

**PROBIOTICS- A NEW MILEU IN PERIODONTICS****Betsy Thomas<sup>1\*</sup>, Meera Avadhani<sup>2</sup> and Khandigae Mahalinga Bhat<sup>3</sup>**<sup>1</sup>Professor & Head Department of Periodontology, MCODS, Manipal, Manipal University.<sup>2</sup>Post Graduate Student Department of Periodontology, MCODS, Manipal, Manipal University.<sup>3</sup>Professor, Department of Periodontology, MCODS, Manipal, Manipal University.Article Received on  
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Periodontology,  
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Manipal University.**ABSTRACT**

Periodontal diseases are chronic in nature with the potential to attack diverse age groups. Our understanding on periodontal disease etiology has undergone many transformations starting from the very old specific plaque hypothesis proposed by Bass & Johns in 1915 to the present ecological plaque hypothesis by P.D. Marsh in 1994. Today, though we are equipped with various treatment modalities, we still are being intimidated with disease recurrence. Now, the question is "Are we truly able to eliminate the causative bacteria present at the site with all these available options? " We are moving from pillar to post to address this problem. Why not let's search a medicine from our own kitchen in the form of fermented curds ? The answer is yes in the form of "Probiotics". The concept of probiotics seems logical as it high-

lights the age old saying which goes as "A Thorn can be taken out by a thorn". Similarly, probiotic therapy utilizes the beneficial microbiota to combat with the pathogenic ones. It was Elie Metchnikoff during the early 1900's made this observation that the Bulgarians who relied on the fermented foods, rich in specific microbiota lived a relatively longer and healthy life.

**KEYWORDS:** Bacterial replacement therapy, prebiotics, designer probiotics, synbiotics.**INTRODUCTION**

From the antibiotic era we are probably moving on to probiotic phase - a new avenue in an attempt to overcome the effects of harmful bacteria. Bacterial homeostasis is believed to be one of the important reasons why the disease progression varies from person to person.<sup>[1]</sup> By

populating the periodontal pocket or gingival sulcus with probiotics, the pathogenic bacteria may be minimized in these sites which is a sort of 'Bioengineering of Microbiota'.

The concept of probiotics falls under "Ecological Plaque hypothesis" proposed by P.D Marsh (1991).<sup>[2]</sup> With the emergence of multi-resistant strains, antibiotic resistance has become a booming problem that has led scientists to develop novel means for fighting infectious diseases. Also there has been a major shift in treatment options from nonspecific to specific approach. Presently treatment options propose altering ecology of niches, in order to modify pathological plaque to a biofilm of commensalisms. And probiotic usage is one such strategy.

## HISTORY

They have a long and strong history dating back to the 1st decade of 1900 when the Ukrainian bacteriologist Elie Metchnikoff found that certain Bulgarians lived a longer, pain-free and disease-free lives. He attributed their healthy longevity to their diet. The diet consisted of yogurt, sour dough, bread and buttermilk. Dr. Metchnikoff discovered that these fermented foods contained friendly beneficial bacteria that were able to take rotten putrescence food and digest them to release by-products that were full of nutrients and which destroyed the foul odor.<sup>[3]</sup> These friendly bacteria that kept the potential pathogens from causing disease were termed Probiotics.

The term 'probiotic', meaning "for life", is derived from the Greek language. It was first used by Lilly and Stillwell in 1965 to describe, "substances secreted by one microorganism which stimulates the growth of another".<sup>[3]</sup>

## DEFINITIONS AND TERMINOLOGY

### Probiotic

"Probiotics are live microorganisms which when administered in adequate amounts, confer a health benefit on the host." - WHO/FAO report (2002).

"Probiotic is a live microbial food ingredient that, when ingested in sufficient quantities, exerts health benefits on the consumer".

- International Life Science Institute (ILSI) Europe.

### Replacement Therapy

The term Replacement therapy, coined by Teughels et al(2007)<sup>[4]</sup> also called as Bacteriotherapy or bacterial interference has been sometimes used interchangeably with

probiotics. It refers to the basic idea of replacing pathogenic bacteria by supplying commensals, which have some characteristics for oral adherence.

### **Prebiotics**

The term 'prebiotic' was introduced by **Gibson and Roberfroid**.<sup>[5]</sup> It is a non-digestible food ingredient that confers benefits on the host by selectively stimulating the growth and/ or activity of one bacterium or a group of bacteria in the colon, and thus improves the host health. e.g. fructo oligosaccharides, gluco oligosaccharides, inulin and maltodextrin.

### **Synbiotics**

The term synbiotic confers the combined administration of prebiotics with probiotics to provide definite health benefits by synergistic action. Because the word alludes to synergism, this term should be reserved for products in which the prebiotic compound selectively favors the probiotic compound.<sup>[6]</sup>

### **Designer Probiotics**

These are genetically modified probiotics with enhanced properties. For example, a recombinant strain of *Lactobacillus* that expressed antibodies targeting one of the major adhesions of *S. mutans* (antigen I/II) was able to reduce both the viable counts of *S. mutans* and the caries score in a rat model.

The treatment modality of using probiotics is not new to the field of medicine. Several systemic diseases were intervened using probiotics like Acute diarrhea, Crohn's disease,<sup>[1]</sup> Urogenital infections, Oropharyngeal infections, cancers and management of cardiovascular diseases as well.

One important aspect of using probiotics is that they address the problems arising from the routine and non-judicious use of anti-biotics especially the emergence of bacterial resistance.

### **PROBIOTICS**

The first probiotic species to be introduced in research was *Lactobacillus acidophilus* by Hull et al. in 1984,<sup>[7]</sup> followed by *Bifidobacterium bifidum* by Holcomb et al. in 1991.<sup>[8]</sup>

The various means of administration of probiotics for oral health purpose that have been studied are Lozenges, tablets, cheese, yoghurt, mouth rinse, capsules etc.

The advantage of incorporating probiotics in to dairy products lies in their potential to neutralize acidic conditions.

Common bacteria used as probiotics are *Lactobacillus* species, *Bifidobacterium* species, *Propionibacterium* species, *Streptococcus* species, *Escherichia* species and *Enterococcus* species.

*Delio vibrio bacteriovorous* is a newer probiotic strain introduced few years back. Of all these organisms, *Lactobacillus* sp. and *Bifidobacterium* sp. are commonly used. These bacteria are generally regarded as safe (GRAS) because they can reside in the human body causing no harm and, on the other hand, they are key microorganisms in milk fermentation and food preservation and used as such from the dawn of mankind.

The role played by these resident bacteria cannot be ignored as they protect the host through the development of immune system,<sup>[9]</sup> helps in maintaining healthy oral tissue by influencing expression of mediators such as intracellular adhesion molecule 1 (ICAM-1), E-selectin and IL-8,<sup>[10]</sup> modulating immune responses and enhancing cellular homeostatic mechanisms.<sup>[11]</sup>

## MECHANISM OF ACTION OF PROBIOTICS

The mechanism of action vary according to the specific strain or combinations of strains used, the presence of prebiotics and the condition that is being treated, as well as the stage of the disease process in which the probiotic is administered.<sup>[12]</sup> Stomatova and Muerman (2009)<sup>[13]</sup> highlighted the possible mechanism of action of these probiotics as follows

- Inhibition of pathogen adhesion, colonization and biofilm formation.
- Inhibition of pathogen growth by various substances
- Modulation of inflammatory pathways induced by pathogens
- Inhibition of collagenases and reduction of inflammation associated products.

Probiotics reduce the inflammatory response by inhibiting the production of proinflammatory cytokines through actions on NFκB pathways and also by increasing production of antiinflammatory cytokines such as IL-10.

Probiotics can also modify the surrounding environment by modulating the pH and/or the oxidation–reduction potential, which may compromise the ability of pathogens to become established (Fig: 1).

A combination of probiotic strains is often used to increase the beneficial effects. Prebiotics also exert direct effects on the host; independent of their effects on resident bacterial populations.<sup>[14]</sup> These include stimulation of expression of IL-10 and interferon  $\gamma$ , enhancement of IgA secretion, modulation of inflammatory responses to pathogens and stabilization of the gut mucosal barrier. Additionally, prebiotics with enhanced function have been designed. These oligosaccharide derivatives contain sugars that are specific epithelial cell receptors to which pathogens adhere and they, therefore, provide "decoy" adhesion sites and cause pathogens to adhere to luminal contents rather than to epithelial cells.<sup>[15]</sup>

### POPULAR PROBIOTIC STRAINS

There are certain criteria<sup>[16]</sup> to be fulfilled for an organism to be considered ideal probiotic strain. They are - Ability to persist, High cell viability, resistant to low pH and acids, able to interact or to send signals to immune cells, adhesion to cancel the flushing effect, should be of human origin, resistance to processing and influence local metabolic activity.

#### Lactobacilli

These constitute about 1% of the cultivable oral microflora. The species commonly found in saliva are The species most often found in saliva are *Lactobacillus acidophilus*, *Lactobacillus casei*, *Lactobacillus fermentum*, *Lactobacillus plantarum*, *Lactobacillus rhamnosus* and *Lactobacillus salivarius*.<sup>[17]</sup>

Probiotic strains from *Lactobacillus* genera include...

- *L. acidophilus* NCFM(world's most researched strain), *L.acidophilus* Rosell- 52, *L.acidophilus* UBLA-34
- *L. johnsonii*
- *L. casei. shirota*
- *L. rhamnosus* GR-1
- *L. gasseri*
- *L. reuteri* MM53

Those species generally found in dairy products include *L. acidophilus*, *L. casei*, *L. fermentum* and *L. rhamnosus*.<sup>[18]</sup> However, it is not yet sure whether their presence in the oral cavity is a result of frequent consumption of dairy products or whether oral cavity is genuinely their natural habitat.<sup>[19]</sup>

**Probiotic properties of *Lactobacillus* sp**

**Sookhee et al (2001)**<sup>[20]</sup> isolated 3790 strains of lactic acid bacteris from the oral cavity of 130 individuals. They observed that those isolates belonging to *Lactobacillus paracasei* ssp. *paracasei* & *L.rhamnosus* had a higher capacity to antagonize important oral pathogens, including *S.mutans* & *P.gingivalis*.

*Weissella cibaria* which was earlier classified under the genus *Lactobacillus* is a gram +ve facultative anerobic lactic acid bacterium that has been isolated from humans. It is known to be detected in fermented foods and is considered a potential probiotic agent, **Bjorkoth et al(2002).**<sup>[21]</sup>

**Bifidobacterium**

Both Bifidobacterium and *Lactobacillus* belong to the Lactic Acid Bacteria group(LAB). These two genera do not include any significant pathogenic species and their dominance in the faeces of breast-fed babies is thought to impart protection against infection.<sup>[22,23]</sup> The health interest of the Bifidobacterium genus is reflected in the commonly-accepted definition of prebiotics: food ingredients that selectively stimulate the growth and activity of bacteria in the gut, usually bifidobacteria (bifidogenic effect) and lactobacilli thus procuring health benefits.<sup>[24]</sup>

Bifidobacterium *infantis* strain has been shown to exert a broad spectrum of antimicrobial properties through production of antimicrobial compounds, unrelated to acid production, which inhibit the growth of pathogens.<sup>[25]</sup> Interestingly, Fujiwara et al.<sup>[26]</sup> recently described a protein factor produced by Bifido-bacterium *longum* SBT 2928, with a molecular weight of at least 100 000, which inhibited adhesion of enterotoxigenic *Escherichia coli* strain Pb176 which expresses colonization factor adhesion II, to the gangliotetrasylceramide GA1 molecule in vitro. Two strains of bifidobacteria were found to produce an antibacterial lipophilic factor (or several factors) with an estimated molecular weight of <3500.<sup>[25]</sup>

In experimental conditions, *B. longum* increases the immunological and defensive functions of germ free mice.<sup>[27,28,29]</sup> Bifidobacterium *breve* YIT4064 enhances antigen specific IgA-antibody directed against rotavirus in the mouse.<sup>[30]</sup>

Probiotic strains from Bifidobacterium genera include- *B.bifidum*, *B.longum* and *B.infantis*.

Thus, due to their outstanding host protective properties, the LAB group of strains are very popular and henceforth are commonly used for making probiotic formulations.

One important factor to be discussed is the transit time they reside in the oral cavity which is generally considered to be very busy all the time. Addressing this issue Haukioja et al(2006)<sup>[31]</sup> performed a trial where they assessed the survival and adherence to oral surfaces of various probiotics used by the dairy industry specifically the Lactic acid group of bacteria. They observed that all the strains tested survived well in saliva but differed in their abilities to adhere, the *Lactobacillus* genus exhibited a higher adherence capacity when compared to *Bifidobacterium* species. Subjects who consumed *L.rhamnosus* in the form of yogurt on a daily basis hosted this organism in the saliva for up to 3 weeks after discontinuing yogurt consumption. These findings were contradicted by the observations made by Yli-knuuttila et al(2006)<sup>[32]</sup> who said that *L.rhamnosus* strain only temporarily colonizes the oral cavity and for attaining long term benefits consistent consumption of the probiotic is recommended.

However, both these studies inferred that probiotic strains do stay in the oral cavity when consumed through commercial formulations. *Streptococcus salivarius* K12 strain can also be of a probiotic source because of its production of salivarin - a lantibiotic with inhibitory activity towards *S.pyogenes*. *Streptococcus Oralis* and *Streptococcus Uberis* have been shown to inhibit the growth of pathogens both in the laboratory and animal models.<sup>[33]</sup> The ideology of this Replacement Therapy (Guided Pocket Regeneration) has sustained a long journey in the field of dentistry. Though most of the times, both the terms were used synonymously, they differed in certain aspects.

#### DIFFERENCES BETWEEN PROBIOTIC THERAPY AND REPLACEMENT THERAPY<sup>[34]</sup>

Probiotic Therapy	Replacement Therapy
1. Generally used as dietary supplements. Can be used by individual.	1. Effector strain is not ingested and is applied directly at the site of infection by the clinician.
2. Able to exert a beneficial effect without permanently colonizing the site.	2. Colonization of the site by the strain is essential.
3. Involves a transient microbiological change.	3. Involves a dramatic and a long-term change in the indigenous microflora.
4. Has a minimal immunological impact.	4. Exerts beneficial effects by influencing immune system. It is directed at displacing or preventing colonization of a pathogen.

### Probiotics and Periodontal Diseases

Various studies have reported the capacity of lactobacilli to inhibit the growth of Periodontopathogens, including *P. gingivalis*, *Prevotella intermedia* and *A. actinomycetemcomitans*.<sup>[20,35]</sup>

A parallel open label placebo controlled study conducted by Hillman et al(1988)<sup>[36]</sup> on 24 gnotobiotic rats, including single baseline application of *S.sanguis* resulted significant decrease in the levels of *Aggregatibacter actinomycetom comitans* when compared with placebo groups. The authors attributed this interaction to the H<sub>2</sub>O<sub>2</sub> producing ability of *S.sanguis*.

Pozhartiskaia M M et al,(1994)<sup>[37]</sup>- Acilact, a Russian probiotic complex of 5 live lyophilized lactic acid bacteria, claimed to improve both clinical and microbiological parameters in gingivitis and mild periodontitis patients.

Grudianov et al(2001)<sup>[38]</sup> using a mixture of probiotics, reported improvements in clinical signs of gingivitis. Probiotics have also been employed as anti-mutagenic and anti-cariogenic agents.

Narva M et al(2004)<sup>[39]</sup> made an in vitro observation and inferred that during the fermentation process in milk, *L.helveticus* produces short peptides that act on osteoblasts and increase their activity on bone formation. They also said that these bioactive peptides could thereby contribute to the decrease in bone resorption associated with periodontitis.

Volozhin et al(2004)<sup>[40]</sup> has shown that a collagenous periodontal dressing containing *L.casei* 37 can significantly reduce the number of periodontal pathogens and extend remission periods up to 10-12 months. This might be due to the inhibitory effect of probiotics on the growth of pathogens thus altering the composition of oral biofilm.

In a study by Koll-klaise et al(2005),<sup>[35]</sup> the prevalence of lactobacilli, particularly *Lactobacillus gasseri* and *L. fermentum*, in the oral cavity was greater among healthy participants than among patients with chronic periodontitis.

Krasse et al (2006)<sup>[41]</sup> evaluated the role of *L. reuteri* against gingivitis. A parallel, double blind, randomized, placebo controlled study with 59 patients having moderate to severe gingivitis were selected. *L. reuteri* strains were administered via chewing gums twice a day

for 2 weeks at a concentration of  $2 \times 10^8$  CFU along with scaling and root planing. After 2 weeks, the clinical parameters were improved in the group consuming probiotic chewing gums.

3 plausible possibilities have been revealed out regarding *L.reuteri* on periodontal disease.

- First, *L.reuteri* is known to secrete 2 bacteriocins (reuterin and reutericyclin) which inhibit the growth of a wide variety of pathogens -Talarico T L et al(1988)<sup>[42]</sup> & Ganzle M G et al (2000).<sup>[43]</sup>
- Second, *L.reuteri* has a strong capacity to adhere to host tissues, thereby competing with pathogenic bacteria - Mukai T et al (2002).<sup>[44]</sup>
- Third, the recognized anti-inflammatory effects of *L.reuteri* on the intestinal mucosa, leading to inhibition of secretion of pro-inflammatory cytokines could be the foundation for a direct or indirect beneficial effect of this bacterium on people with periodontal disease - Ma D et al (2004)<sup>[45]</sup> & Pena J A et al(2005).<sup>[46]</sup>

Matsuoka et al(2006)<sup>[47]</sup> conducted a parallel open labelled study on 84 subjects consuming *L. salivarius* T1 2711 tablets 5 times a day for 8 weeks and showed decrease in bleeding on probing and *P.gingivis* counts. This was one of the earlier studies conducted on a large sample and for a relatively long period of 8 weeks.

Kang et al (2006)<sup>[48]</sup> in a cross over, open label placebo controlled study including 72 subjects evaluated the efficacy of a probiotic, *W. cibaria* CMS1 rinse. Subjects were instructed to rinse in the morning, afternoon and evening with a 15 ml rinse after brushing. There was a significant reduction in plaque scores in the probiotic rinse group which suggested that *W. cibaria* isolates possessed an ability to inhibit biofilm formation. (Fig 2). Riccia et al (2007)<sup>[49]</sup> assessed the anti-inflammatory effects of *L.brevis* prepared in the form of a lozenge in a group of patients with chronic periodontitis. After 4 days of lozenge usage, significant improvements were observed in the plaque index, Gingival index and bleeding on probing for all the subjects. Also, a significant reduction in salivary levels of PGE2 and MMP's were also observed. The authors attributed the beneficial anti-inflammatory effect of *L.brevis* to.

- *L.brevis*'s capacity to prevent the production of Nitric oxide(NO), & consequently the release of PGE2 and the activation of MMP's induced by the NO.

- *L.brevis* may also be antagonistic, leading to a reduction in the quantity of plaque - improvement in gingival index.

Teughels et al, (2007)<sup>[4]</sup> conducted a split mouth study on beagle dogs with artificially created pockets. Bacterial pellets of *S. sanguis* KTH-4, *S. salivarius* TOVE and *S. mitis* BMS were applied locally in pockets at 1,2 and 4 weeks. They showed decreased counts of anaerobic bacteria and *C. rectus* with decreased pocket recolonization and bleeding on probing when compared with controls.

Nackaerts et al. (2008)<sup>[50]</sup> analyzed radiologically the alveolar bone around the teeth that received root planing and the alveolar bone around the teeth that received root planning and repeated sub-gingival application of the bacterial mixture. These authors observed that the bone density within periodontal pockets treated with beneficial bacteria improved significantly after 12 weeks, while this improvement was not statistically significant for the positive control pockets.

Mayanagi et al(2009)<sup>[51]</sup> studied the effect of *L. salivarius* WB21 tablets on periodontopathic bacteria in a double blind, placebo controlled, randomized clinical trial on 66 healthy subjects. The results showed significant reduction in the sum total of five periodontopathic bacteria: *A. actinomycetemcomitans*, *P. intermedia*, *P. gingivalis*, *T. denticola* and *T. forsythia* in the probiotic group compared to the placebo group.

Staab et al(2009)<sup>[52]</sup> observed the reduction of MMP-3, elastase activity on 50 students with plaque induced gingivitis after having 65ml of Yakult daily, giving a daily probiotic dose of 100 billion bacteria per 100 ml for 8 weeks containing *L. casei* species. Yakult's *L. casei* strain Shirota is one of the most studied probiotic strains.

Van Essche et al (2009)<sup>[53]</sup> have reported that *B. bacteriovorus*, attack prey on and kill *A. actinomycetemcomitans*, thus suggesting a potential scope for the role of *B.bacteriovorus* in the prevention and treatment of periodontitis.

Twetman et al (2009)<sup>[54]</sup> used *L. reuteri*-containing chewing gum in 42 healthy patients and assessed its effects on crevicular fluid volume, cytokine (interleukin-1 $\beta$ , interleukin-6, interleukin-10, and TNF- $\alpha$ ) levels, and bleeding on probing. Crevicular fluid volume, as well as TNF- $\alpha$  and interleukin-8 levels, and bleeding were significantly reduced.

A study was done by Vivekananda M R et al (2010)<sup>[55]</sup> to evaluate the effects of *Lactobacilli reuteri* (Prodentis) alone and in combination with scaling and root planing (SRP) in a double blind, split mouth, randomized, placebo-controlled clinical trial of 30 volunteers with chronic periodontitis. *L. reuteri* (Prodentis) lozenges  $1 \times 10^8$  CFU were used twice daily for 20 days. At the end of 20 days, there was significant reduction in plaque index, Gingival index, Gingival bleeding index, Probing pocket depth reduction and Clinical attachment gain in SRP+ prodentis group followed by placebo group. This was one of the few trials where an attempt was made to assess the probing pocket depths and clinical attachment levels.

Teughels et al (2011)<sup>[56]</sup> conducted a systematic review on the microbiological and clinical effects of probiotics on periodontal health. Three animal and 11 in vivo human studies were retrieved. Many of the retrieved studies were pilot in nature. There was a high degree of heterogeneity between the studies. The author concludes by saying that the currently available data indicate an effect of probiotics on the oral microbiota and a more limited effect on clinical periodontal outcome measures. They also stressed on the need for further large randomized trials with a focus on the change in clinical parameters.

Teughels et al(2014)<sup>[57]</sup> performed a randomized placebo-controlled clinical trial to evaluate the effects of *Lactobacillus reuteri*-containing probiotic lozenges as an adjunct to scaling and root planing (SRP) amongst 30 chronic periodontitis patients. All patients received one-stage full-mouth disinfection and randomly assigned over a test (SRP + probiotic) or control (SRP + placebo) group. The lozenges were used two times a day for 12 weeks. Clinical and microbiological parameters were assessed at baseline, 3, 6, 9 and 12 weeks after the therapy. At 12 weeks there was a significant reduction in the number of *P.gingivalis* in the test group compared to controls.

Periodontal works are sparse and need validation by large randomized trials. It can be said probiotics are still in “infancy” in terms of periodontal health benefits, but surely have ope.

### **Residence Time of Probiotics in The Oral Cavity**

An important aspect regarding the use of probiotics and their subsequent effect on the oral cavity is the quality time which the probiotic strains reside in the oral cavity sustaining conditions of constant salivary & gingival crevicular fluid washings and the rapid turnover of the tissues.

Several observations suggested that permanent or long term colonization of probiotic strains in the oral cavity demands a routine usage of probiotic formulations.<sup>[32]</sup>

Latency time of probiotic *S. salivarius* K12, 4 tablets/day for 3 days, was assessed in the oral cavity in a 35-day follow-up, by Horz et al. (2007).<sup>[67]</sup> Probiotic could be found on oral mucous membrane, tongue and in stimulated saliva for more than 3 weeks, with a gradually reduced *S. salivarius* K12 level being detected beginning 8 days after treatment withdrawal.

## COMMERCIAL PROBIOTIC FORMULATIONS

### Gum Periobalance

This is probably the first probiotic specifically formulated to fight against periodontal disease marketed by Sunstar, Etoy, Switzerland. It contains a patented combination of two strains of *L. reuteri* specially selected for their synergistic properties in fighting cariogenic bacteria and periodontal pathogens. Each dose of lozenge contains at least  $2 \times 10^8$  living cells of *L. reuteri* Prodentis. Single daily dosage every day, either after a meal or in the evening after brushing their teeth would be recommended, to allow the probiotics to spread throughout the oral cavity and attach to the various dental surfaces.

### PerioBiotic

PerioBiotic™ Toothpaste is a mild, non-irritating and fluoride-free toothpaste. It contains Dental-Lac™, a patent pending functional *Lactobacillus* dental hygiene probiotic. Research on Dental-Lac™, a specific *Lactobacillus paracasei* strain, demonstrates its ability to kill off harmful strains of oral bacteria including *Streptococcus mutans*, a significant contributor to dental caries, tooth decay and periodontal disease.

In addition, PerioBiotic™ contains two active ingredients that have been shown in research to promote dental and oral health via their cavity-fighting abilities: xylitol and calcium glycerophosphate.

### Bifidumbacterin, Acilact , Vitanar ( marketed by Alfarm Ltd., Moscow, Russia)

This probiotic preparation is a complex of five live lyophilized lactic acid bacteria, claimed to improve both clinical and microbiologic parameters in gingivitis and mild periodontitis patients.<sup>[38]</sup> After routine mechanical debridement, 2 tablets to be dissolved in the mouth, three times a day for 20-30 days for improved outcome.

**Wakamate D (Wakamoto Pharmaceutical Co., Tokyo, Japan)**

This probiotic tablet contains  $6.5 \times 10^8$  colony forming units (CFU) per tablet of *Lactobacillus salivarius* WB21 and xylitol (280 mg/ tablet) was originally prepared to contribute for the intestinal microbial balance by providing acid tolerant *L. salivarius* WB21.

**Prodentis (BioGaia, Stockholm, Sweden)**

This probiotic lozenge<sup>[55]</sup> is a blend of two *Lactobacillus reuteri* strains containing a minimum of  $1 \times 10^8$  colony forming units (CFU) for each of the strains DSM 17938 and ATCC PTA 5289.

**Bion**

A combination of pre & probiotic commercially available in Indian market has 0.48 billion spores of *L.bifidum* & *S.thermophilus*, 0.10 billion spores of *Sacharomyces boulardi* along with 300mg of fructo-oligosacharides. It is prescribed as a single dose daily before food in the morning.

**ADVERSE REACTIONS**

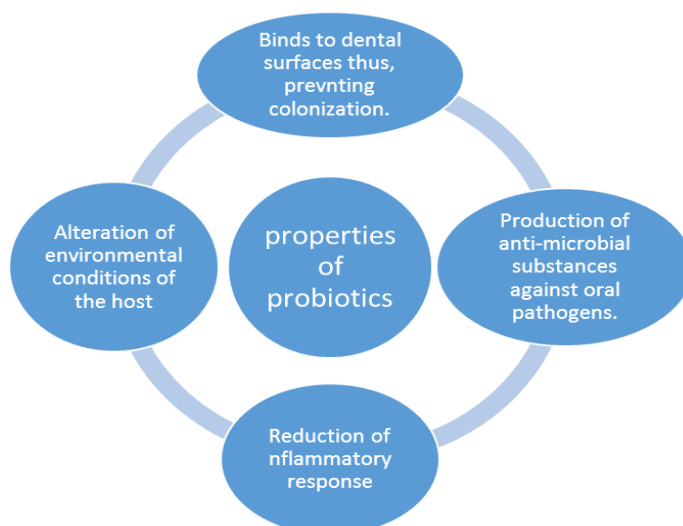
Although no serious adverse events have been described in clinical trials, systemic infections associated with specific probiotics have been noted.

Some cases of bacteraemia and fungemia have been reported in immunocompromised individuals in gut syndrome and chronic diseases. *Lactobacillus endocarditis* was reported after dental treatment in a patient taking *L. rhamnosus*.<sup>[68]</sup>

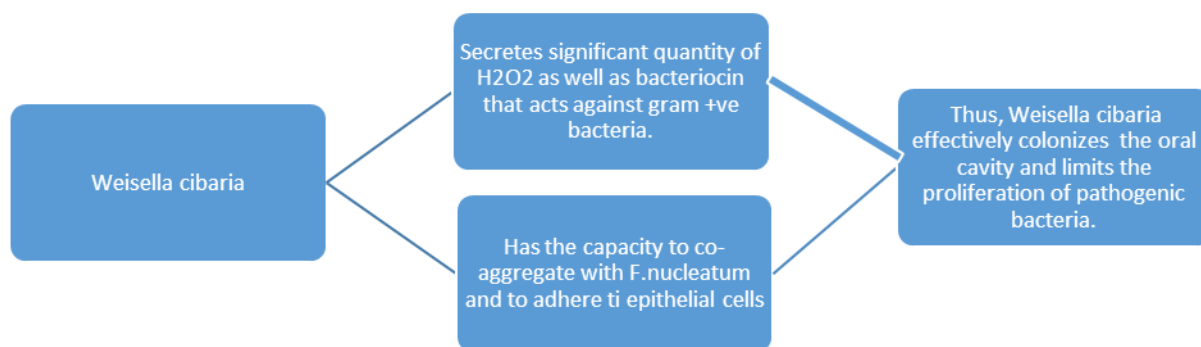
Liver abscess was reported in an individual on *L. rhamnosus* GG.<sup>[69]</sup>

Stimulation of immune system by probiotics showed degradation in autoimmune diseases, and transferred antibiotic resistance to pathogens.<sup>[68]</sup>

Hence, it is clear that careful selection of the strain to be ingested for a particular disease is important, and the mode and time of the administration as well as the age of the subject taking probiotics is crucial.



**Fig 1: Mechanism of action of probiotics**



**Fig 2: Host beneficial properties of Weisella**

## CONCLUSION

The oral cavity with a well maintained balance of different species may be a potential source for health-promoting probiotic bacteria. The use of probiotics in oral care applications is gaining momentum. In today's world, it would be the right time to change the way bacteria are treated. There is increasing evidence that the use of probiotic strains can deliver oral health benefits. Probiotics, counterparts of antibiotics are free from issues of developing resistance and being body's own resident flora are most easily accepted by the host.

In conclusion, the presently available literature suggests that probiotics might offer opportunities to modify the etiopathogenesis and secure periodontal health by either direct microbiological interactions or by immunomodulatory interactions.

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