

**Probiotics And Prebiotics In Periodontal Diseases**Dr. Alladi Vaishnavi<sup>1</sup>, Dr. Sania<sup>2</sup>, Dr. Sadiya Khattoon<sup>3</sup>, Dr. Parv Agarwal<sup>4</sup>**Correspondence Author: Dr. Alladi Vaishnavi**, Kothiwal Dental College & Research Centre, Moradabad, (U.P.), 244001, INDIA.**Conflicts of interest:** None to Declare**Introduction**

Microorganisms have been used for hundreds of years by our ancestors in various food and beverages, and recently have undergone clinical research for their ability to prevent and cure a variety of diseases. In recent years, novel insights have been gained into the role of bacterial micro flora in health and disease.<sup>1</sup>

There is a long history of recommending the use of microorganisms, particularly lactic acid bacteria, to promote health. The oldest traces date back to classical Roman literature when Plinius Secundus maior wrote that fermented milk products could be beneficial for the stomach. The Nobel prizewinning scientist Eli Metchnikoff is seen as one of the pioneers of modern probiotic research. In “The Prolongation of Life”, written in the beginning of the 20th Century, he claimed that Bulgarians lived longer than other populations, due to the consumption of fermented milk.<sup>2</sup> However, it was not until 1965 that the word probiotic itself was introduced by Lilly and Stillwell as “substances produced by microorganisms that stimulate the growth of another”.<sup>3</sup> This term, the antonym of antibiotics, is derived from the Greek language and literally means “for life”. Since the 1960s, several definitions have been proposed.<sup>4-9</sup> The currently used definition is: “probiotics are living microorganisms which, when administered in adequate amounts, confer a health benefit for the host”, and has been approved by the World Health Organization (WHO) and the United Nations Food and Agriculture

Organization (FAO). In the 1990s, another related term was introduced: prebiotics. These are to date defined as non-digestible food ingredients that beneficially affect the host by selectively stimulating the growth/or activity of one or a limited number of bacteria, that can improve host health. When a product contains both probiotic and prebiotics, the term synbiotic applies. The first probiotic species introduced into research were *Lactobacillus acidophilus* by Hull, et al. in 1984 and *Bifidobacterium bifidum* by Holcomb, et al. in 1991.<sup>10</sup>

Periodontal disease is a chronic, inflammatory disease affecting the supporting structures of the teeth, i.e., the connective tissue attachment, periodontal ligament, and alveolar bone. It results from the interplay of a Gram-negative bacterial infection and the host response in susceptible individuals. The disease may result in bone loss, bleeding and erythema of the gingival tissue, and mobility of the teeth. Methods of treatment often include the mechanical removal of the bacteria with or without antibiotics in combination with improved oral hygiene techniques.<sup>11</sup>

Due to an increase in antibiotic resistance, and because both periodontal disease and dental caries are results of bacterial action, new treatment methods have been explored. Among them, probiotic approaches are being evaluated.

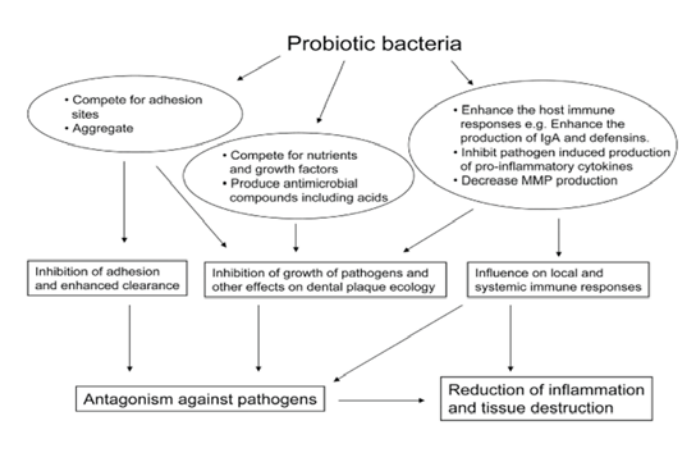
**Replacement therapy<sup>12</sup>**

Replacement therapy/ bacteriotherapy /bacterial interference is sometimes used interchangeably with

probiotics .Although both approaches use live bacteria, there are some slight difference

Probiotic Therapy	Replacement Therapy
"Probiotics are generally used as dietary supplements"	"Effector strain is not ingested and is applied directly on the site of infection"
"Rarely dramatic and long term microbiological change"	"Involves dramatic and long term change in the indigenous microbiota"
"Probiotics are able to exert a beneficial effect with out permanently colonizing the site"	"Colonization of the site by the effector strain is essential"
"Exerts beneficial effect by influencing the immune system"	"Has a minimal immunological impact"

#### MECHANISM OF ACTION<sup>10</sup>



#### STRAINS

A probiotic is listed by the genus, species and an alphanumeric designation. In the scientific community, there is an agreed nomenclature for microorganisms- For example -*Lactobacillus Casei* DN-114 001 or *Lactobacillus Rhamnosus* GG.<sup>13</sup>

Table – Nomenclature for microorganisms

Genus	Species	Strain Designation
<i>Lactobacillus</i>	<i>Rhamnosus</i>	GG
<i>Lactobacillus</i>	<i>Casei</i>	DN-114 001

#### DIFFERENT PROBIOTIC STRAINS<sup>12</sup>

<i>Lactobacillus</i> species	<i>Bifidobacterium</i> species	<i>Streptococcus</i> species	<i>Enterococcus</i> species	<i>Escherichia coli</i>	<i>Fusobacterium</i> species
<i>L. Acidophilus</i>	<i>B. bifidum</i>	<i>S.Lactis</i>	<i>E.fecalis</i>		
<i>L. casei</i>	<i>B.longum</i>	<i>S.cremoris</i>	<i>E.faecium</i>		
<i>L. Rhamnosus</i>	<i>B.breve</i>	<i>S.diacetylactis</i>			

#### CHARACTERISTICS OF PROBIOTIC STRAINS<sup>14</sup>



#### DOSING

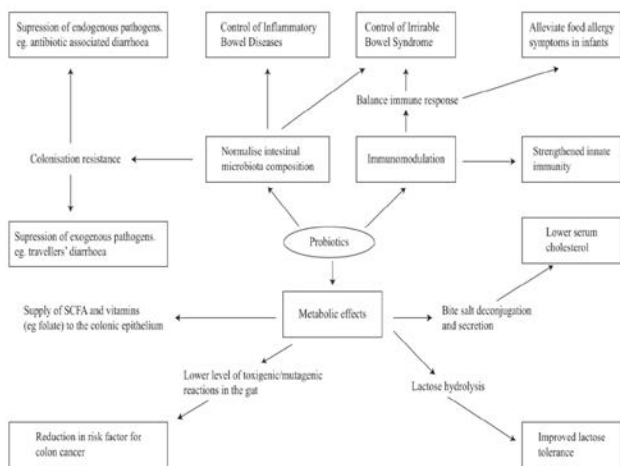
Probiotics are available in a wide variety of preparations including powder, capsules and liquids. Most studies use twice a day daily doses (BD) but there is no evidence that once daily dosing is not enough. The CFU's in these preparations can vary tremendously between brands. They should be protected from light, refrigerated and not to be taken with food and antibiotics (gap of at least 2 hrs between the two). Dry powders in bottles which have to be reconstituted should be stored in dark or amber colored

bottles and reconstituted with cool water but, the stability (probiotics viability) tends to go down with time.<sup>15</sup>

**DIFFERENT PROBIOTIC PRODUCTS AVAILABLE IN INDIA ARE:<sup>12</sup>**

SOME PROBIOTIC PRODUCTS IN INDIA	FORMULATION
Nestle Nesvita	Yoghurt
Yakult	Drink
Amul	Ice cream,Buttermilk
Mothers dairy	B Activ yoghurt,Buttermilk,Nutrifit
Bifilac	Capsules/Sachets
Becelac PB	Capsules/Sachets
Gut pro	Capsules

**PROPOSED HEALTH BENEFITS STEMMING FROM PROBIOTIC CONSUMPTION<sup>16</sup>**



**PROBIOTICS AND PERIODONTAL DISEASES**

Periodontitis is a multifactorial disease that encompasses the hard and soft tissue, microbial colonization (with or without invasion), inflammatory responses and adaptive immune responses. The complexity of the local tissue components, including bacteria and/or their products and virtually all aspects of host response mechanisms, has complicated our ability to elucidate the critical protective functions in the tissues and has continually provided

evidence for the potential of host destructive factors as the ultimate causative parameters in the disease. Treatment of periodontal diseases in recent years has moved towards an antibiotic/antimicrobial model of disease management. Probiotics might be a promising area of research in the treatment of periodontitis.

Probiotics lower the pH so that plaque bacteria cannot form dental plaque and calculus that causes the periodontal disease.<sup>17</sup>

Probiotics make an excellent maintenance product because they produce antioxidants. Antioxidants prevent plaque formation by neutralizing the free electrons that are needed for the mineral formation. Probiotics are able to breakdown putrescence odours by fixating on the toxic gases (volatile sulphur compounds) and changing them to gases needed for metabolism.<sup>10</sup>

Presence of *S.Oralis* and *S.Uberis* provided a good indication of health of periodontium.<sup>12</sup>

Koll *et.al*<sup>18</sup>, characterized 22 strains of orally isolated lactobacilli with regard to antimicrobial activities on oral pathogens including periodontopathic bacteria and tolerance to environmental stress in vitro.

Shimazaki *et.al*<sup>19</sup> showed the relationship between the intake of dairy products such as milk, cheese and lactic acid foods (yoghurt and lactic acid drinks) and periodontitis.

Teughels *et.al*<sup>20</sup> conducted a study in which seven presumed beneficial bacteria were examined for their ability to interfere, exclude, or displace *A. actinomycetemcomitans* from epithelial cells in vitro and resulted in the hypothesis that bacterial interactions interfere with *A.actinomycetemcomitans* colonization of epithelial cells in vitro, and demonstrated the potential beneficial effects of *S.mitis*, *S.salivarius*, and *S.sanguinis*. Staab and co-workers<sup>21</sup> also concluded that probiotic milk has a beneficial effect on gingival inflammation.

Shimauchi et al<sup>22</sup> studied the effect of probiotic intervention using lactobacilli on the periodontal condition of volunteers without severe periodontitis in which freeze dried *Lactobacillus salivarius* WB21- containing tablets oral placebo were given to volunteers. The results indicate that probiotics could be useful in the improvement / maintainance of oral health in subjects at a high risk of periodontal diseases.

Essche and co-workers<sup>23</sup> found in his studies that *B.bacteriovorus* as a living antibiotic was used for the prevention and treatment of periodontitis .

### PROBIOTIC 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. More 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 methanethiol.

Kang and colleagues<sup>24</sup> reported the capacity of various strains of *W.Cibaria* to inhibit the production of volatile sulphur compounds by *F nucleatum*. They concluded that this beneficial effect resulted from the production of hydrogen peroxide by *W.Cibaria*, which inhibited the proliferation of *F.nucleatum*.

A recent study showed that certain bacterial species, including *Atopobium parvulum*, *Eubacterium sulci* and *Solobacterium moorei*, predominate on the dorsal surface of the tongue among people with halitosis. Conversely, another species, *Streptococcus salivarius*, was detected most frequently among people without halitosis and is therefore considered a commensal probiotic of the oral cavity. *S.salivarius* is known to produce bacteriocins, which could contribute to reducing the number 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.

Burton and co workers<sup>25</sup> in their study used a broadly-active antimicrobial (chlorhexidine) to effect temporary depletion of the oral microbiota and then have attempted to repopulate the tongue surface with *Streptococcus salivarius* K12, a benign commensal probiotics. The objective of this is to prevent re-establishment of non desirable bacterial populations and thus help limit the recurrence of oral malodour. In the preliminary trials of the use of a chlorhexidine rinse followed by strain K12 lozenges, the majority of subjects with confirmed halitosis maintained reduced breath levels of volatile sulphur compounds for atleast 2 weeks. Thus, concluded that probiotic bacterial strains originally sourced from the indigenous oral microbiotas of healthy humans may have potential application as adjuncts for the prevention and treatment of halitosis.

Iwamoto and co workers<sup>26</sup> studied whether oral administration of lactobacilli alters the degree of halitosis and clinical conditions associated with halitosis. Twenty patients with genuine halitosis were given  $2 \times 10^9$  *Lactobacillus salivarius* WB21 and 280mg of xylitol per tablet. The dose through out the test period was maintained at three tablets per day, taken orally after eating and xylitol in tablet form daily. Oral malodour and clinical parameters were evaluated at the same time of day for each patient after 2 and 4 weeks.it was seen that all patients were positive for *L. salivarius* DNA in their saliva at 2 weeks, although 12 patients were negative for this organism at baseline. Oral malodour parameters significantly decreased at 2 weeks in the subjects with physiologic halitosis. The scores of an organoleptic test

and bleeding on probing significantly decreased at 4 weeks. It was concluded that oral administration of probiotic lactobacilli primarily improved physiologic halitosis and therefore, may have beneficial effects on bleeding in the periodontal pocket.

### PREBIOTICS

The concept of prebiotics came to light during mid-nineties of the twentieth century (Gibson et al., 1995). Prebiotics pass through the digestive system without being broken down by the digestive enzymes i.e. reach the large intestine in an intact form. Once these non-digestible carbohydrates pass into the intestines, they serve as a feast for the probiotic bacteria that live there. Prebiotics of proven efficacy are able to modulate the gut microbiota by stimulating indigenous beneficial flora while inhibiting the growth of pathogenic bacteria therein. Preferred target organisms for prebiotics are species belonging to the *Lactobacillus* and *Bifidobacterium* genera. The most efficient prebiotics may also reduce or suppress numbers and activities of organisms seen as pathogenic.<sup>14</sup>

Most of the prebiotics used as food adjuncts, such as inulin, fructooligosaccharides, lactulose, dietary fiber and gums, are derived from plants. Two of the best-known prebiotics are inulin and trans-galactooligosaccharides (TOS) occur naturally in foods such as garlic, onion, leeks, shallots, Asparagus, spinach, Jerusalem artichokes, chicory, peas, beans, lentils, oats and bananas.

Prebiotic oligosaccharides taking interest amongst food researchers and are getting more global attention than other functional foods because of their multipronged beneficial effects including gut health, higher mineral absorption, lowering of cholesterol, immune system stimulation, pathogen exclusion, etc<sup>14</sup>

### MECHANISM OF ACTION

- Enhance the growth of resident commensal gut bacteria particularly bifidobacterium and lactobacilli .

- Cellobiose has the additional property of downregulating virulence factors of *Listeria monocytogenes*.

- They may also exert a direct effect on the host by stimulating expression of IL-10, Interferon  $\gamma$ , enhancement of IGA secretion, and modulation of inflammatory responses in pathogens.<sup>27</sup>

### ARE PREBIOTICS A VIABLE ALTERNATIVE OR ADJUNCT?

It is recognized that the resident oral microbiota persists by catabolizing endogenous nutrients such as salivary proteins and glycoprotein's and gingival Crevicular fluid. For a rational approach to the development of oral prebiotics and the manipulation of resident microbiota, it is essential to know which species can be considered to promote health and to gain some understanding of their metabolic needs and interactions.

Koli-klais *et.al*<sup>28</sup> found that homo fermentative lactobacilli particularly *L.gasseri* were more prevalent in healthy rather than periodontally diseased sites.

Hojo *et.al*<sup>29</sup> also found *L. gasseri* as well as *L.salivarius* and *L.fermentum* to be more prevalent in healthy sites but not exclusive to health. Counts of bifidobacteria were particularly high in a group of well-maintained periodontitis subjects, indicating that these bacteria are better able to colonize sites that have undergone plaque removal. Thus, it is possible that prebiotic therapy promotes the growth of certain bifidobacteria and lactobacilli , which may enhance periodontal health.

### CONCLUSION

Effective use of probiotics has the potential to decrease patients exposure to antimicrobials. With the current focus on disease prevention and the quest for optimal health at all ages, the probiotics market potential is enormous. Health professionals are in an ideal position to help and guide their clients toward appropriate prophylactic and therapeutic uses of probiotics that deliver the desired

beneficial health effects. There are many probiotic products at the market place and most have supporting evidence behind the advertised health claims. New legislation governing the labelling of probiotics, such as indicating the species, strain and number of bacteria present is likely to come into force in the near future.

With the increasing popularity of probiotic products, consumers frequently demand that the health properties of probiotics strains be preserved in the products sold and that there is at least a theoretical chance that the health effects of the probiotic strains will be evident after consumption.

Probiotics should not be considered a panacea for health, but can be incorporated into a balanced and varied diet to maximize good health.

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