ejpmr, 2017,4(06), 413-424

SJIF Impact Factor 4.161

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

PROBIOTICS - A BOON TO PREVENTIVE DENTISTRY!

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Article Received on 27/03/2017 **Article Revised on 17/04/2017** **Article Accepted on 07/05/2017**

ABSTRACT

Probiotics utilize the naturally occurring bacteria so as to confer health benefits. Several studies have suggested the probiotics use for oral health purposes. Although these organisms are naturally present in food and water, they can also be added to some foods because of their beneficial effects on human health. The aim of this review is to understand the actual mechanism of action of probiotic bacteria in the oral cavity and summarize their observed effects with respect to oral health.

KEYWORDS: probiotics**,** dental caries**,** periodontal diseases.

INTRODUCTION

The normal microflora of intestine is considered to be metabolically active but as yet unexplored organ of the host defense.[1] Before birth, the gastrointestinal tract is sterile but as the newborn child is exposed to bacteria in the environment and in the diet, the colonization process begins.[2] During and shortly after birth, the epithelial surfaces in the oral cavity become colonized by various species of the native microflora that tend to persist in the mouth, and it is possible that they compete with other bacteria and prevent the growth of those that may colonize later.[3,4] During the first month of life, the importance of diet on bacterial colonization of the gut have been explored and breastfed children are dominated by bifidobacteria and lactobacilli while formula-fed children have more bacteroides, clostridia, and enterobacteriaceae.[5,6] The first bacteria to colonise the colon are facultatively anaerobic strains such as Escherichia coli and streptococci. The type of bacteria that subsequently colonise the gut depends largely on the feeding habits of the infant. Breast-fed infants usually develop a different gut flora to those on formula feeds.[7,8] A major reason for this difference may be that breast milk contains a 'bifidus' factor i.e. glycoprotein containing glucose, galactose, fructose and N-acetyl glucosamine, which stimulates the growth of specific bifidobacteria at the expense of other species present in milk.[9,10] An early installation and colonization of probiotics in the oral environment would be the first step for possible long-term success, but there are limited data available to support this event.[11] Hence, they are viable bacteria that are beneficial for the host by improving its intestinal microbial equilibrium.[12,13] Probiotic bacteria are natural inhabitants of the intestinal flora and majority of the strains and species are taken from healthy humans although there are some which originate from fermented food.[14] Probiotics, literally meaning 'for life', microbes which exert health-promoting influences in mammals.[15] Probiotics may modify the microbial balance of the host by reducing the overgrowth of the pathogens. New methods such as probiotics to replace pathogens of the microflora by using harmless bacteria are now being widely used to combat infections.[16] Current time demands treatment by the elimination of specific bacteria as well as alteration in bacterial ecology by using probiotics.[17] In fact, the findings may support a “metabolic summative effect” in which probiotic therapy is a connecting link between oral and general health; the oral cavity is influenced by general health.[18,19] The first species introduced into probiotic research were Lactobacillus acidophilus and Bifidobacterium Bifidum and a number of potential health benefits have been suggested such as reduced susceptibility to infections, reductions in allergies, and lactose intolerance, as well as regulation of blood pressure and serum cholesterol values.[20] A combination of strains can enhance adherence in a synergistic manner.[21] Probiotics, in particular, are known to have a role in prevention or treatment of some diseases.[22]

Definitions

In 1965, Lilly and Stillwell[23] defined probiotics as "Substances produced by microorganisms that promote the growth of other microorganisms."

In 1974, Parker[24] termed probiotics as "Organisms and substances that contribute to intestinal microbial balance."

In 1989, Fuller[25] defined probiotics as "A live microbial feed supplement that beneficially affects the host animal by improving its intestinal microbial balance."

In 1992, Havenaar and Huis Int Veld[26] changed the concept of probiotics as "A viable monoculture or mixed-culture of microorganisms that, when applied to animal or human, benefits the host by improving the properties of the native microflora."

In 1996, Schaafsma[27] defined probiotics as "Living microorganisms that, when ingested in a certain amount, exert health benefits beyond inherent basic nutrition."

In 1999, Naidu et al.[28] termed probiotics as "A microbial dietary adjuvant that beneficially affects the physiology of host, by modulating mucosal and systemic immunity, as well as by improving nutritional and microbial balance in the intestinal tract."

In 2001, Schrezemeir and de Vrese[29] defined probiotics as "A preparation or substance with suitable microorganisms in ample amount, which modify the microflora (by implantation or colonization) in a compartment of the host and as such exert benefit to the host."

In 2001, World Health Organization (WHO) and the United Nations Food and Agriculture Organization (FAO) report[30] defined probiotics as "Live microorganisms that, when taken in adequate amounts, confer a health benefit to the host."

In 2002, Marteau et al[31] defined them as "microbial preparations or cells components of microbes that have health benefits and well-being."

The oral cavity is an ecosystem with rich and diverse micro biota in it. There is a lot of metabolic activity taking place in the oral cavity. (Figure 1)[24,32]

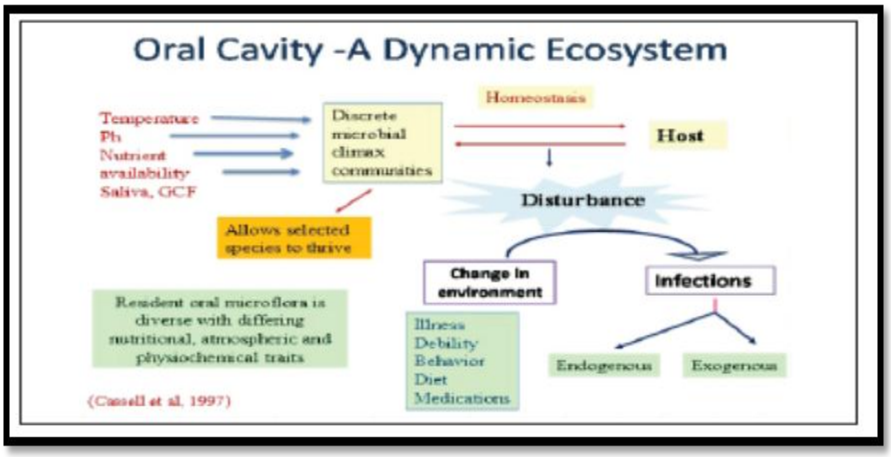

Figure 1: showing Oral cavity - a complex ecosystem.

A dental disease is observed even with a slight alteration in local environment. This promotes the potential pathogens to compete and take this advantage under appropriate conditions. Then, the pathogens increase in great numbers to predispose a site to disease. The probiotic method which may be very effective in removal of pathogenic microbes from the oral cavity.[25,33] An essential condition for a microorganism to act as an oral probiotics is its capacity to adhere to and colonize various surfaces of the oral cavity.[34]

A good probiotic agent needs to be non-pathogenic, nontoxic, and resistant to gastric acid, adhere to gut epithelial tissue and produce antibacterial substances.[25] (Figure:2).

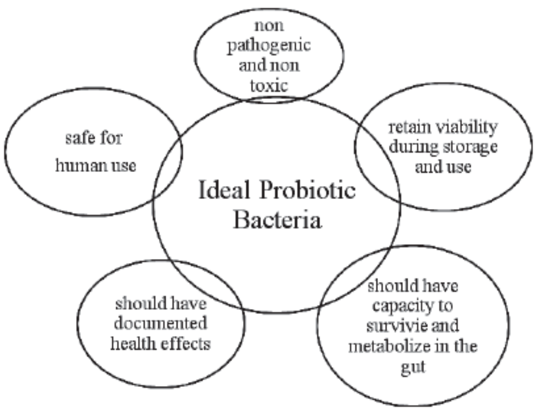

Figure 2: Characteristics of Ideal probiotic bacteria

History

The concept of useful microorganisms to promote health is very old and can even be traced back to the classical Roman literature where food fermented with microorganisms was used as a therapeutic agent.[35]

Figure 3: Elie Metchnikoff (1845–1916)

The modern history of probiotics dates back to 1877, when Pasteur and associates noted the growth of anthrax bacilli in co-cultures.[36] The idea of probiotics was given by Ukrainian bacteriologist and Nobel Laureate Ilya Metchnikoff (1908), while studying the flora of the human intestine, he developed a theory that senility is caused by certain poisoning body 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 and which was well-received. Probiotic organisms are thought to act through a variety of mechanisms including the competition with potential pathogens for nutrients or for adhesion sites, including toxins degradation, formation of antimicrobial products, and local and systemic immunomodulation.[37-39] Metchnikoff proposed that the lactic acid-forming strain Lactobacillus bulgaricus is able to replace pathological intestinal microbiota. He suggested that 'the dependence of the intestinal microbes on food makes it possible to adopt measures to alter the flora in our bodies and to override the harmful microbes by useful microbes'.[23] (Figure 3)[40] Henry Tisser, who also worked at the Pasteur institute, isolated a bacterium named Bacillusbifidus communes, which was later reclassified as to the genus Bifidobacterium.[41] He observed that children with diarrhea had in their stools a low number of these bacteria characterized by a unique, Y shaped morphology. On the contrary, these "bifid" bacteria were abundant in healthy children. He suggested that these bacteria could be administered to patients with diarrhea to help restore a healthy gut flora.[20] In 1917, Professor Alfred Nissle, Germany, isolated a strain of Escherichia coli from the feces of soldiers who remained healthy despite the fact that most of their comrades suffered from diarrhea.[42] Later, in 1935, certain strains of Lactobacillus acidophilus were found to be active when implanted in the human digestive tract.[43] The term 'probiotics', the exact opposite of term 'antibiotics', was introduced in 1965 by Lilly and Stillwell. They showed that several species of protozoa, during their slower rate of growth, produce substances that prolong the growth among other species.[25] Lactobacillus rhamnosus GG, ATCC 53103 (LGG), is the most widely studied probiotic bacterium. It was originally found in human intestine in 1985 and named after its discoverers, those were Sherwood Gorbach and Barry Goldin.[44] The importance of living cells in probiotics was emphasized by Fuller, in 1989.[33] In the following decades, intestinal lactic-acid bacterial species with alleged health promoting properties were introduced as probiotics, emphasising the beneficial effects on the host.[45]

Composition

Probiotics contain mostly strains of genera Lactobacillus and Bifidobacterium. Lactobacillus species from which probiotic strains have been isolated include L. acidophilus, L. johnsonii, L. casei, L. rhamnosus, L. gasseri, and L. reuteri. Bifidobacterium strains consisted of B. bifidum, B. longum, and B. infantis.[11,46-48] There are different probiotic strains available as shown in [Table 1][49]

Table 1: Different probiotic strains

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

Another probiotic species, Bifidobacterium DN-173 010, when consumed once daily with yogurt showed a significant reduction of salivary S. mutans, whereas no significant reduction was found in lactobacilli levels.[47] Polonskaya was the one who first described that probiotics such as Lactobacillus acidophilus strains may inhibit the in vitro growth of other bacteria.[50] Nikawa et al. reported that consumption of yoghurt containing Lactobacillus reuteri (L. reuteri) for 2 weeks lowered the concentration of S. mutans in the saliva by up to 80%.[48] In a study done by Nase et al. they found that children consuming milk containing probiotic, particularly those

3-4 years of age, had smaller number of dental caries and low salivary counts of S. mutans than controls. These promising results suggest a potentially beneficial application of probiotics for the prevention of dental caries.[46] It has been suggested that the invasive operative caries treatment might be challenged by probiotic approach with subsequent less invasive intervention in clinical dentistry.[51]

The first one is the concentrated culture added to a beverage or food such as fruit juice. The second one is the probiotics inoculated into prebiotic fibres. The third one is that probiotic inoculated into a milk-based food or dairy products such as milk, milk drink, yoghurt, yoghurt drink, cheese, kefir, biodrink. The last one is that the concentrated and dried cells packaged as dietary supplements or non-diary products such as power, capsule, gelatin tablets.[32] Cheese might indeed be an ideal vehicle for administering probiotics to humans for purposes of promoting oral health.[52,53] Eating cheese enhances remineralization and prevents demineralization of enamel and may lower the cariogenic S. mutans levels in saliva.[54] There are various means of probiotic administration for oral health purposes as shown in (Table 2)[32] and different test strains considered as probiotics (Table 3)[32]

Table 2: Different means of probiotic administration for oral health purposes

Vehicle	*Strain*	*Outcome*	*Reference*
Lozenge	*S. salivarius*	Reduces oral VSC levels	Burton *et al* (2005)
Straw, tablet	*L. reuteri* ATCC 55 730	*S. mutans* level reduction	Çaglar *et al* (2006)
Yoghurt	*Bifidobacterium* DN-173 010	Reduction of salivary *S. mutans*	Çaglar *et al* (2005b)
Cheese	*L. rhamnosus* GG; *Prorionibacterium* JS	Reduced risk of high yeast counts and hyposalivation	Hatakka *et al* (2007)
Rinse solution	*W. cibaria*	Reduction of VSC	Kang *et al* (2006)
Capsule, liquid	*L. sporogenes, L. bifidum, L. bulgaricus, L. thermophilus, L. acidophilus, L. casei, L. rhamnosus*	Increased salivary counts of lactobacilli without significant decrease in *S. mutans* counts	Montalto *et al* (2004)
Yogurt drink	*L. rhamnosus* GG	Temporary oral cavity colonization	Yli-Knuuttila *et al* (2006)

Table 3: Test strains considered probiotics in the oral cavity

Test strain	*Reference*	*Type of experiment*	*Feature tested*	*Result*
S. salivarius	Burton *et al* (2006a)	*In vivo*	Reduction of VSC	Reduced VSC levels
L. rhamnosus GG *L. acidophilus* *L. casei*	Busscher *et al* (1999)	*In vitro* *In vivo*	Inhibition of *S. mutans*	Positive correlation to *S. mutans* inhibition
L. reuteri	Çaglar *et al* (2006)	*In vivo*	Inhibition of *S. mutans*	Reduced *S. mutans* levels
Bifidobacterium DN-173 010	Çaglar *et al* (2005a)	*In vivo*	Inhibition of *S. mutans*	Reduces levels of caries pathogens
L. rhamnosus GG *Propionibacterium freudenreichii* ssp. *shermanii* JS	Hatakka *et al* (2007)	*In vivo*	Inhibition of *C. albicans*	Reduce high yeast counts
L. rhamnosus *L. paracasei* *L. johnsonii*	Haukioja *et al* (2006a)	*In vitro*	Adherence Survival in saliva	Better adherence than bifidobacteria
L. rhamnosus GG *L. casei* *L. reuteri*	Haukioja *et al* (2006b)	*In vitro*	Inhibition of *S. mutans*	Inhibit *S. mutans* adhesion to salivary pellicle
W. cibaria	Kang *et al* (2005)	*In vitro*	Adherence	S-protein positively affects adhesion
W. cibaria	Kang *et al* (2006)	*In vivo*	Reduction of VSC	Inhibited production of VSC
L. casei Shirota *L. acidophilus*	Lima *et al* (2005)	*In vitro*	Adhesion	Different pattern of adhesion according to the test strain
L. rhamnosus GG	Yli-Knuttila *et al* (2006)	*In vivo*	Adherence	Only temporary colonization in oral cavity

Dairy products supplemented with probiotics are a natural means of oral administration and easily adopted in dietary regime.[32] A formulation of approximately 10^8 probiotic bacteria per gram or millilitre with daily intake of 1.5–2 dL is recommended and the dairy products should preferably be nonsweetened and contain only natural sugar.[55] Stecksén-Blicks[56] C 2009, studied effect of long-term consumption of milk supplemented with probiotic lactobacilli and fluoride on dental caries and general health in preschool children. Similarly Caglar Esber[57] 2005, showed in his study that probiotic bifidobacteria in yogurt may reduce the levels of selected caries-associated micro-organisms in saliva. Chinnapa Anitha[58] et al 2013, compared mutans streptococci levels in saliva, before and after consumption of probiotic ice-cream and curds. Thereby, several authors arrived at the conclusion that probiotic products could act as a possible substitute for dislodging pathogenic microorganisms by probiotic bacteria and can prevent enamel demineralization. Twetman Svante[59] 2008, concluded that daily consumption of ice-cream containing probiotic bifidobacteria may reduce the salivary levels of mutans streptococci in young adults. In a study addressing the survival of bacteria in saliva and their adherence to oral surfaces, Haukioja et al tested the colonization potential of different commercially available probiotics in which Lactobacillus and Bifidobacterium strains were formed from the dairy industry. The results cast light on several controversial points reflecting mechanisms of colonization in the oral cavity. All test strains demonstrated 24-h survival rates in saliva but their binding capacity to the saliva-coated surfaces varies among different strains. Lactobacilli showed better adherence than bifidobacteria. Because of that lactobacilli may compete for the same binding sites on saliva coated hydroxylapatite with F.nucleatum which explains their lower colonization capacity. This tendency indicates that probiotics might affect the oral biofilms and modify resident microflora. He defined a novel mechanism whereby lactobacilli and B. lactis Bb12 affected the composition of salivary pellicle on hydroxyapatite and thereby inhibited S. mutans adherence in vitro.[60,61] A specially designed straw with a reservoir containing probiotics has also been presented by Caglar et al who compared two non-dairy delivery methods, a Life top straw (BioGaia AB, Stockholm, Sweden) and a lozenge on the effectiveness of L. reuteri to reduce the number of S. mutans. Both ways of consumption showed significant reduction in salivary S. mutans levels in half of the patients when compared with subjects who received placebo. Caries prophylaxis with chewing gum containing L. reuteri Prodentis is also recommended. Consumed twice daily this was marketed to regulate S. mutans counts in the oral cavity.[33]

C. Holz[62] et al, did a randomized, an in vivo study of three groups examined the short-term effect on ingestion of sugar-free candies containing 0 (placebo), 1 or 2 mg/candy piece of heat-killed L. paracasei DSMZ16671 on salivary mutans streptococci counts before and after consumption of the candies.

Mechanism of action of probiotics

Probiotic organisms act through a variety of potential mechanisms

a) Compete with potential pathogens for nutrients and growth factors or enterocyte adhesion sites and involved in altering the pH of the gut.
b) Disintegration of toxins, production of antimicrobial substances, and antioxidants.
c) And local and systemic immunomodulation, by stimulating T-lymphocytes for replication. Develops a mucosal barrier, activates immune system, forms short chain fatty acids, helps in the metabolism of bile acids, and also synthesis vitamins.[33]

Potential mechanism of probiotic bacteria is (Figure 4)[63]

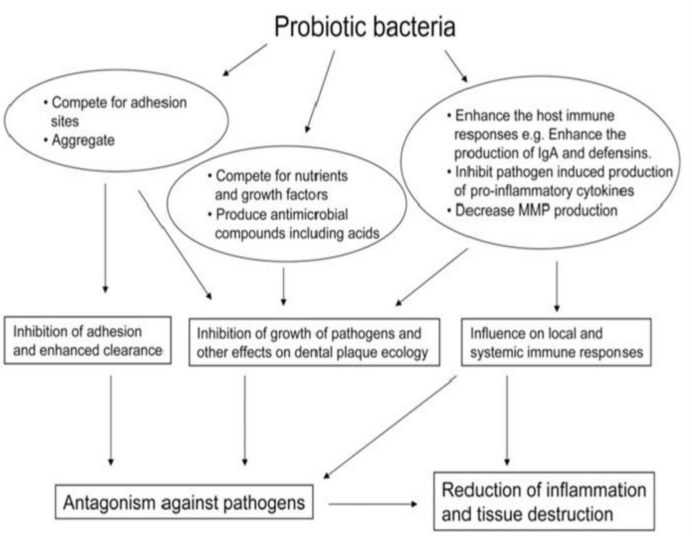

Figure 4: Potential mechanisms by which probiotic bacteria could affect oral health

Basically, probiotics help in binding oral microorganisms to proteins and biofilm formation. They inhibit plaque formation through its complex ecosystem by compromising bacterial attachments.[64] Probiotics have been shown to normalize an increased permeability. Binding is considered to be the initial stage in pathogenesis, and binding of bacteria to the intestinal mucosa or mucus may allow the colonization.[65-67] Probiotics compete with pathogens for binding sites and available substrates, however.[68,69] Adhesion to the intestinal mucosa is considered important for the beneficial health effects.[67,70] The mechanism of adhesion to oral surfaces is an issue of importance for the long-term probiotic effect of the microorganisms.[64]

Fusobacterium nucleatum plays an important role as a bridge-organism that facilitates the colonization of other bacteria by co-aggregation.[71] Many authors have reported that the co-aggregation abilities of lactobacilli species might form a barrier that prevents colonization of pathogens, through inhibiting substances were generated by Lactobacillus species.[72,73] The indirect interactions of probiotics are effective in the process of removing harmful bacteria and stabilizing normal conditions. Probiotics regulate permeability and help to develop colonies in oral microflora with less pathogenic species.[14,24,32,60,74-75] Modulation of host immune response - Probiotics strengthen the immune system and help prevent disease. Probiotics stimulate dendritic cells resulting in expression of helper T cell (Th1) response, which modulates immunity.[76] One mechanism of action of probiotics is suggested to be their modulation of host immune response. Immune inductive sites in the oral cavity are within the diffuse lymphoid aggregates of the Waldeyer's ring.[77] Dendritic cells scattered in mucosal surfaces are pivotal in the front-line bacterial recognition (antigen presentation) and in activating T-cell responses.[78]

Lactobacilli are highly acidogenic and aciduric, and grow optimally under slightly acidic environment. They are considered a part of the normal oral flora and comprise about 1% of the cultivable species.
Bifidobacteria is present in small amounts in the normal oral biofilm. It is important to emphasise that all lactic acid bacteria (or bifidobacteria) are not probiotics and does not possess the ability to confer health benefits for the host.[79] Hypothetical mechanisms of probiotic action in the oral cavity (figure 5)[80]

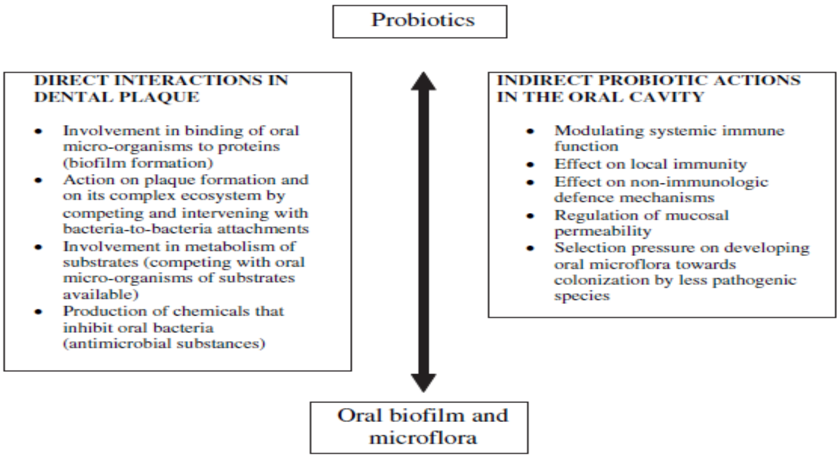

Figure: 5 Hypothetical mechanisms of probiotic action in the oral cavity.

Probiotics and dental caries

Regarding caries, a periodic consumption of fermentable carbohydrates can lead to an acidic environment which favors certain microflora, e.g. mutans streptococci and lactobacilli, reducing the biofilm diversity and resulting in enamel demineralization.[19] First, lactobacilli in general are hardly involved in the initiation of cavities. Second, not all Lactobacillus spp. have a caries-inducing effect.[81] In the oral cavity, bifidobacteria are prevalent in deep caries lesions and may play an important role in the progression of caries.[82]

Streptococcus mutans has been considered as one of the major virulent of the caries-producing microorganisms. It can colonize the tooth surface and initiate plaque formation by its ability to form extracellular polysaccharides from sucrose, in the presence of enzyme glucosyltransferase, usually through water-insoluble glucan, Inhibiting colonization of S. mutans on the tooth surface is believed to prevent the formation of dental plaque and development of dental caries.[83] Juneja[84] A et al 2012, evaluated the changes in mutans streptococci counts in saliva after short term probiotic intervention and its delayed effects on salivary mutans streptococci count. With in dentistry, studies with L. rhamnosous GG, L. reuteri have proven their potential in interacting with S. mutans by lowering the number of caries pathogen, thus suggesting a role of probiotics in caries prophylaxis.[85-87] Lactobacillus rhamnosus GG and L. Casei[88,89] have proved their potential to hamper growth of oral streptococci. Definite S. mutans count reduction after a 2-week consumption of yoghurt containing L. reuteri. A temporary reduction in S. mutans was observed during the periodic intake of yogurt and few days after cessation of consumption, indicating the necessity of continual probiotic use in order to achieve an effect.[32] First, probiotic bacteria must attach to the tooth surface where cariogenic bacteria reside. Secondly, they must become a part of the biofilm that develops on teeth. Finally, they must compete with cariogenic bacteria. All this process helps to show how probiotic effect against carries by drastic reduction of the levels of cariogenic bacterial growth.[30] A new promising approach to preventing dental caries is thus by upsetting the cariogenic biofilm by the use of probiotics also referred to as Replacement therapy.[23] Polonskaya[50] first described the phenomenon that probiotics such as Lactobacillus acidophilus strains may inhibit the vitro growth of other bacteria. In a study addressing the survival of bacteria in saliva and their adherence to oral surfaces, tested the colonization potential of several probiotics which are commercially available and various Lactobacillus and Bifidobacterium strains obtained from the dairy industry. The results cast light on several controversial points reflecting mechanisms of colonization in the oral cavity. All test strains demonstrated 24-h survival rates in saliva but their binding capacity varies to the saliva-coated surfaces. Lactobacilli showed better adherence property than bifidobacteria. Thereby, lactobacilli may compete with F. nucleatum for the same binding sites on saliva coated hydroxylapatite which explains their lower colonization capacity. This fact indicates that probiotics might affect the formation of oral biofilms and modify resident microflora. He defined a novel mechanism whereby lactobacilli and B. lactis Bb12 affected the composition of salivary pellicle on hydroxyapatite and thereby inhibited S. mutans adherence in vitro.[6162] When combination of fluoride and probiotic bacteria are consumed they seemed more potent than the probiotic supplement or fluoride consumed separately.[90]

Probiotics and periodontal disease

The probiotics was used primarily for enhancing oral health in the treatment of periodontal inflammation.[91] Various authors concluded probiotics effect on periodontal health (Figure 6)[92]

Study	No. of participants	Age range (years)	Strain	Vehicle, time	Authors' conclusion
Hallström et al	18	–	*L reuteri* ATC 55730 and *L reuteri* ATC PTA 5289	Tablets, 3 wk	During experimental gingivitis, daily intake of probiotic lozenges did not significantly affect the PI, GI, and BOP measurements.
Iniesta et al	40	20–24	*L reuteri* DSM 17938 and *L reuteri* ATC PTA 5289	Tablets, 8 wk	No clinical impact of the probiotic use in gingivitis patients could be demonstrated concerning PI and GI.
Krasse et al	59	–	*L reuteri* (2 formulas)	Chewing gums, 2 wk	In patients with moderate to severe gingivitis a significant reduction in PI for both probiotic groups was shown in contrast to no reduction in the placebo group. In one of the probiotic groups a significantly higher reduction of the GI compared with the placebo group was shown.
Riccia et al	26	24–51	*L brevis*	Lozenges, 4 d	With the use of the probiotic lozenges all clinical parameters (GI, PI, BOP, calculus, and temperature sensitivity) decreased significantly in periodontitis patients.
Shah et al	30	14–35	*L brevis*	Lozenges, 2 wk	The administration of a probiotic tended to lead to a significant decrease in PI, GI, PPD, and CAL at 2 mo in aggressive periodontitis patients.
Shimauchi et al	66	–	*L salivarius* WB21	Tablets, 8 wk	GI, PI, and BOP scores were improved after intervention, but no significant differences between placebo and probiotic group could be shown.
Slawik et al	28	20–33	*L casei* strain *Shirota*	Milk drink, 4 wk	Daily consumption of a milk drink reduces the effect of plaque-induced gingival inflammation associated with a higher plaque score due to the high carbohydrate content of the probiotic milk drink.
Staab et al	50	–	*L casei* strain *Shirota*	Milk drink, 8 wk	Beneficial effect of the probiotic milk drink on gingival inflammation in experimental gingivitis patients.
Szkaradkiewicz et al	38	31–46	*L reuteri* ATC PTA 5289	Tablets, 2 wk	Improved clinical parameters (GI, PPD, CAL) after probiotic use in chronic periodontitis patients. The measurements in the probiotic group were significantly lower than in the control group.
Teughels et al	30	–	*L reuteri* DSM 17938 and *L reuteri* ATC PTA 5289	Tablets, 12 wk	Significantly more pocket depth reduction and attachment gain in the moderate and deep pockets in the probiotic group when compared with the control group.
Twetman et al	38	–	*L reuteri* ATC 55730 and *L reuteri* ATC PTA 5289	Chewing gums, 2 wk	BOP improved statistically significantly after probiotic usage.
Vicario et al	20	44–65	*L reuteri* ATC 55730 and *L reuteri* ATC PTA 5289	Tablets, 4 wk	Probiotic usage improved PI, BOP, and PPD in non-smoking patients with initial-to-moderate chronic periodontitis. In the control group no statistically significant changes could be shown.
Vivekananda et al	30	35–50	*L reuteri* DSM 17938 and *L reuteri* ATC PTA 5289	Lozenges, 3 wk	In chronic periodontitis patients PI, GI, GBI, PPD, and CAL were significantly more reduced in the patients where scaling and root planing were supplemented with a probiotic compared with scaling and root planing alone.

–, not reported/only mean age reported; BOP, bleeding on probing; CAL, clinical attachment level; GBI, gingival bleeding index; GI, Gingival Index; PI, Plaque Index; PPD: probing pocket depth.

Figure: 6 Various authors concluded probiotics effect on periodontal health

Another issue in oral pathology, chronic periodontitis, could also benefit from orally administered probiotics. Decreased gum bleeding and reduction in gingivitis has been observed with the application of L. reuteri. It was reported that resident lactobacilli flora inhibits the growth of Porphyromonas gingivalis and Prevotella intermedia in 82% and 65%, respectively.[17,93] Probiotics lower the pH so that microorganisms cannot form dental plaque and calculus that cause oral inflammation. Antioxidants intercept stain and plaque formation by neutralizing the free electrons which are essential for mineral formation.[83] Teughels[94] et al. reported that the subgingival application of preparation which includes Streptococcus sanguis, Streptococcus salivarius, and Streptococcus mitis after scaling and root planning significantly suppressed the re-colonization of Porphyromonagulae (canine P. gingivalis) and P. intermedia in a beagle dog model. The use of probiotic chewing gum containing L.reuteri ATCC 55730 and ATCC PTA 5289 also decreased levels of pro-inflammatory cytokines in GCF,[95] and the use of L. brevis decreased MMP (collagenase) activity and other inflammatory markers in saliva. B. subtilis seemed to reduce the number of periodontal pathogens.[96] Periodontal dressings with Probiotics containing optimal concentration of 10^8 CFU $ml)^{-1}$ were shown to reduce the number of most commonly isolated periodontal pathogens: Bacteroides sp., Actinomyces sp. And S. intermedius, and also C. albicans.[97] Other studies using Lactobacillus species (L brevis, L salivarius WB21) show significant decreases in gingivitis and plaque index when the results at the end of the probiotic usage are compared to baseline data.[98-100] S.oralis (previously called S.Sanguis type II) and S.uberis are common in healthy periodontal subjects and diminish in number where periodontal pathogens are abundant. The use of a probiotic compound containing S.oralis and S.uberis inhibit the growth of periodontal pathogens by producing hydrogen peroxides. These have two beneficial effects; one being that they whiten the teeth and additionally they also oxidize volatile sulfur compounds produced by bacteria which are responsible for halitosis.[101] The possible mechanism in the VSC reduction is the production of hydrogen peroxide which is formed by W. cibaria that prevents the proliferation of F. nucleatum. Streptococcus salivarius, can also be used as an oral probiotic, has shown inhibitory effect on VSC by competing for colonization sites with species causing an increase in levels of VSC and further reported that S. salivarius strain K12 produced two lantibiotic bacteriocins, compounds that prevent development of gram-positive bacteria which are said to be responsible for halitosis.[102-104] They have great potential for the control of halitosis and prevention of several other oral bacterial infections.[105] Kang[106] et al have shown a definite inhibitory effect on production of volatile sulphur compounds by F. nucleatum after ingestion of W. cibaria both in vitro and in vivo. Beneficial Effects of probiotics on periodontal health (Figure 7)[107]

Evidence	Studied by
Streptococcus oralis and S. Uberis have been shown to inhibit the growth of pathogens both in vitro and in vivo. The presence of these organisms is an indicator of good periodontal health.	Hillman JD et al 1985
On oral administration of Lactobacillus salivarius in tablet form, it was inferred that plaque index and probing pocket depth was reduced in patients who were smokers when, compared to a placebo group.	Shimauchi H et al 2008
Subgingival application of beneficial bacteria S. sanguis, S. salivarius, S. mitis, has been shown to delay re-colonization by periodontal pathogens, reduce inflammation and improve bone density and bone levels in beagle dogs.	Teughels W et al 2007
Bdellovibriobacteriovorus, 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.	Van Essche M et al 2009
Probiotic mouth rinse is effective in reducing plaque accumulation and gingival inflammation.	Harini PM et al 2010
L.reuteri Prodentis lozenges when consumed showed plaque inhibition, anti-inflammatory, and antimicrobial effects. The study proposed that probiotics could serve as a useful adjunct or alternative to periodontal treatment when scaling and root planing might be contraindicated.	Vivekananda MR et al 2010
Routine intake of lactic acid foods may have a beneficial effect on periodontal disease.[10]	Shimazaki Y et al. 2008
Probiotic strains overall showed a stronger inhibition of the periodontal pathogens, and these observations underline the therapeutic potential of applications that stimulate oral health by the application of beneficial effector strains.[11]	Van Essche M et al 2013
Probiotic supplementation (i) reduces attachment and alveolar bone loss in rats with periodontitis and (ii) can protect the small intestine from reactive changes induced by periodontitis.[12]	Messora MR et al 2013
Probiotics lower the pH so that plaque bacteria cannot form dental plaque and calculus that causes the periodontal disease.[13]	Patil SS 2011

Figure 7: Beneficial Effects of probiotics on periodontal health

Future perspectives

The use of probiotics is an emerging area of research in the field of oral healthcare. One ambitious and promising example is the generation of an S. mutans strain with a complete deletion of lactate hydrogenase which significantly reduced cariogenicity.[108] High titers of antibodies against human cariogenic bacteria, S. mutans and S. sobrinus, were produced in bovine colostrum by a vehicle of fermented milk. [64] Another option could be to enhance the properties of a potentially beneficial strain. One example is the construction of an L.paracasei strain with a functional scFV (single chain variable fragment) antibody binding to the surface of Porphyromonas gingivalis.[109]

CONCLUSION

Literature reveals that specific strains of probiotic microorganisms confer benefits to the health of the host and are safe for human use. However, considerable work is required to affirm the benefits of probiotics. Probiotics are, nevertheless, a new, interesting field of research in oral microbiology and oral medicine. The research is still in the initial stage. The idea of probiotics casts new light on the connections between diet and health, including oral health.

Probiotics can be used with caution in immunocompromised patients, and contraindicated in premature infants and patients with central venous access in place. Finally, possibilities to genetically modify or engineer potential probiotic strains may offer totally new visions need to be studied.

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