

## REVIEW ARTICLE

**Probiotics – A Review And Its Role In Dentistry**Prabhavati Benakanal<sup>1</sup>, Ramnarayan BK<sup>2</sup>, Chaya M David<sup>3</sup>**ABSTRACT**

Probiotics are live microorganisms. They improve intestinal microbial balance upon administration to host in adequate amounts and thereby confer a health benefit to the host. They not only stimulate health promoting flora but also suppress pathogenic microorganism which are capable to cause and spread diseases. Hippocrates age –old quote ‘Let food be thy medicine and medicine be thy food’ holds good in incorporating probiotics in the diet to conquer health beneficial effect from them. Probiotics and prebiotics are categorized under functional foods and implication of their role in human health and disease has become the most promising area in the field of medicine. The pioneer work on probiotics has mainly focused on gastrointestinal tract, and concluded that they strengthen the immune system to combat allergies, stress, exposure to toxic substances and other diseases.

The use of probiotic plays an important aspect in dentistry too ever since the oral infections occupied the prime space among the other infections affecting the humans. The use of probiotics has reemerged as a means to restore and boost the beneficial microbes in our bodies.

Much more scientific developments are needed to have a better understanding of these tiny forms of lives in order to broaden their potential applications. This article emphasizes on the concepts of probiotics and its implications in dentistry.

**Keywords:** Probiotics, prebiotics, dairy products, oral health, lactobacillus

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**INTRODUCTION**

Live microorganisms were one of the components of diet in past century. They have been used in the diet by incorporating them in food and alcoholic fermentations. Microbial cultures in the form of cultured dairy products have been used for thousands of years, which yielded health benefit to the host by preventing and curing a variety of diseases.<sup>1</sup>

The primary function of the human gastrointestinal tract is to aid in digestion and absorption of nutrients and excretion of waste end products. The human gut contains 10 times more bacteria than cells elsewhere in human body. This vast biomass consists of over 400 known bacterial species. They generate intense metabolic activity and are of key importance for human health. The injudicious use of antibiotics, exposure to toxics in the form of polluted water and food has led to the disruption of the ecosystem. This causes destruction of beneficial bacteria leaving resistant ones, pathogenic. Antibiotic resistance, with the emergence of multiple resistant strains, is an increasingly important global problem. This is the time to shift the pattern of treatment from specific bacteria elimination to altering bacterial ecology by probiotics. In this regard probiotics play as innovative tool which are nothing but the dietary supplements containing potentially beneficial bacteria or yeasts. They are beneficial as they stimulate health promoting flora and also suppress pathogens which cause and spread diseases.<sup>2</sup>

The oral infections occupied the prime space among the other infections affecting the humans hence the use of probiotic plays an important aspect in dentistry too. Probiotics strengthen the immune system by fighting against allergies, stress, exposure to toxic substances and other

diseases. There are reports of their beneficial use in HIV infection and cancers, mostly the colorectal carcinomas but their use in premalignant and malignant oral disorders is yet to be probed.<sup>3</sup>

## HISTORICAL PERSPECTIVES

The use of living microorganisms in the diet has a long history. Fermented milk was the first recorded probiotic for human consumption. The role of fermented milk in human diet was known in Vedic times. The Ukrainian bacteriologist and Nobel Laureate Metchinkoff over a century ago suggested that the long healthy life of Bulgarian peasants was due to consumption of fermented milk products. Accelerated aging is because of auto-intoxication (chronic toxemia)<sup>1</sup>, which is due to the toxins produced by gut microflora. The experiments were conducted on Bulgarian peasants to know the cause on longevity. The results showed that longevity is due to consumption of large quantities of sour milk by which the pathological reaction (auto-intoxication) might be removed and life expectancy could be enhanced by implanting lactic acid bacteria from Bulgarian yogurt. He believed that when consumed, the fermenting bacillus (*Lactobacillus*) positively influenced the microflora of the gut, decreasing "putrefaction" (decomposition) and toxic microbial activities there.<sup>1</sup>

In 1965 Lilley and Stillwell introduced the term probiotics. Later in 1991, Holcomb identified *Bifidobacterium bifidum*. In 1994, the WHO deemed probiotics to be the next most important in immune defense system when commonly prescribed antibiotics are rendered useless by antibiotic resistance. The use of probiotics in antibiotic resistance is termed as "Microbial interference therapy".<sup>2</sup> These incidences paved way for a new concept of probiotics in medicine and dentistry. The first clinical trials in the 1930s focused on the effect of probiotics on constipation, and research has steadily increased since then.<sup>2</sup>

Gibson & Roberfroid described positive health effects for "prebiotics" which were defined as "non-digestible food ingredients that beneficially affect the host by selectively stimulating the growth, activity or both, of one or a limited number of bacterial species already resident in the

colon". The expression "synbiotic" designates the synergistic combination of pre and probiotics, a concept which looks most promising but still remains in its infancy.<sup>4</sup>

## Definitions of probiotics

Probiotic is derived from Latin word "pro"-for and Greek word "biotic"- life. The various definitions of probiotics are as follows.

1. Substances secreted by one microorganism that stimulate another microorganism. Lilley and Stillwell -1965.<sup>5</sup>
2. According to World Health Organization and the Food and Agriculture Organization of the United Nations "Probiotics are live microorganisms which when administered in adequate amounts, confer a health benefit on the host."<sup>6</sup>
3. The US Food and Drug Administration (FDA) uses other terms for live microbes for regulatory purposes; Live microbes used in animal feeds are called "Direct-fed Microbials" and when intended for use as human drugs, they are classified as "Live Biotherapeutics".<sup>7</sup>

## Subcategories of the general term Probiotic include<sup>7</sup>

1. Probiotic Drugs – intended to cure, treat or prevent disease.
2. Probiotic Foods-which include foods, food ingredients and dietary supplements.
3. Direct Fed Microbials- Probiotics for animal use.
4. Designer Probiotics –genetically modified probiotics.

## Selection and ideal requisites of a probiotic

Fuller in 1989 listed the following as features of a good probiotic.<sup>8</sup>

1. It should be a strain, which is capable of exerting a beneficial effect on the host animal, e.g. increased growth or resistance to disease.

2. It should be non-pathogenic and non-toxic.
3. It should be present as viable cells, preferably in large numbers.
4. It should be capable of surviving and metabolizing in the gut environment e.g. resistance to low pH, organic acids acid and bile.
5. It should be stable under storage and field conditions.
6. Microorganism has to be microbiologically characterized and subjected to randomized clinical trials.
7. Principally it has to be of human origin, scientifically demonstrating beneficial physiological effects and proving being safe for human use.
8. It has to be effectively able to adhere to the target tissue.

### Constituents of probiotics

Probiotics can be yeast, bacteria or moulds. However most commonly, bacterial species are predominant. Some of these species are

**a) Lactic acid producing bacteria (LAB) :**

*Lactobacillus acidophilus, sporogenes, plantarum rhamnosum, delbrueck, reuteri, fermentum, lactus, cellobiosus, brevis*

*Bifidobacterium-bifidum, infantis, longum, thermophilum, animalis*

*Streptococcus-lactis, cremoris, alivarius, intermedium*

**b) Non lactic acid producing bacterial species;**

*Bacillus, Propionibacterium, Leuconostoc Pedococcus, Enterococcus, E.Faecium*

**c) Non pathogenic yeasts and moulds;**

*A.cerevisiae, A.niger, A. oryzae, C. Kluyveri, Saccharomyces boulardii.*

**d) Non spore forming and non flagellated rod or coccobacilli**

The majority of probiotics are bacteria with the species of *Lactobacillus* and *Bifidobacterium* being the most common type of bacteria used.<sup>2</sup>

*L. rhamnosus GG, ATCC 53103 (LGG)* is the most widely studied probiotic bacterium. Probiotics for oral health purpose can be administered in the body by various means like lozenges, tablets and capsules, cheese, yoghurt, liquid, mouthrinse.<sup>9</sup>

### PROBIOTICS IN ORAL HEALTH

Much of the research work in probiotics has focused on the gastrointestinal tract and concluded that probiotics are effective in the treatment of digestive related diseases. The use of probiotics plays an important aspect in dentistry too. These can be introduced into the oral cavity at much higher concentration to gain health beneficial effect. The drawback related to use in oral cavity is many of the beneficial bacteria are destroyed by the hydrochloric acid in the stomach. It is avoided by freezing the bacteria and put them in a pill. Most of the probiotics used are in dairy forms and contain calcium that reduces demineralization of teeth.

#### Some of the hypothetical mechanism of probiotics action in the oral cavity is by

- Direct interaction in dental plaque – the two bacterial Probiotic strains namely *Streptococcus thermophilus* and *Lactococcus lactis* are able to adhere to saliva coated hydroxyapatite and are successfully incorporated into a biofilm. These strains modulate the growth of the oral bacteria and diminish the colonization of *Streptococcus oralis*, *Actinomyces naeslundii* and *Streptococcus sobrinus*.
- Involvement in binding of oral micro-organisms to proteins
- Action on plaque formation and on its complex ecosystem by competing and intervening with bacterial attachments.
- Involvement in metabolism of substrate and production of chemicals that inhibit oral bacteria.

#### Indirect probiotic actions are also featured such as

1. Modulating systemic immune function.
2. Effect on local immunity.
3. Effect on non-immunologic defense mechanisms.
4. Regulation of mucosal permeability.
5. Probiotics as antioxidants and produce antioxidants.
6. Prevent plaque formation by neutralizing the free electrons.<sup>10</sup>

### Role of probiotics in Dental Caries

Dental caries is one of the most common diseases in the world and can lead to pain, tooth loss, infection. The formation of plaque on the surface of a tooth is a multistep mechanism. Initial attachment of *S. mutans* is followed by its multiplication and accumulation, leading to a sessile community known as a biofilm. Biofilms are very stable communities that can tolerate low pH, antimicrobial products, and nutrient / oxygen deprivation. *S. mutans* also produces a bacteriocin, (mutacin), which is active against other streptococcal species and non-streptococcal gram positive bacteria.

The production of mutacin leads to the efficient colonisation of this pathogenic microbe inside the oral cavity resulting in dental caries. Streptococcus species are acidogenic. They cause demineralisation of the tooth enamel by creating a low pH environment in dental plaque. With the diversity of the oral microflora and the mechanisms of action of beneficial bacteria, it seems acceptable that probiotics would have a favourable effect on the reduction of dental caries.<sup>11</sup> The various studies conducted looking at the effect of oral probiotics on dental caries is listed in table 1.

### Role of probiotics in Periodontal Disease

Periodontal disease can be classed into two types; gingivitis –inflammation of the gingiva and periodontitis – progressive disease that affects all supporting tissues of the teeth. The main pathogenic agents causing periodontitis are *P. gingivalis*, *Treponema denticola*, *Tannerella forsythia* and *Aggregatibacter actinomycetemcomitans*. These pathogens have a complex advantage of possessing a variety of virulent factors that allow them to colonise the subgingival sites, escape the host's defence system and cause damage to the whole tooth structure. The prevalence of *Lactobacillus gasseri* and *L. fermentum* in the oral cavity was compared between healthy individuals and those with chronic periodontitis by Koll-Klais and team. They found that growth of periodontopathogens was inhibited by lactobacilli and demonstrated the influence of lactobacilli in the oral cavity of a healthy individual.<sup>16</sup> Theoretical

possibilities for probiotics to affect periodontal health are shown in figure 1.<sup>17</sup>

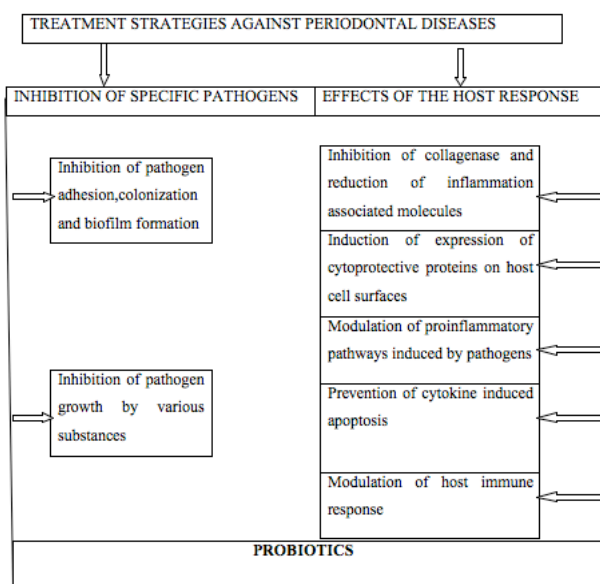
### Role of probiotics in Halitosis

There are a number of reasons for halitosis (bad smelling breath) which includes consumption of particular foods, metabolic disorders and respiratory tract infections. But commonly it is associated with an imbalance of the commensal microflora of the oral cavity. Kazor and team looked at the species of bacteria found on the tongue of patients suffering from halitosis and compared the findings with subjects who were considered healthy.<sup>18</sup> The species found to be most associated with halitosis were *Atopobium parvulum*, *Eubacterium sulci*, *Fusobacterium periodonticum*. In the same study, *Streptococcus salivarius* was found to be the most prevalent in the healthy subjects, and this is thought to be due to the capability of *S. Salivarius* to produce bacteriocins which could contribute to reducing the number of bacteria that produce VSCs.<sup>11</sup>

### Role of probiotics in infections and oral diseases

*Candida albicans* is a leading cause of infection in oral cavity. It is particularly common in the elderly and in immunocompromised patients. The strains which reduce *C. albicans* in oral cavity are *L. rhamnosus* GG and *Propionibacterium freudenreichii* which was shown by Hatakka et al (2007) after consuming these organisms in the form of cheese. The effects of various *Lactobacillus* strains in oral cavity were studied by Koll et al (2008) and the results showed that most strains suppressed growth of periodontal pathogens, including *actinomycetemcomitans*, *Porphyromona gingivalis*, *P. intermedia*, and cariogenic *S. Mutans*. No inhibition was found for *C.albicans* growth. A study was conducted by Hasslöf P et al (2010) to investigate the ability of a selection of lactobacilli strains, used in commercially available probiotic products, to inhibit growth of oral mutans streptococci and *C. albicans* in vitro by agar overlay method. The strongest inhibition on *Candida albicans* was displayed by the two *L. plantarum* strains and *L. reuteri* ATCC 55730.

The research work focused on the implications of probiotics on AIDS showed that progression of AIDS can be slowed by probiotic bacteria. Lactobacillus strains had produced proteins capable of binding a particular type of sugar (mannose) found on HIV envelope. This binding of sugar enables the colonization of the bacteria on the mucosal lining of the mouth and digestive tract. One strain secreted abundant mannose binding protein particles into its surroundings and neutralized HIV by binding to its sugar coating. They also described that immune cells trapped by lactobacilli formed a clump. This configuration would immobilize any immune cells harbouring HIV and prevent them from infecting other cells.<sup>2</sup>



**Figure-1:** Theoretical possibilities for probiotics to affect periodontal health.<sup>17</sup>

### Role of probiotics in orthodontic treatment

Fixed orthodontic appliances are considered to affect dental health due to accumulation of microorganisms that may cause enamel demineralization, which can be clinically visible as white spot lesions. This white spot lesion formation is due to imbalance between mineral loss and mineral gain.

Cildir et al. in 2009 conducted a clinical study with probiotics and found out that daily consumption of fruit yogurt with Bifidobacterium animalis subsp. Lactis DN -173010 could reduce the salivary levels of mutans streptococci in orthodontic patients with fixed appliances. Further studies are needed to clarify if this

approach is an alternative strategy for prevention of demineralization and white spot formation during orthodontic treatment.<sup>19</sup>

### Role of probiotics in oral cancer

There is very minimal evidence in literature showing the anticancer effects of probiotics. Probiotics can interfere at various stages of cancer process, of which mainly cause interference with chromosomal and DNA damage. However, more research is required to develop specific regulations on their consumption.<sup>2</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 an informal evidence among patients in 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.<sup>20</sup>

### SAFETY OF PROBIOTICS

Probiotics are considered as safe and are easily available in the market throughout the world. US Food and Drug Administration (FDA) classified probiotics as a nutritional product rather than as a pharmaceutical product which made them easily accessible without prescription. Bacteremia or sepsis from lactobacilli is extremely rare as evidenced by epidemiologic studies. Numerous probiotics have a long history of safe use and no health concerns have been observed. However there are, isolated reports of fungemia with Saccharomyces following its use as a probiotic especially in immunocompromised patients.<sup>21</sup>

### STATUS OF PROBIOTICS IN INDIA

In India, probiotics are often used as animal feed supplements for cattle, poultry and piggery. It is rarely used for human beings among whom spor-

**Table-1:** A brief overview of some of the studies conducted looking at the effect of oral probiotics on dental caries.<sup>11</sup>

Reference	Strain	Study
Náse et al, 2001 <sup>12</sup>	L. rhamnosus	Supplementing 1-6 year old children with L. rhamnosus for 7 months significantly reduced the risk of dental caries
Strahnic et al, 2007 <sup>13</sup>	L. salivarius & L. Fermentum	Both strains showed antagonistic activity on the growth of S. mutans and Streptococcus pneumonia. L. salivarius was able to survive an environment of low pH as that produced by a high number of S. mutans.
Chung et al, 2004 <sup>14</sup>	L. fermentum	L. fermentum was found in the saliva of healthy children. This strain significantly inhibited the formation of the insoluble glucan produced by S. mutans. It did not affect the multiplication of this pathogenic strain, but it completely inhibited the adherence onto cuvette walls
Stamatova et al, 2007 <sup>15</sup>	L. rhamnosus & Lactobacillus bulgaricus	Inhibitory effects against P. gingivalis, Fusobacterium nucleatum & streptococcal spp
Koll-Klais et al, 2005 <sup>16</sup>	Various lactobacilli strains	69% of these strains inhibited S. mutans, 82% inhibited P. Gingivalis

**Table-2:** Effect of probiotics on human disease<sup>23</sup>

Disease	Probiotic	Assessment	Effect
Asthma	Lactobacillus acidophilus,oral(live)	Serum IgE & IL-4 Lymphocyte proliferation	No alterations
Rotavirus infection	L.GG,Oral (live)	Diarrhea,Serum total IgA & IgM and anti-rotavirus IgM & IgG	Duration of diarrhea decreased;Increased anti-rotavirus IgA
Crohn's disease & juvenile arthritis	L.casei,oral (live)	Anti beta-lactoglobulin IgA-secreting cells	Number increased

olac, *Saccharomyces boulardii* and yogurt (*L. bulgaricus* + *L. thermophilus*) are the most common ones. The preparation made from *Sporolactobacilli* strain is marketed as Sporolac, acts as an alternate to B-complex 80 capsules. In India, only sporulating lactobacilli are produced and they are sold with some of the antibiotic preparations.<sup>1</sup>

## FUTURE TRENDS OF PROBIOTICS

The World Health Organization considered Probiotics to be the next-most important immune defense system when commonly prescribed antibiotics are rendered useless by antibiotic resistance. Probiotics can be used as passive local immunization against dental caries. High titers of

in India, which is a probiotic given to paediatric patients. ViBact (which is made up of genetically modified *Bacillus mesentericus*) is the latest and recent addition to the list of probiotics in India. It antibodies can also be directed against human cariogenic bacteria produced in bovine colostrums over the vehicle of fermented milk. Research is directed at the reduction of severity and occurrence of mucosal lesions, specifically aphthous ulcers.<sup>22</sup> Studies with probiotic bacteria indicate that select strains have the potential to be beneficial to human health (Table 2). Studies that have used animal models of human diseases demonstrate that probiotic bacteria have the ability to alter immunologic responses (Table 3).<sup>23</sup> The basic of probiotic nanotechnology applications is currently in the development of

**Table-3:** Probiotic effects in rodent models of human disease<sup>23</sup>

Disease model	Probiotic	Assessment	Effect
Insulin-dependent diabetes mellitus	Lactobacillus casei, oral (live)	Tcell markers, splenic cytokines	Decreased CD4+ cells IFN gamma and IL-2
Insulin-dependent diabetes mellitus	Lactobacillus casei oral (heat-killed)	Splenic B and T cell number and production of IFN gamma and IL-2,4,5,6,10	Decreased incidence of diabetes, increased CD4+Bcells, decreased CD8+ T cells, decreased IFN gamma and increased IL-2
Collagen-induced arthritis(CIA)	Lactobacillus casei shirota, oral (live)	Joint swelling, Delayed Hypersensitivity, collagen stimulated IL-4 and interferon gamma production by spleen cells	Decreased CIA, anticollagen antibodies
Influenza immunization	Bifidobacterium bifidus -oral	Respiratory tract infection and antiinfluenza virus IgG	Protection against lower respiratory tract infections, Higher serum IgG levels.

Nano-encapsulated probiotics. Applications of nanotechnology in organic food production require precaution, as little is known about their impact on environment and human health.<sup>23,24</sup>

## CONCLUSION

Probiotics represent a new area of research in medicine. Current findings on the potential use of probiotics against oral conditions are very encouraging. As the evidence for beneficial effect of probiotics on periodontitis is less than dental caries, if dental caries can be prevented then periodontitis is less likely to occur. More research is needed in this area, but the use of probiotics to manage the oral microflora is looking to be a very effective adjunct way to control oral conditions that affect so many people worldwide.

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