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Review Article

The Use of Probiotics in Prevention and Treatment of Oral Diseases

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Abstract

Objectives: The use of probiotics is in management and prevention of many systemic diseases is a well-known medical practice, while the use of probiotics in dentistry is not yet well recognized. The aim of this study is to present a review that describes the role of probiotics in prevention and management of oral diseases, including caries, periodontal diseases and other intra oral pathological conditions.

Data/Sources: The authors conducted searches through the following sources: Pub Med, Cochrane, and Researchgate. The used search terms were: probiotics, oral diseases, dental caries and periodontal diseases. No restrictions were made on language or date of publishing.

Study Selection: Original articles discussing the use of probiotics in management and prevention of oral diseases including caries and periodontal diseases were selected for review in this study. A thorough review of each article was performed by the authors and a description of probiotics, mechanisms of action, and current uses of Probiotics as oral therapeutics, safety of use and future requirements are presented.

Conclusion: As further research regarding the proper strains, doses and vehicles is needed, the use of probiotics in dental practice shows high potentials and is a promising treatment modality in management and prevention of various oral diseases.

Keywords: *Probiotics; Symbiosis; Caries Prevention; Periodontal Diseases; Oral Diseases*

Introduction

Humans are described as macro-species, who live in symbiosis with microbes which are described as micro-species; however, humans are defined as *Holobionts* while microbes are defined as *Symbionts*. The association between host and *Symbionts* affects the fitness of the *Holobiont* within its environment, and it often governs the physiological homeostasis of the balance between host well-being and dysfunction [1]. Lately, interest has been gained in probiotics and its role in prevention and/or treatment of oral diseases as well as its usefulness in many other medical fields. Probiotic science teaching is sometimes placed within non-traditional, complementary or alternative medicine, depending on the training programmes. Health professionals like chiropractors, naturopaths and herbalists routinely use products that contain probiotics in their practices.

As a definition, the term probiotics was derived from the Greek words, meaning "for life" [16]. In 1960, Lilly and Stillwell introduced the word probiotics as "Substances produced by microorganisms that stimulate the growth of another". Other researchers described Probiotics approach as the modification of a human microbiota by exogenous administration of microbial cells (or cell components), aimed at benefiting the host's health [2]. In 1990 the term Prebiotics was introduced. It was defined as non-digestible food ingredients that beneficially affect the host by selectively stimulating the growth and/or activity of one or a limited number of bacterial species. The combination of both Prebiotic and Probiotic is known as symbiotic which is beneficial to oral health. Since then, several definitions had been proposed, but the currently used definition that is approved by the World Health Organisation (WHO) and the United Nations Food and Agriculture Organisation (FAO) in 2002 is; "Probitics are living microorganisms which when administered in adequate amounts confer a health benefit for the host" [3].

Studying oral microbiology is important for the prevention and treatment of oral pathosis along with other systemic diseases. With the slow progress of isolating new antibiotics coupled with the increase of emerging resistant pathogenic bacteria, it has become imperative to try and enhance the use of living therapeutics. Probiotics form the cornerstone of such biotherapy [4]. Bacteria in the oral cavity have access to the blood stream through gingival crevices, and have been identified as causative agents in a number of systemic diseases; as the association between periodontal diseases and cardiovascular diseases [5]. Also, glycemic control in diabetic patients is adversely affected by periodontal diseases [6]. In addition, studies have found that there is an increased risk for diabetes onset in patients with periodontitis [5]. Other researchers found a correlation between oral bacteria which can cross brain barrier, and Alzheimer's disease [6].

Aim of the Study

The aim of this review was to shed light on the latest uses of probiotics in dental practice.

Data/Sources and Study selection

Searches conducted by the authors included PubMed, Cochrane, Researchgate and Google search. The search terms used were: Probiotics, oral diseases, dental caries and periodontal diseases. No restrictions were made on language or date of publishing. Original articles discussing the use of probiotics in management and prevention of oral diseases including caries and periodontal diseases were selected for this study. A thorough review of each article was performed by the authors and a description of Probiotics, mechanisms of action, and current uses of Probiotics as oral therapeutics, safety of use and future requirements are presented.

Discussion

Criteria of helpful probiotics that can be used in oral therapy

A good probiotic should be a non-pathogenic strain that can benefit a host by being able to withstand low pH of the host's gut in order to stay viable during presentation and storage [7]. Probiotics used for oral health therapy should adhere to oral tissues counteracting pathogenic bacteria without lowering the oral pH while metabolizing sugar [8].

Mechanisms of action for management and prevention of oral diseases

The mechanism of action in oral cavity is either direct or indirect. Direct mechanism includes the binding of probiotics to plaque/biofilm through binding to protein. It competes with pathogenic bacteria on the attachment to plaque and on substrate, and it secrets chemicals to inhibit other oral bacteria from binding, and by this way it improves human health. The secreted chemicals are antimicrobial peptides or proteins called Bacteriocins. These antimicrobials attack other pathogens present in the same ecological environment [9].

Indirect mechanism involves modulating systemic and local immunity, and producing antioxidants [10]. Generally speaking, in order to prevent and/or treat oral diseases, probiotics can act through the modulation of the host's inflammatory processes, inhibits formation of plaque, and decrease counts of disease-causing microorganisms.

Because probiotics are not able to colonize and adhere permanently in oral cavity, a compliance of continuous administration is needed [11].

By these mechanisms, the effect of harmful bacteria is minimized or eradicated by the presence of otherwise harmless Probiotic [7].

Oral cavity is an example of a complex ecosystem which is inhabited by more than 700 bacterial species present on the tongue, teeth, gums, inner cheeks, palate and tonsils [12]. *Streptococcus mutans* is an example of bacteria present in the oral microbiota that produces bacteriocin called mutacin. Its presence is highly associated with initiation of dental caries. Tests had been conducted with the aim of introducing probiotics which could replace *Streptococcus mutans* and significantly reduce the incidence of caries [13].

Researchers studied the effect of binding probiotics to different compounds; such as fluoride, xylitol and chlorhexidine. Results showed that there was no statistical difference detected on cariogenic bacterial count when combining probiotics with fluoride or xylitol [14]. However, it was found out that pre-treatment with chlorhexidine can result in long-lasting reduction in salivary *S. mutans* [15].

Strains that can be used in a probiotic product for treatment of oral diseases

***Streptococcus salivarius* (BLIS K-12 and M18):** *Streptococcus salivarius* is one of the most numerous beneficial bacteria found in the mouth of healthy individuals. However, only a small percentage of people have *S. salivarius* with BLIS K-12 or M18 activity. The K-12 strain was discovered when scientists examined a healthy child, who did not develop sore throat for several years. *S. salivarius* BLIS M18 appears in the mouth of newborns within hours after birth. K-12 strain of *S. salivarius* secretes powerful antimicrobial molecules called BLIS (Bacteriocin like Inhibitory Substances) which are lethal to harmful bacteria. M18 strain produces several bacteriocins and

enzymes (dextranase and urease) which prevent biofilm formation and inhibit *Streptococcus mutans;* bacteria which is associated with the initiation of dental caries [5].

***Streptococcus thermophilus*:** Is one of the sub-species of *Streptococcus salivarius* that may provide many of the same benefits of *S. salivarius* strains. *Streptococcus thermophilus* is normal inhabitant of the oral cavity, oropharynx and upper respiratory tract, which colonizes a few hours after birth [5].

***Lactobacillus*:** Many types of lactobacillus bacteria are used as probiotics*. Lb. acidophilus* has the ability to produce hydrogen peroxide, and antibacterial substances lactocidin and acidophilin. It aids in the production of niacin, folic acid and pyridoxine. It may also lower serum cholesterol. *Lb. acidophilus* has an effective antimicrobial action against *Staphylococcus aureus*, *Salmonella, E. coli, Rotavirus and Candida albicans*. *Lb. acidophilus* is found in small intestine, vagina, urethra and cervix in both humans and animals, and is present naturally in yogurt. Another *Lactobacillus* is *Lb. salivarius* which may inhibit bacteria *H. pylori*, *Lb. salivarius* has also shown to affect the number of periodontal pathogens in plaque. *Lactobacillus paracasei* is another *Lactobacillus* which is naturally found in fermented products, as well as yogurt and raw milk. *Lactobacillus reuteri* is a gram-positive bacterium that is found in most mammals' intestines originally isolated from human breast milk. *Lb. reuteri* produces reuterin, an antimicrobial substance that is effective against *Rotavirus* [16].

Potential applications of probiotics

Probiotics were widely used in food industry and in manufacturing of different kinds of dairy beverages. Nowadays probiotics have wider uses. Despite that many probiotics products have not been properly documented or clinically proven, they are still presented as reliable products by the companies [17]. This brings attention to the need to establish proper standards and guidelines that ensure the effectiveness of probiotic products presented. Probiotics are now used in the following conditions:

1. **Antibiotic-associated diarrhoea:** This type of diarrhoea is associated with the use of antibiotics [17], such as clindamycin, cephalosporins and penicillins. The cause of which was linked to *Clostridium difficile*. *Lb. acidophilus, Saccharomyces boulardii* yeast was found to be effective against this type of diarrhoea because it is resistant to stomach acids and bile salts, and reach the intestine after oral administration [18].
2. **Chronic bowel conditions:** Inflammatory diseases and bowel syndromes such as Crohn's disease are known to benefit from a combination of probiotics strains; lactobacilli, bifidobacteria, *Streptococcus salivarius* [19]. *Lb. salivarius* was also found to reduce flatulence in patients suffering from irritable bowel syndrome, and reduces flatulence, however, *Lb. salivarius*, *Lb. acidophilus* inhibits gram negative bacteria *H. pylori* which is associated with gastritis and peptic ulcers [20].
3. **Enhance immune response:** *Lactobacillus casei* among other probiotics strains was found to increase phagocytic activity of natural killer cells [21].
4. **Fighting Rotavirus infections:** *Lactobacillus reuteri* is effective in infants and children suffering from Rotavirus infections [22]. It is also effective against antibiotic-associated diarrhoea, traveller's diarrhoea and diarrhoea caused by *Clostridium difficile*. Its antimicrobial actions also eradicate *H. pylori*, which is the bacteria associated with peptic ulcer [22].
5. **Reducing the risk of cancer:** It has been found that modifying the gut microbiota reduces the risk of gastro intestinal cancer. Intestinal instillation of lactobacilli and bifidobacteria containing probiotics decrease β-glucuronidase and carcinogen levels in the GIT [23]. Other strains like *Lb. casei Shirota* present in a Japanese milk-based drink appear to reduce the risk of cancer recurrence in the urinary bladder. Another study related the decrease in carcinogenic aflatoxin levels in the lumen with the presence of different types of bacteria as *Propionibacterium* SP [23].
6. **Allergy:** The composition of vaginal microbiota was shown to influence the asthmatic condition of born children. Studies had connected the colonization of *Ureaplasma urealyticum* during pregnancy with infant wheezing. Asthma in newborns was also associated with taking antibiotics during pregnancy. *Lb. rhamnosus* GG given to pregnant women and newborns was shown to cause significant reduction in early atopic diseases [24].
7. **Surgical infections:** Studies had found that *Lb. fermentum* RC-14 had the ability to prevent *Staphylococcus aureus* post-surgical wound infections while other species like *Lb. plantarum* had the ability to minimize the risk of post-operative infections in liver transplant [25].

Probiotics and their effect on oral ecosystem

Bacterial species that colonised in the oral cavity live in homeostasis with the host, but any disturbances in the balance can initiate oral diseases as dental caries and periodontal diseases.

Probiotics can influence the oral microbial community by one of the following mechanisms:

1. Probiotic bacteria or their products can modulate the humoral or cellular immune system.
2. It can produce antimicrobial substances as lactic acid, hydrogen peroxide and bacteriocin-like substances that can directly inhibit periodontal pathogens or indirectly by competing with the pathogenic bacteria for their nutrients, or by restricting the adhesion of pathogens on surfaces [26].

The role of probiotics in controlling caries

Dental caries and periodontal diseases are considered as the most common oral diseases. The prominent generations that colonise on different surfaces of the oral cavity are: *Streptococcus* sp., *Veillonellaceae* sp., *Neisseria* sp., *Haemophilus* sp., *Actinomyces* sp., *Prevotella* sp., *Capnocytophaga* sp., *Treponema* sp., *Eikenella* sp., *Staphylococcus* sp., *Porphyromonas* sp. and *Fusobacterium* sp. In dental caries there is an increase in acidogenic and acid-tolerating species, such *as mutans streptococci* and *lactobacilli* and other species [27].

The etiology of dental caries includes four factors; the presence of cariogenic bacteria, a susceptible host, nutrients and time. To stop the progression of this process, different approaches can be used; such as diet counselling, fluoride application and mechanical plaque removal [26].

Because caries is considered an infectious disease, attempts were made to overcome the growth and spread of bacteria causing dental caries and probiotics had shown its potential effect in reducing the proliferation and adherence of cariogenic bacteria of which *Lactobacillus* sp. and *Bifidobacterium* sp. were the most commonly used [28].

Streptococcus mutans is the main bacteria involved in the initiation of tooth decay. *S. salivarius* BLIS M-18 was found to inhibit *Streptococcus mutans* which should help in preventing the occurrence of dental caries [29]. The first study that investigated the role of probiotics in inhibition of oral streptococci was performed by Meurman., *et al.* in 1995. Another *in vitro* study has demonstrated the ability of *Lactobacillus rhamnosus GG* to inhibit oral *Streptococcus mutans* in children [30]. *Lb. plantarum 299V* and *Lb. plantarum 931* were the most potent inhibitors of *S. mutans* strains [31]. In another human trial, done by Cgler., *et al*. there was a significant decrease in *S. mutans* following the introduction of probiotic ice-cream containing *Bifidobacterium lactis* [32].

In a systematic review done by Cagetti., *et al*. probiotics have demonstrated the capacity to reduce *Streptococcus mutans* count. A continuous regular almost daily intake is required to reach the goal of reducing *Streptococcus mutans* count in saliva and/or plaque [28].

The effect of probiotics on periodontal disease

Gingivitis is characterized by an inflammation and bleeding from the gingiva, which upon its progression may result in periodontitis. Periodontitis involves additional inflammation of supporting periodontal ligaments and alveolar bone, however, gingivitis is reversible when treated properly while periodontitis is irreversible [27].

The bacterial biofilm that forms the dental plaque consists of bacteria and bacterial byproducts, and of exopolysaccharides polymers that are made up of sugar residues [27].

Gingivitis and periodontitis are the result of the presence of pathogenic bacteria within the dental plaque that release inflammatory cytokines resulting in activated host immune response, and consequent destruction of soft tissue and bone. Local and systemic administration of antibiotics was found to be ineffective on the treatment of periodontitis. Treatment of periodontal disease involves mechanical scaling and root planning along with optimizing oral hygiene measures. Treatment with probiotics includes restoring the number of beneficial bacteria, modulating the host's inflammatory process and reducing the pathogenic microorganisms count. Probiotics inhibit endogenous pathogens as well as prevent super infection with these pathogens [33].

Grudianov., *et al.* in 2002 found that probiotics bacteria reduced the number of pathogenic bacteria in biofilm; making them one of the earliest researchers who reported the beneficial effects of probiotics on periodontal disease [34]. Twetman., *et al.* [35] investigated the effects of probiotics on gingival inflammation. They found out that a formula of probiotics consisting of *Lb. reuteri ATCC SS730 and Lb. reuteri ATCC PTA 5289* and if administered in chewing gum for one week, was able to modulate the immune responses related to the periodontal disease. In 2007 Noordin., *et al.* [36] studied the effect of Niacin which can be extracted from the probiotic *Lactococcus lactis*, and is incorporated in mouth rinse for 32 days, on the reduction of plaque accumulation and gingivitis. Another study found out that probiotics *Bacillus subtilis* E-300 can also inhibit pathogens associated in periodontal disease [37]. Clinical studies in humans that have explored treatment of the periodontal diseases using probiotic therapy without clinical treatments like scaling, have reported minimal benefits such as reduction of gingival bleeding. However, studies that involved probiotics as an adjunct to clinical periodontal treatment report a much better improvement in the clinical status of patients compared to clinical treatment alone [38].

The effect of probiotics on halitosis

Halitosis and breath malodor are general terms used to define an offensive odor emanating from someone's breath. Oral malodor is the result of microbial degradation of proteins present in saliva, food debris, plaque and post nasal drip by anaerobic bacteria resulting in the production of volatile sulfur compounds. These bacteria are located on the dorsum of the tongue and they produce volatile sulfur compounds, valeric acid, butyric acid and putrescine that cause malodor [37].

Current treatments focus on either nonselective anti-bacterial therapy, or the use of agents that mask the odor [39]. Non-selective anti-bacterial treatment consists of mechanical and chemical reduction of bacterial count. These treatments are expensive and complex and only result in short term reduction of number of bacteria that cause malodor, which recovers to its original numbers again. For example, Chlorhexidine is antimicrobial chemical that is effective in treatment of malodor but only if used daily [40]. The introduction of beneficial bacteria to fight the odor-causing bacteria is recommended for treatment of halitosis. The pre-emptive colonization of a bacterial strain that doesn't produce odours will prevent the growth of odour-causing microorganisms. As the dorsum of the tongue is the origin of most halitosis problems, the selected probiotic strain should be able to live within this ecosystem. *Streptococcus salivarius K12* effectively colonizes in the oral cavity including the dorsum of the tongue. The K-12 strain secretes BLIS (Lantibiotic bacteriocins), salivaricin A and B which inhibit the bacteria responsible for malodour. Administration of *S. salivarius* probiotics provides a long-term breath support and treatment of halitosis [41].

Masdea., *et al*. also showed that *S. thermophilus* might reduce the volatile sulfur compound level by inhibition of *Porphyromonas gingivalis* growth and neutralizing volatile sulfur compounds [42].

Different doses of probiotics are recommended for treatment of halitosis depending on the severity of the condition. Till this day, chlorhexidine is advised to be used as pretreatment in resistant cases where more potent antimicrobial treatment is required [39].

The effect of probiotics on oral candidiasis

Candidiasis can significantly degrade the quality of life of elderly and immune compromised patients. This disease causes a variety of mucosal infections affecting the gastrointestinal tract, respiratory and genital tracts. *Candida albicans*, a polymorphic yeast, contribute to the pathogenesis of this mucosal infection [26].

Probiotics have the potential to reduce the prevalence of oral candida in elderly as investigated by Hatakka and co-workers in 2007 [43]. *S. salivarius* K12 may inhibit the invasion of *C. albicans* into mucous surfaces acting as a useful probiotic against oral candidiasis [44].

A very recent study done by Mette Rose Jørgensen., *et al.* investigated the antifungal potential of the probiotic bacterium *Lactobacillus reuteri (DSM 17938 and ATCC PTA 5289)* against six oral Candida species (*C. albicans, C. glabrata, C. krusei, C. tropicalis, C. dubliniensis,* and

C. parapsilosis). The results confirmed the ability of *L. reuteri* to inhibit growth of five out of six oral *Candida* species, while no probiotics effect was noticed against *C. krusei* [45].

Other oral effects of probiotics

Probiotic lozenges can reduce the effects of chemotherapy or radiation induced mucositis as well as haemophilia induced oral ulcerations [46,47].

Vehicles (carrier system) for probiotics

Probiotics can be introduced in different vehicles (Table).

Carrier	Probiotic
Milk	*Lb. casei* strain Shirota
Chewing Gum	*Lb. reuteri* ATCC 55730
Milk	*Lb. rhamnosus* GG
Ice-cream	*Bifidobacterium lactis* Bb-12
Cheese	*Lb. rhamnosus* LC 705
Yoghurt	*Bifidobacterium* DN-173
Lozenge	*S. salivarius* k12
Tooth paste	*Lb. paracasei*

Table: Examples of probiotic strains and carrier types.

It can be provided in four basic forms:

1. Food or beverages (fruit juice).
2. Prebiotic fibers.
3. Milk-based products.
4. Dried cells packages as powder, capsule, gelatin tablets.
5. Tooth paste: In a recent study, performed by the University of Split Croatia, probiotics containing tooth paste was found to be effective in the prevention of oral infectious diseases. *Lb. paracasei* containing tooth paste had strong antimicrobial activity especially against *Candida albicans*. It was even stronger than Hexitidine mouth wash which is well known in management of *C. albicans* [48].

Safety

Guidelines for the evaluation of probiotics were set by a joint working group of the FAO and WHO in May 2002. The guidelines defined minimum requirements to substantiate health claims of a certain probiotic. Safety assessment is an important part of these guidelines [49]. Probiotics are living microorganisms, which could potentially infect the host. Although, rare systemic infections have been reported, the use of probiotic in food has been considered safe for human consumption [50]. However, probiotics used to treat oral pathosis should not relocate antibiotic resistance genes and should maintain genetic stability in the oral microflora [51]. Care must be taken when administering viable bacteria to immune compromised patients and those who suffer intestinal bleeding [52].

In January 2016, the US Food and Drug Administration issued a letter of no objection for the safety of *S. salivarius K12* as Generally Recognized as Safe (GRAS) [5].

Probiotics in the future

Probiotics for oral health is a promising and attractive research topic. The use of probiotics in management of oral conditions needs further researches. The proper strains, doses and vehicles for prevention and treatment of different oral conditions should be addressed.

Conclusion

Promising results were demonstrated on the effect of Probiotic strains on oral health in the prevention and treatment of dental caries, and its effect on periodontal diseases as well as on its role in controlling halitosis and other oral diseases.

Bibliography

1. Eberl G and M Lochner. "The development of intestinal lymphoid tissues at the interface of self and microbiota". *Mucosal Immunology* 2.6 (2009): 478-485.

2. Guglielmetti S., *et al*. "A dairy bacterium displays in vitro probiotic properties for the pharyngeal mucosa by antagonizing group A streptococci and modulating the immune response". *Infection and Immunity* 78.11 (2010): 4734-4743.

3. FAO/WHO. "Report of a joint FAO/WHO expert consultation on guidelines for the evaluation of probiotics in food". World Health Organization and Food and Agriculture Organization of the United Nations, London Ontario Canada (2002).

4. Sari A Mahasneh and Adel M Mahasneh. "Probiotics: A Promising Role in Dental Health". *Dentistry Journal* 5.4 (2017): 26.

5. Joseph L Evans. "Agro food industry Hi tech" (2016).

6. Shoemaker DK and Allen SJ. "The microbiome and disease: reviewing the links between the oral microbiome, aging, and Alzheimer's disease". *Journal of Alzheimer's Disease* 43.3 (2015): 725-738.

7. Rangare Lakshman Anusha., *et al*. "The magic of magic bugs in oral cavity: Probiotics". *Journal of Advanced Pharmaceutical Technology and Research* 6.2 (2015): 43-47.

8. Gungor OE., *et al*. "Who will win the race in childrens' oral cavities? Streptococcus mutans or beneficial lactic acid bacteria?" *Beneficial Microbes* 4.3 (2013): 237-245.

9. Cotter PD., *et al*. "Bacteriocins: developing innate immunity for food". *Nature Reviews Microbiology* 3.10 (2005): 777-788.

10. Meurman JH. "Probiotics: Do they have a role in oral medicine and dentistry?" *European Journal of Oral Sciences* 113.3 (2005): 188-196.

11. Teughles W., *et al*. "Probiotics and oral healthcare". *Periodontology* 48 (2008): 111-147.

12. Dewhirst FE., *et al*. "The human oral microbiome". *Journal of Bacteriology* 192.19 (2010): 5002-50017.

13. Hillman JD., *et al*. "Construction and characterization of an effecter strain of Streptococcus mutans for replacement therapy of dental caries". *Infection and Immunity* 68.2 (2000): 543-549.

14. Jindal G., *et al*. "A comparative evaluation of probiotics on salivary mutans streptococci counts in Indian children". *European Archives of Paediatric Dentistry* 12.4 (2011): 211-215.

15. Aminabadi NA., *et al*. "Effect of chlorhexidine pretreatment on the stability of salivary lactobacilli probiotic in six- to twelve-year-old children: A randomized controlled trial". *Caries Research* 45.2 (2011): 148-154.

16. OE Gungor., *et al*. "Probiotics: can they be used to improve oral health?" *Beneficial Microbes* 6.5 (2015): 647-656.

17. G Reid., *et al*. "Potential uses of probiotics in dental practice". *Clinical Microbiology Reviews* 16.4 (2003): 658-672.

18. Beaugerie L., *et al*. "Antibiotic-associated diarrhoea and Clostridium difficile in the community". *Alimentary Pharmacology and Therapeutics* 17.7 (2003): 905-912.

19. Gionchetti P., *et al*. "Oral bacteriotherapy as maintenance treatment in patients with chronic pouchitis: a double blind, placebo-controlled trial". *Gastroenterology* 119.2 (2000): 305-309.

20. Canducci F., *et al*. "A lyophilized and inactivated culture of Lactobacillus acidophilus increases Helicobacter pylori eradication rates". *Alimentary Pharmacology and Therapeutics* 14.12 (2000): 1625-1629.

21. Matsuzaki T and J Chin. "Modulating immune responses with probiotic bacteria". *Immunology and Cell Biology* 78.1 (2000): 67-73.

22. Majamaa H., *et al*. "Lactic acid bacteria in the treatment of acute rotavirus gastroenteritis". *Journal of Pediatric Gastroenterology and Nutrition* 20.3 (1995): 333-338.

23. Hosoda M., *et al*. "Effect of administration of milk fermented with lactobacillus acidophilus LA-2 on fecal mutagenicity and microflora in the human intestine". *Journal of Dairy Science* 79.5 (1996): 745-749.

24. Kalliomaki M., *et al*. "Probiotics and prevention of atopic disease: 4-year follow-up of a randomised placebo-controlled trial". *Lancet* 361.9372 (2003): 1869-1871.

25. Rayes N., *et al*. "Early enteral supply of lactocacillus and fiber versus selective bowel decontamination: a controlled trial in liver transplant recipients". *Transplantation* 74.1 (2002): 123-127.

26. Laleman I and Teughles W. "Probiotics in the dental practice: a review". *Quintessence International* 46.3 (2015): 255-264.

27. Saha S., *et al*. "Probiotics as oral health biotherapeutics". *Expert Opinion on Biological Therapy* 12.9 (2012): 1207-1220.

28. MG Cagetti., *et al*. "The use of probiotics strains in caries prevention: a systematic review". *Nutrition* 5.7 (2013): 2530-2550.

29. Nase L., *et al*. "Effect of long-term consumption of a probiotic bacterium, Lactobacillus rhamnosus GG, in milk on dental caries and caries risk in children". *Caries Research* 35.6 (2001): 412-420.

30. Solderling EM., *et al*. "Probiotic Lactobacilli interfere with Streptococcus mutans biofilm formation in vitro". *Current Microbiology* 62 (2010): 618-622.

31. Hasslof P., *et al*. "Growth inhibition of oral mutans streptococci and candida by commercial probiotics lactobacilli- an invitro study". *BMC Oral Health* 10 (2010): 18.

32. koglar E., *et al*. "Short-term effect of ice-cream containing Lactis Bb-12 on the number of salivary mutans streptococci and Lactobacilli". *Acta Odontologica Scandinavica* 66.3 (2008): 154-158.

33. Roberts FA and Darveau RP. "Beneficial bacteria of the periodontium". *Periodontology* 30 (2002): 40-50.

34. Grudinov AL., *et al*. "Use of probiotics bifidumbacterin and Acilact in tablets therapy of periodontal inflammations". *Stomatolgiia* 81.1 (2002): 39-43.

35. Twetman S., *et al*. "Short term effect of chewing gums containing probiotics Lactobacillus reuteri on the levels of inflammatory mediators in gingival crevicular fluid". *Acta Odontologica Scandinavica* 67.1 (2009): 19-24.

36. Noordin K and Kamin S. "The effect of probiotics mouth rinse on plaque and gingival inflammation". *Annals of Dentistry* 14.1 (2007): 19-25.

37. Tsubura S., *et al*. "The effect of Bacillus subtilis mouth rinsing in patients with periodontitis". *European Journal of Clinical Microbiology and Infectious Diseases* 28.11 (2009): 1353-1356.

38. Robert P Allaker and Abish S Stephen. "Use of Probiotics and Oral Health". *Current Oral Health Reports* 4.4 (2017): 309-318.

39. Loesche WJ and Kazor C. "Microbiology and treatment of halitosis". *Periodontology* 28 (2002): 256-279.

40. Burton JP., *et al*. "A preliminary study of the effect of probiotics Streptococcus salivarius K12 on oral malodour parameters". *Journal of Applied Microbiology* 100.4 (2006): 754-764.

41. Young A., *et al*. "Inhibition of orally produced volatile sulfur compounds by zinc, chlorhexidine or cetylpyridinium chloride- effect of concentration". *European Journal of Oral Sciences* 111.5 (2003): 400-404.

42. Masdea L., *et al*. "Antimicrobial activity of Streptococcus salivarius K12 on bacteria involved in oral malodour". *Archives of Oral Biology* 57.8 (2012): 1041-1047.

43. Hattaka K., *et al*. "Probiotics reduce the prevalence of oral candida in the elderly-A randomized controlled trial". *Journal of Dental Research* 86.2 (2007): 125-130.

44. Sanae A Ishijima., *et al*. "Effect of Streptococcus salivarius K12 on the in vitro growth of Candida albicans and its protective effect in an oral candidiasis model". *Applied and Environmental Microbiology* 78.7 (2012): 2190-2199.

45. Mette Rose Jørgensen., *et al*. "Probiotic Lactobacillus reuteri has antifungal effects on oral Candida species in vitro". *Journal of Oral Microbiology* 9.1 (2017): 1274582.

46. Sharma A., *et al*. "Lactobacillus brevis CD2 lozenges reduce radiation and chemotherapy-induced mucositis in patients with head and neck cancer a randomized double-blind placebo-controlled study". *European Journal of Cancer* 48.6 (2012): 875-881.

47. Niscola P., *et al*. "Aphtus oral ulceration and its successful management by lactobacillus brevis CD2 extract in adult haemophlilic patients". *Hemophilia* 18.3 (2013): 78-79.

48. Amizik Ivana P., *et al*. "Antimicrobial efficacy of probiotic-containing toothpastes: an in vitro evaluation". *Medicinski Glasnik* 14.1 (2017): 139-144.

49. Food and Agriculture Organization of the United Nations and World Health Organization. Guidelines for the evaluation of probiotics in food. Food and Agriculture Organization of the United Nations and World Health Organization Working Group Report (2002).

50. Reid G. "Safety of lactobacillus strains as probiotic agents". *Clinical Infectious Diseases* 35.3 (2002): 349-350.

51. Grajek Gr., *et al*. "Probiotics, prebiotics and antioxidants as functional foods". *Acta Biochimica Polonica* 52.3 (2005): 665-671.

52. Marteau PR. "Probiotics in clinical conditions". *Clinical Reviews in Allergy and Immunology* 223 (2002): 255-273.

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