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### ABSTRACT:

The development of resistance to a range of antibiotics by some important pathogens has raised the possibility of a return of humans to the pre-biotic dark ages. The time has come to shift the paradigm of treatment from specific bacteria elimination to altering the bacterial ecology by probiotics. Probiotics are dietary supplements containing potentially beneficial bacteria and has been found beneficial to the host health. Probiotic is “a live microbial food ingredient that, when consumed in ample volume, exerts health-benefits on the consumer. They help in stimulating health promoting flora and also suppressing pathogens which cause and spread diseases. In the medical field, probiotics are used mainly for the treatment of gastrointestinal diseases. Recently, probiotics are being used as a treatment for various oral diseases including dental caries, periodontitis, oral candidiasis, halitosis and many more. The aim of this review is to examine the mechanisms of probiotic bacteria and the use of these probiotics in the oral cavity.

**Key words:** Probiotics, oral cavity, systemic health.

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**I**NTRODUCTION  
 The human gut contains 10 times more bacteria than cells elsewhere in the human body. The enormous biomass consists of over 400 known bacterial species that generate intense metabolic activity and are of key importance for human health. This ecosystem gets disrupted when exposed to toxics in the form of polluted water and food as well as injudicious use of antibiotics. Antibiotic resistance, with the emergence of multiple resistance strains, is an increasingly important global problem. This causes destruction of beneficial bacteria, leaving resistant ones, pathogenic. Of late, it has been realized by health care professionals and prompted them to seek alternative therapeutic options. One such alternative is the use of beneficial bacteria, the probiotics, which stimulate health-promoting indigenous flora reverting back the change.<sup>1,2,3</sup> They repopulate the beneficial bacteria, which can help kill pathogenic bacteria and fight against infection. Probiotics administered orally, may benefit oral health

by preventing the growth of harmful microbiota or by modulating mucosal immunity in the oral cavity.<sup>1</sup>

### Definition

According to the currently adopted definition, by **WHO/Food and Agriculture Organization (2002)**, probiotics are: “Live micro-organisms, which when administered in adequate amounts confer a health benefit on the host.”<sup>1,3,5</sup>

**International Life Science Institute Europe** suggested a definition according to which a probiotic is “a live microbial food ingredient that, when consumed in ample volume, exerts health-benefits on the consumer.”<sup>1,3,5-15</sup>

### HISTORY

The idea of probiotics dates back to the first decade of 1900s, when the Ukrainian bacteriologist and Nobel Laureate Metchinkof (1908) studying the flora of the human intestine developed a theory that senility in humans is caused by poisoning of the body by the products of some of these bacteria. To prevent the multiplication of these organisms he proposed a diet

containing milk fermented by lactobacilli, which produce large amounts of lactic acid that could increase the life span of humans. The concept of probiotics was thus born and a new field of bacteriology was opened.<sup>1,15,16</sup> Lilley and Stillwell (1965) introduced the term ‘probiotics’, the antonym of term ‘antibiotics’. Mann and Sporing in 1974 discovered that the fermented yogurt reduced the blood serum cholesterol. The first probiotic species to be introduced in research was *Lactobacillus acidophilus* by Hull et al in 1984, followed by *Bifido bacterium bifidum* by Holcomb et al in 1991.<sup>2,5,8,12,13,15-21</sup>

**MECHANISM OF ACTION**

Probiotics are broadly categorized in two genus *Lactobacillus* and *Bifidobacterium*. While other microorganisms also classified into this group includes yeasts and moulds e.g., *Saccharomyces cerevisiae*, *Aspergillus niger*, *Aspergillus oryzae*, *Schizosaccharomyces boulardii*.<sup>22</sup>

Numerous mechanisms regarding their mode of action have been proposed<sup>23-27</sup> including the following:

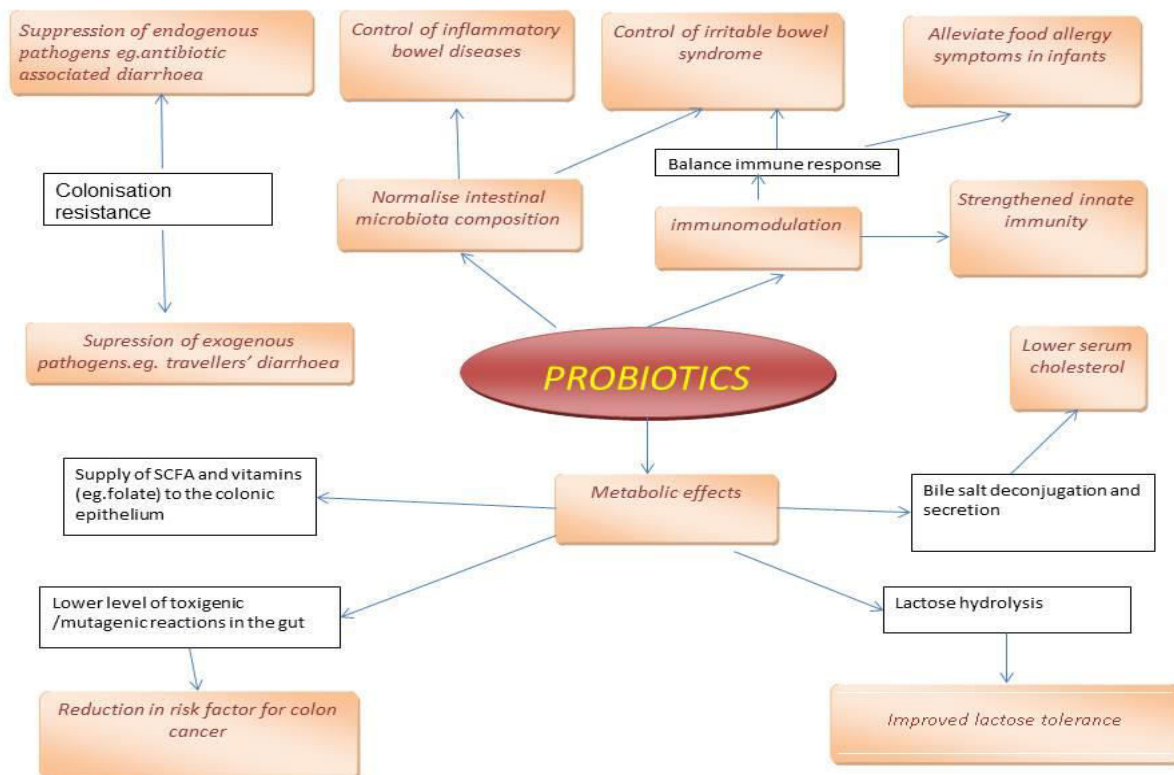
- Prevention of adhesion of pathogen to host tissues.
- Stimulation and modulation of the mucosal immune system by reducing the production of pro-inflammatory cytokines through action on NFκB

pathways, increasing the production of anti-inflammatory cytokines such as IL-10, and also by enhancing IGA defenses and influencing dendritic cell maturation.

- Improvement of intestinal barrier integrity and upregulation of mucin production.
- Killing or inhibiting the growth of pathogens through the production of bacteriocins or other products such as acids or peroxides, which are antagonistic toward pathogenic bacteria [Figure 1]

**CHARACTERISTIC OF A GOOD PROBIOTIC:**

1. Should be capable of exerting a beneficial effect on host animal like increased growth or resistance to disease.
2. Should have high cell viability.
3. Should be capable of surviving and metabolizing in the gut environment like resistance to low pH and organic acids.
4. Should be stable and capable of remaining viable for periods under storage and field conditions.
5. Able to interact or to send signals to immune cells.
6. Should be of human origin.
7. Should be non-pathogenic and non-toxic.
8. Should reinstate and replace intestinal microflora.<sup>1,2,4,8,10,15,17-20</sup>



**Figure1:** Proposed health benefits stemming from probiotic consumption.<sup>28</sup>

### **Different general forms of commercially available probiotics**

1. **Yakult**- probiotic dairy product made by fermenting mixture of skimmed milk with a special strain of bacterium *Lactobacillus casei* Shirota.
2. **Probiotic juice**- deliver a powerful daily dose of live and active probiotic cultures of *Lactobacillus plantarum* 299v, a well studied probiotic strain formulated for daily digestive health
3. **Choconat**- includes nature's "good bacteria"<sup>6</sup>
4. The latest and recent addition to the list of probiotics in India is made up of genetically modified *Bacillus mesentericus*, which act as an alternate to B-complex capsules. Only sporulating *Lactobacilli* are used with some antibiotic preparations.<sup>17</sup>

### **PROBIOTICS – ROLE IN SYSTEMIC HEALTH**

Traditionally, probiotics have been associated with gut health, and most clinical interest has focused on the prevention or treatment of gastrointestinal infections and diseases; however, during the last decade, an increasing number of established and proposed health effects of probiotic bacteria have been reported, including enhancement of the adaptive immune response, treatment or prevention of urogenital and respiratory tract infections, and prevention or alleviation of allergies and atopic diseases in infants.<sup>29,30</sup> Several investigators have also suggested probiotics for oral health purposes. Interestingly, probiotics are also suggested to increase the lifetime of voice prosthesis by inhibiting the adhesion of unwanted microbes.<sup>31-33</sup>

### **PROBIOTICS – ROLE IN ORAL HEALTH**

Probiotics are useful in promoting oral health and in prevention of dental caries and periodontal diseases. Probiotic bacteria is recently being used in dentistry as oral replacement therapy where probiotics adhere to dental tissues as a part of the biofilm or plaque and compete with the cariogenic and periodontal pathogens for colonization and hence prevent caries, gingivitis and improve oral health. A great advantage is the ease of administration in the oral cavity. Live cultures can be used in patient's mouth as there is no danger from stomach acidity as in the GIT. One of the most important benefits of probiotics in the oral cavity is the reduction of inflammation. Probiotics can help fight harmful bacteria in the oral cavity and helps in maintenance of healthy teeth and gums. Since probiotics is an all natural treatment it should not have any side effects.<sup>16</sup>

### **PROBIOTICS AND DENTAL CARIES**

Dental caries is a multifactorial disease of bacterial origin that is characterized by acid demineralization of

the tooth enamel. To have a beneficial effect in limiting or preventing dental caries, a probiotic must be able to adhere to dental surfaces and integrate into the bacterial communities making up the dental biofilm. It must also compete with and antagonize the cariogenic bacteria and thus prevent their proliferation. The advantage of incorporating probiotics into dairy products lies in their capacity to neutralize acidic conditions. For example, it has already been reported that cheese prevents demineralization of the enamel and promotes its remineralisation.<sup>9,15,34,35</sup> Several studies suggest that consumption of products containing probiotic *Lactobacilli* or *Bifidobacteria* could reduce the number of mutans streptococci in saliva.<sup>36-44</sup>

### **PROBIOTICS AND PERIODONTAL DISEASE**

The main pathogenic agents associated with periodontitis are *Porphyromonas gingivalis*, *Treponema denticola*, *Tannerella forsythia* and *Aggregatibacter actinomycetemcomitans*. These bacteria have a variety of virulent characteristics allowing them to colonize the sub-gingival sites, escape the host's defense system and cause tissue damage. The persistence of host's immune response also constitutes a determining factor in progression of the disease. Studies have proven that prevalence of *Lactobacilli*, particularly *Lactobacilli gasseri* and *Lactobacilli fermentum*, in the oral cavity was greater among the patients with chronic periodontitis. Various studies have reported the capacity of *Lactobacilli* to inhibit the growth of periodonto-pathogens, including *P.gingivalis*, *Prevotella intermedia* and *A.actinomycetemcomitans*. Together these observations suggest that *Lactobacilli* residing in the oral cavity could play a role in the oral ecological balance.<sup>9,13</sup> Recently Van Essche et al.<sup>45</sup> have reported that *Bdellovibrio bacteriovorus*, attack, prey on and kill *Aggregatibacter actinomycetemcomitans*, thus suggesting a potential scope for the role of *Bdellovibrio bacteriovorus* in the prevention and treatment of periodontitis. Hojo et al.<sup>46</sup> suggested that *Bifidobacterium* inhibit some black pigmented anaerobes by competing for an essential growth factor vitamin K.

### **PROBIOTICS AND HALITOSIS**

Halitosis has many causes including consumption of particular foods, metabolic disorders, respiratory tract infections but in most cases it is associated with an imbalance of the commensal microflora of the oral cavity. Most specifically, halitosis results from the action of anaerobic bacteria that degrade salivary and food proteins to generate amino acids which are in turn transformed into volatile sulphur compounds, including hydrogen sulphide and methane thiol. *Streptococcus salivarius*, was detected most frequently among people without halitosis and is therefore considered a

commensal probiotic of the oral cavity.<sup>9,34</sup> *S. salivarius* is known to produce bacteriocins, which could contribute to reducing the number of bacteria that produce volatile sulphur compounds. The use of gum or lozenges containing *S. salivarius* K12 (BLIS technologies Ltd., Dunedin, New Zealand) reduced levels of volatile sulphur compounds among patients diagnosed with halitosis.<sup>9</sup>

Only a few clinical studies have found different probiotic strains or products to be efficacious. The studied strains include *E. coli* Nisle 1917, *S. salivarius* K12, three *Weissella confusa* isolates, and a lactic acid forming bacterial mixture, not specified by the authors of that work.<sup>47-50</sup>

### PROBIOTICS & ORTHODONTIC TREATMENT

Fixed orthodontic appliances are considered to jeopardize dental health due to accumulation of microorganisms that may cause enamel demineralization, clinically visible as white spot lesions. Furthermore, the complex design of orthodontic bands and brackets may create an ecological environment that facilitates the establishment and growth of cariogenic mutans streptococci strains. White spot lesion formation can be seen as an imbalance between mineral loss and mineral gain and recent systematic reviews have examined methods to prevent this side effect of orthodontic treatment. Studies are needed to clarify if use of probiotics can be effective as an alternative strategy for prevention of demineralization and white spots.<sup>1</sup>

### PROBIOTICS AND CANDIDIASIS

The main species of *Candida* in the oral cavity are *C. albicans*, *C. glabrata*, *C. tropicalis*, *C. pseudotropicalis*, *C. guilliermondii*, *C. krusei*, *C. lusitanae*, *C. parapsilosis*, *C. stellatoidea* and *C. dubliniensis*, and that *C. albicans* is the most aggressive. In an attempt to increase preventive measures and treatment of candidiasis, bacterial microbiota plays an important probiotic role. However, mechanism of action of probiotics against candidiasis is still not well known.<sup>51</sup> Thus, the literary findings show positive and negative results of the effect of probiotics on *Candida*. As an example, a study analyzed the coexistence of *Lactobacillus acidophilus* and *Candida* in a healthy mouth and the results revealed that there is a balance between the two species, namely *Candida* nutritional stimulants serve as the *Lactobacillus* and these control the excessive growth of *C. albicans* by producing lactic acid.<sup>52</sup>

*Candida* species constitute part of the commensal oral flora in about 50% of healthy subjects,<sup>54</sup> but are able to cause a clinically apparent lesion if the immune defenses are breached either on the local or systemic level. One study has shown that subjects who consumed

cheese containing the probiotic *L. rhamnosus* exhibited reduction in the prevalence of oral candida which subsequently may confer protective effect against oral candidiasis. However, others investigated the effect of various lactobacilli and could not find any effect on oral *Candida*. This may be partly explained by the finding of the *ex vivo* experiment which demonstrated a profound but variable ability of commercially available strain of lactobacilli probiotics to inhibit the growth of *C. albicans* possibly due to low pH milieu produced by the lactobacilli.<sup>54</sup>

### PROBIOTICS AND VOICE PROSTHESIS

There is no research regarding relationship between dental restorative materials and probiotics. However in larynx, the second barrier after oropharynx, probiotics strongly reduce the occurrence of pathogenic bacteria in voice prosthetic biofilms. There is anecdotal evidence among patients in The Netherlands that the consumption of buttermilk, which contains *Lactococcus cremoris*, *Lactococcus lactis* spp. that can produce antimycotics and other substances, prolongs the lifetime of indwelling voice prostheses. Recent research has suggested that consumption of 2kg/day of Turkish yogurt effectively eliminates biofilm formation on indwelling voice prosthesis, possibly related to the presence of *Streptococcus thermophilus* and *Lactobacillus bulgaricus* in Turkish yogurt. Lactobacilli have long been known for their capacity to interfere with the adhesion of uropathogens to epithelial cells and catheter materials, while *S. thermophilus* can effectively compete with yeasts in their adhesion to substratum surfaces, like silicone rubber. Further research should be carried out to determine if it is possible to treat other infections of the upper digestive tract, like esophagitis, with probiotic containing dairy products rather than with antibiotics.<sup>11,54</sup>

Evidence suggests that probiotics can also reduce the risk of hypo-salivation and feeling of dry mouth.<sup>20</sup>

### FUTURE PROSPECTS

Probiotics can be used as passive local immunization against dental caries. High titres of antibodies can also be directed against human cariogenic bacteria produced in bovine colostrums over the vehicle of fermented milk. Early mucosal colonization with *E. coli* bacteria in newborns stimulates mucosal immune system to produce specific antibodies as well nonspecific secretory immunoglobulins. Research is directed at the reduction of severity and occurrence of mucosal lesions specifically aphthous ulcers.<sup>3</sup>

### CONCLUSION

With the fast evolving technology and integration of biophysics with molecular biology, designer probiotics poses huge opportunity to treat diseases in natural and

non-invasive way. The interest in oral probiotics has been growing during the last decades. Probiotic bacteria seem to affect both oral microbiota and immune responses. In India, with the growing interest in self care and optimum health at all ages' recognition of a link between diet and health has never been stronger. Since mouth is the gateway of the body and the oral cavity reflects the systemic health of the individual, it is the need of the hour to find probiotics which maintain and improve the oral health conditions. Systematic studies and randomized control trials are needed to find out the best probiotic/ prebiotic strains and means of their administration in different oral health conditions.

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