sciendo

Journal of Health Study and Medicine

2024, Article 2
pp. 39–58
DOI 10.2478/jhsm-2024-0002

The Use of Probiotic Preparations in Caries Prevention and Treatment

Submitted: 11 November 2024; Accepted: 14 June 2024; Published: 28 June 2024

Aleksandra Anna Bernaś[1]
https://orcid.org/0009-0005-1997-1733

Sebastian Kłosek[2]
https://orcid.org/0000-0001-9694-0950

[1] Student Scientific Circle, Department of Oral Pathology, Medical University of Lodz, Poland
[2] Department of Oral Pathology, Medical University of Lodz, Poland

Corresponding author

Aleksandra Anna Bernaś
Student Scientific Circle, Department of Oral Pathology
Medical University of Lodz, Poland
aleksandra.bernas@stud.umed.lodz.pl

Abstract

The article delves into the potential of probiotics and synbiotics as alternative approaches to preventing and treating dental caries. Probiotics are live, non-pathogenic microorganisms combined with non-living substances (prebiotics) that support their growth and activity. Probiotics, including strains of Lactobacilli, Bifidobacterium, Streptococcus, secrete various compounds, such as antimicrobial substances, bacteriocins, and enzymes, which help combat cariogenic bacteria. Research suggests that early administration of probiotics can establish a stable oral ecosystem and decrease the risk of dental caries.

Synbiotics, a combination of probiotics and prebiotics, offer a synergistic approach to promoting oral health. Prebiotics like glucomannan hydrolysate, arabinose, xylose, and xylitol support the growth of beneficial bacteria while hindering the proliferation of cariogenic strains. The use of synbiotics, particularly in children, has shown promise in reducing the incidence of dental caries.

Overall, this review highlights the growing interest in probiotics and synbiotics as potential solutions to addressing the complex issue of dental caries. These alternative methods offer the potential to rebalance the oral microbiota and reduce the prevalence of this widespread oral health problem. Nonetheless, further research is needed to confirm their efficacy and long-term effects in preventing and treating dental caries.

Key words: *probiotics, synbiotics, dental caries, oral cavity, microbiota*

Introduction

It has been estimated that the human microbiome is inhabited by 3.8 x microorganisms [1]. The oral cavity biofilm is considered to be a substantial and the second, after the intestine, largest (at about 1000 species) biofilm of multispecies of bacteria (about 700 species), fungi (including yeasts), viruses (mainly bacteriophages), archaea, and protozoa multicellular structure of microorganisms in the human body [1–9].

The composition of the microbiome is individual and diverse for each person and the viral composition additionally depends on the gender [1, 5]. This ecosystem is influenced by interspecies interactions and the host-microbial relationship. If one of the microbes becomes more numerous or dominant and the immune response is impaired, it can shift the balance, which changes the relationship from a mutualistic system to dysbiosis [1, 3, 10]. Three main mechanisms contribute to the unbalanced microbiome state: the loss of beneficial organisms, the loss of microbial diversity, and the predominance of pathogenic microorganisms [1].

It is difficult to maintain a constant oral environment because numerous exogenous and endogenous factors influence the disruption of homeostasis [2]. These include drug use, smoking, the host`s lifestyle, oral hygiene, the environment, pH fluctuations, salivary gland disease, diabetes, antibiotics, everyday mechanical forces (brushing, rinsing, chewing), oxygen and nutrient availability [2, 3].

Teeth surfaces are excellent places for bacteria to dwell on, which results in dental plaque formation. It concerns especially *Streptococcus* species producing surface adhesins, which helps to create a primary biofilm layer in the mouth [1]. Dental plaque is a particular factor in the appearance of dental caries due to the fact that it surrounds the tooth surfaces and starts reacting with carbohydrates leading to the fermentation process. The acids formed as a result of this reaction significantly lower the pH on the tooth surface and dissolve its tissues [11].

The fact that the place of occurrence of specific species of bacteria depends on their preference for a given area has been confirmed. For example, dental plaque is inhabited by: *Veillonella parvula, Veillonella dispar, Capnocytophaga* and *Corynebacterium genera. Veillonella atypica* may be found on the tongue dorsum surface [1].

One of the most common oral pathologies – dental caries, which affect approximately 44% of the world's population, are associated with the phenomenon of reduced pH [5, 12]. Approximately 2 billion people have teeth permanently affected by caries and 520 million children with deciduous teeth suffer from this multifactorial condition [13].

Despite the decline in the number of people suffering from this disease, it continues to be a global burden on society [5].

The health of every organ is essential for general health, and that includes the oral cavity. The absence of dental caries and other oral complaints such as: periodontitis, missing teeth, chronic oral and face pain, birth defects, oral ulcerations, and oral cancer is considered by the WHO to be a complete oral health [4].

Research is constantly looking for the most effective methods to maintain the microbiome balance and decrease the risk of ailments in the oral cavity, with the most limited side effects. [13] Among the most commonly used are: AMPs (antimicrobial peptides), nano-sized drug delivery systems, EPM disruption techniques, agents that enhance the immune response (antibiotic course), and above all appropriate oral hygiene enriched with the use of mouth rinses and dental floss [1].

In order to avoid the occurrence of dysbiosis, relatively new therapeutic and prophylactic methods using probiotics and synbiotics can be used [14]. They successfully modify and restore the state of the oral cavity microecosystem in both health and disease [1, 3].

The following review covers the most common oral ailment – caries, and alternative treatments for it with probiotics and synbiotics.

Probiotics

Probiotics are preparations containing live, non-pathogenic microorganisms combined with not-living substances, such as dietary fibers (e.g., oligosaccharides, phenolic acids, polyunsaturated fatty acids), that nourish them called prebiotics. Together they create synbiotics [5, 15]. These complexes mainly consist of bacteria of the *Lactobacilli, Bifidobacterium, Streptococcus* and *Weissella* genus and also selected species of *Bacillus subtilis* and *Saccharomyces cerevisiae* [12, 13, 16]. They can be produced in the form of pharmaceutical formulations, dietary supplements, functional foods (e.g., yogurt, milk, cheese, butter) as well as nanoparticles [7, 17].

Some of the best known probiotics occur naturally in large quantities in cow's and human milk – they are lactic acid bacteria. However, nowadays the pharmaceutical companies offer many types, strains, and species of probiotics which provide a huge availability of the probiotic course [18]. The biggest challenge for probiotic preparations is creating non-dairy products which will show high probiotic vitality and resistance, not change consistency, and remain in the oral environment long enough. Studies have shown that the greatest solution to these requirements is provided by orodispersible films (ODFs), which consist of carboxymethylcellulose (CMC), hydroxypropyl methylcellulose (HPMC), gelatin, and release active substances into the dysbiotic oral cavity [17]. For many decades, probiotics have been gaining popularity in general medicine, for example in the treatment of urogenital illnesses, cancer prevention, allergy prophylaxis, vaginal infections, respiratory and especially widely investigated gastrointestinal ailments [7, 16, 18–21]. They have been in use since 1994 to reduce oral infections and more and more researchers confirm their positive impact on limiting the development of oral ecosystem disease. Since then, probiotics preparations have become a successful method supporting the treatment of dental caries and other civilization diseases of the oral cavity: periodontitis, gingivitis, oxidative stress, halitosis, and opportunistic infections, such a candidiasis or oral cavity cancer [4, 6, 16, 18, 20]. Microorganisms called probiotics have become one of the additional or alternative methods to an antibiotic course due to the fact that antibiotic resistance increases and these substances positively affect and improve the oral microflora [18]. Moreover, preventative measures based on probiotic formulations are cheaper than antibiotic treatment. Through numerous mechanisms in the organism, probiotics and related preparations (synbiotics and postbiotics) have been included in the most popular bioactive agents having the capacity to regulate pathogens [15, 19]. Due to the fact that bacteria change the oral environment, probiotic preparations get into antagonistic and synergistic relationships with bacteria dwelling in dental plaque, controlling them and preventing the disturbance of homeostasis [20].

Research confirmed that taking probiotics as early as possible increases the probability of persistent and permanent incorporation of probiotic bacteria into the individual's microbiome and helps to establish a stable oral ecosystem [18].

Modifications of the biofilm are based on three main mechanisms. First is the secretion of antimicrobial substances, such as lactic acid, acetic acid, hydrogen peroxide which damage the epithelium and pathogenic bacteria dwelling in it, bacteriocines – responsible for cariogenic bacteria destruction or inhibition of their growth, enzymes: mutanase, urease and dextranase, biosurfactants reducing adhesion to the mucosa and reducing the level of pro-inflammatory cytokines, collagenase, elastase, prostaglandins E2. The second mechanism relies on the competition for nutrients and adhesion surfaces to the oral tissues. The third factor is the immunomodulatory activity stimulating cellular and humoral immune responses of the host as a result of enlarged IgA production and the activation of macrophages, neutrofils and NK cells, which precedes phagocytosis [5, 7, 23, 12, 13, 15, 16, 18–20, 22].

These mechanisms may result in, among others, restoration of the integrity of the mucosa, degradation of toxins, neutralization of cancer factors, improvement of dysbiosis microbiota, reduction of the creation of CFUs of pathogens, e.g., *Streptococcus mutans*, which is a major factor of caries [12, 17]. Moreover, compound probiotic products increase the colonization of commensal microorganisms, buffer saliva pH (which deteriorates the survival conditions of pathogens), thus preventing dental tissue demineralization (e.g., of enamel) [7, 13, 19]. Before using specific bacteria strains, *in vitro* and *in vivo* examinations should be performed to ensure the right direction of probiotic action to avoid unwanted side effects, like gastrointestinal problems or allergic reactions [20].

From year to year probiotics are gaining popularity in dentistry due to the fact that oral pathologies are common all over the world, due to a diet rich in sugar, neglected oral hygiene, and also the use of stimulants, especially cigarettes. A probiotic therapy can be an effective method of managing oral diseases [4, 15]. Administered in previously adjusted doses, probiotics confer benefit to the host's health by maintaining appropriate microbiological

balance, its metabolism, as well as physiology, decreasing dysbiosis and inflammatory process in the oral cavity [4, 12, 17–19, 21, 22, 24].

Synbiotics

One of the most recent alternative approaches to the treatment of oral disorders is the administration of synbiotics [25]. They are still generating the interest of researchers [26, 27]. They may be found more and more frequently in food and various beverages [15, 27].

When one or many strains of living probiotics are combined with non-digestible, selective food ingredients (prebiotics), then this combination is called synbiotics.

Synbiotics have two management strategies: a synergic one – to obtain one or more health benefits to the host through microorganisms and a complementary one – acting directly against specific pathogens [15].

This synergistic combination of probiotics and prebiotics was created to increase the survivability and implantation of probiotic bacteria and to prevent the overgrowth of pathogens in the oral cavity environment [25].

Prebiotics – one of the components of synbiotics, are mainly carbohydrate compounds (oligosaccharides): fructooligosachharides (FOS), galactooligosaccharides (GOS), xylooligosaccharides (XOS), polydextrose, carbohydrates inulin, lactitol, starch, and glucose-derived oligosaccharides that occur in nutritional products or are synthesized [25, 28]. Prebiotics also occur in the form of phenolic substances, nitrate, proline (amino acid), and polyunsaturated fatty acids [13, 15]. The effect of everyday synbiotics administration, including a combination of probiotics: *Lactobacillus acidophilus, Lactobacillus plantarum, Lactobacillus rhamnosus, Bifidobacterium infantis, Streptococcus thermophilus,* and prebiotics in the inulin and fructan forms, decreases the viscosity and increases the buffering capacity of the host's saliva [10].

Prebiotics strengthen the therapeutic action of probiotics by bacteria multiplication (through enzymes hydrolyzation), metabolic activation and increasing the growth of non-pathogenic, beneficial bacteria in the oral cavity, which boosts immunity and restores the microbiota balance [12, 13, 25, 28].

They also support the suppression of colonization of microbes by preventing the adhesion of pathogenic bacteria to the oral mucosa surfaces, which contributes to dental caries [25, 28].

For instance, N-acetyl-D-mannosamine (the most promising prebiotic), succinic acid, and Met-Pro are responsible for *Streptococcus salivarius* and *Streptococcus oralis* development, and glucomannan hydrolysate (GMH) causes the growth of lactic-acid bacteria [25]. In 2011, the first results showed the positive effect of this combination. GMH prebiotics have also been proven to be an excellent solution as they stimulate the overgrowth of the probiotic *Lactobacillus acidophilus NCFB 1748* over *Streptococcus mutans* and reduce antibodies [10]. *Lactitol* ensures the evolution of *Streptococcus salivarius*. Moreover, this strain does not cause the development of pathogenic microorganisms [13]. Arabinose, xylose, and xylitol affect the growth of *Lactobacilli spp* [25].

In other studies, no relevant results were received after the use of concentrations: 1%, 2%, 3%, 4%, and 5% of GOS and FOS prebiotics on the growth of *Lactobacillus acidophilus* compared to the placebo group [10]. It has been proven that arginine supports the effectiveness of alkalogenic bacteria: *Streptococcus parasanguinis, Streptococcus gordonii,* and *Streptococcus sanguinis* in suppressing oral dysbiosis [10, 25]. Furthermore, the combinations of probiotics: *Lactobacillus fermentum, Lactobacillus plantarum Lactobacillus spp., or Lactobacillus paracasei* with prebiotics: xylitol, arabinose, or xylose seem promising [25]. Nitrate prebiotics can modify dental plaque by restoring the adequate ratio of beneficial bacteria to pathogenic ones. Proline containing up to twenty amino acids has prebiotic properties. Ile-Pro-Ile peptide (diprotin A) provides resistance to the pH decrease in the oral cavity biofilms [13].

Although studies are still being conducted, scientists have already demonstrated positive effects of synbiotic on the therapy of caries.

The role of microbiota in dental caries

Tests have indicated that non-pathogenic, live microorganisms widely recognized as probiotics have a relevant role in eradicating dental caries, a disease with complex etiology. This condition is mainly caused by the occurrence of

cariogenic bacteria as well as a diet high in carbohydrates. The Global Burden of Disease Study in 2019 assessed that 3.5 billion people suffer from oral conditions, especially tooth decay [13]. This multifactorial disease, apart from periodontitis, is one of the most widespread oral health problems throughout the world. This infectious disease, in addition to the deterioration of the patient's health, also diminishes the psychosocial quality of life [10]. It was demonstrated that groups of specific bacteria with common physiological properties (above all *Streptococci, Lactobacilli,* and *Bifidobacteria*), accumulating in supragingival dental plaque as well as a sugar-rich diet (mainly in sucrose, glucose, fructose, and starch) delivering more than 5% of the total energy intake per day, are one of the main causes of the dysbiotic effect. As a result of the accumulation of cariogenic bacteria in oral mucosa and the fermentation of carbohydrates, which release organic acids, the environment acidification proceeds, providing an excellent condition for caries development [2, 5, 11, 12, 19]. These acids lead to the demineralization of tooth tissues, which causes enamel loss [11]. Significant elements in the development of dental caries are also: reduced salivary flow, genetics, age, socio-economy, irregular oral hygiene, tooth susceptibility to caries, inappropriate fluoride intake, high cost of dental help, and the host's immune deficiency [5, 11–13, 18, 19]. To significantly increase the effectiveness of anticaries properties, probiotics have to meet certain requirements, among others: it is necessary for them to connect with dental plaque, inhibit cariogenic bacteria proliferation, and limit carbohydrates metabolism causing the synthesis of organic acids [12].

Streptococcus mutans present in the oral cavity of people with and without dental caries and a few acidogenic and acid-tolerating bacteria species: *Streptococcus sobrinus,* or *Lactobacillus spp*., which have the ability to produce biofilm, synthesize exopolysaccharide (EPS) from sucrose and survive in an acid environment substantially contributing to the occurrence of dental caries [5, 8, 12, 18, 20, 29]. In addition to the above, in recent years it has been shown that *Actinomyces, Lactobacillus, Neisseria, Prevotella, Propionibacterium, Scardovia, Candida albicans,* and Epstein-Barr virus (EBV) are also microorganisms that may lead to this disease [2].

Lactobacillus

The most appreciated feature of *Lactobacillus* is their ability to increase in size and survive in low pH environment [8]. *Lactobacilli* containing probiotics have bactericidal and bacteriostatic effect, which results in the production of hydrogen peroxide, bacteriocins, fatty and organic acids [20]. *Lactobacillus salivarius* are well-examined bacteria . One of the most noteworthy of them is the WB21 probiotic strain, which effectively eliminates cariogenic bacteria in the oral cavity [9]. A short-term intake of *Lactobacillus acidophilus La5* and *Bifidobacterium lactis Bb12* probiotics in the form of yoghurt results in a significant decrease in *Streptococcus mutans* in the saliva of patients who are at a high risk of caries [30].

Lactobacillus reuteri produces and secretes reutin, which is produced by the fermentation of glycerol. As a result of the presence of this substance, these bacteria have an anti-caries effect and effectively prevent periodontal diseases [31]. Yoghurt enriched with this probiotic strain is also effective in reducing the number of *Streptococcus mutans* compared to the control study [30].

In order to neutralize the low level of saliva pH, which leads to the damage of teeth structure, adding milk products with various types of probiotics is advisable [15].

A 10-day *in vitro* study was conducted using bovine enamel samples. The biofilm of cariogenic bacteria was rich in pathogens: *Streptococcus mutans, Lactobacillus rhamnosus,* and *Actinomyces naeslundii*. In this research, the following probiotic preparations were used: *Lactobacillus reuteri* and *Streptococcus oligofermentans*. The results of the research showed that *Lactobacillus reuteri* compared to S*treptococcus oligofermentans* had a better anti-caries effect, while both strains reduced the CFU of cariogenic strains index, neutralized the acidic pH, and inhibited the activity of pathogens in the in vitro trial [31]. In 2021, a study was conducted involving the administration of two species of probiotics: *Limosilactobacillus reuteri DSM 17938* and *Limosilactobacillus reuteri ATCC PTA 5289* to test their effectiveness in reducing the incidence of caries outbreaks in children aged 2 to 5, suffering from ECC (early childhood caries). The study did not show a significant reduction in the recurrence of

early childhood caries, but due to the discontinuation of the study, it is not conclusive [32].

The *Lactobacillus casei* probiotic, belonging to the *Lactobacillus paracasei* group, administered together with the plant polyphenol oxyresveratrol (ORV), demonstrated positive anti-caries results. ORV together with *Lactobacillus casei* has a great competitive advantage over *Streptococcus mutans*, thanks to the stimulation of bacteria to discharge acetic acid [33].

Another species of lactic acid bacteria is *Lactobacillus brevis.* A study of six strains proved that *Lactobacillus brevis KCCM 202399*, isolated from kimchi, reduces the development of *Streptococcus mutans KCTC 5458* biofilm most effectively [34].

In another study, the probiotic strain *Lactobacillus acidophilus* was also taken in the form of yogurt for one month. After this time, in addition to a clear decrease in the number of *Streptococcus mutans* bacteria, an increase in the concentration of IgA in the saliva of the examined patients was observed. Therefore, a probiotic containing *Lactobacillus acidophilus* not only reduces the occurrence of cariogenic pathogens, but also has an immunostimulating effect [35].

Orthodontic treatment increases the probability of dental caries due to food debris remaining between the brackets and the wires of braces. 33 individuals were supplemented with probiotics (3 mg *Lactobacteria*, 2 mg *Glycobacteria*) in the form of tablets during orthodontic treatment. This test revealed that the density of *Streptococci mutans* and *Lactobacilli* did not diminish substantially after this research. Therefore, it is not a satisfactory method to help orthodontic patients to get rid of the problem of dental caries [36].

The newly found *Lactiplantibacillus plantarum VHProbi V38* strain, obtained from fermented cabbage, has strong bactericidal properties against *Streptococcus mutans*. It has been found that it can secrete bacteriocins. On an agar plate, it inhibits the growth and agglutinates cariogenic *Streptococcus mutans* and eliminates pathogenic biofilm, thus becoming a promising candidate to fight caries. In addition, its bactericidal properties were tested against: *Porphyromonas gingivalis, Aggregatibacter actinomycetemcomitans,* and *Fusobacterium nucleatum* causing periodontal diseases [37].

Streptococcus

A successful and direct method of eradication of *Streptococcus mutans* (SM) and *Streptococcus sorbinus* is the application of probiotics rich in *Streptococcus dentisani*, obtained from dental plaque of individuals with no caries and *Streptococcus salivarius M18* (with the strongest clinical potential), discharging bacteriocins inhibiting their harmful operation [18]. In addition, the *Streptococcus salivarius M18* can also secrete dextranase and urease, which are responsible for the decomposition of dextran and hydrolyzation of urea. The above processes increase the alkalinity in the oral cavity and dental plaque is dissolved. After 90 days of taking *Streptococcus salivarius M18* by children, the probability of new outbreaks of caries has decreased [30].

An equally popular probiotic of the *Streptococcus salivarius* species is the *K12* strain. In addition to antibacterial properties, it also copes well with fungal infections. *Streptococcus salivarius K12*, extracted from the surface of the tongue, effectively inhibits the growth of cariogenic biofilm and *Streptococcus mutans* microorganisms. It has been repeatedly tested both on animals and humans, which is why it is a safe therapeutic proposition. It has been proven to secrete two types of bacteriocins: salivaricin A2 and B [21, 29, 38, 39].

It is known that preparations containing chlorhexidine have a strong bactericidal effect. As it turned out, a less popular but also successful method of getting rid of *Streptococcus mutans* in children with active caries is rinsing the mouth with probiotics. *Streptococcus oralis KJ3sm, Streptococcus uberis KJ2sm* as well as *Streptococcus rattus JH145* reduced the amount of cariogenic bacteria as a result of rinsing the mouth twice a day for 14 days [40].

Streptococcus oligofermentans, which discharge hydrogen peroxide (from lactic acid), have the ability to adhere to oral cavity tissues, and show low reaction with dietary carbohydrates [31].

Enterococcus

Studies have also been performed using *Enterococcus faecium CRL 183*, a probiotic known for antifungal activity and disturbing the growth of *Streptococcus*

mutans ATCC 25175 strain [41]. Research indicated that after a regular period of administration of probiotic preparations, there occurred a relevant growth of the pH level, a change in protein complex in saliva that prevents adhesion of pathogens (SM), cariostatic influence in the system enriched with probiotics, and the decrease of *Streptococcus mutans* CFU. However, several tests have not confirmed the effectiveness of the long-term dental caries prevention through maintaining low concentration of *Streptococcus mutans* in the oral biofilm after discontinuation of a probiotic course [12, 18–20].

Synbiotics in dental caries

Glucomannan hydrolysate (GMH) and three other saccharides: arabinose, xylose, and xylitol are prebiotics which are used in synbiotics preparations, eradicating carcinogenic *Streptococcus mutans* [25].

Xylose, xylitol, and arabinose demonstrated high prebiotic potential, and influence on saccharolytic bacteria, thereby regulating the reaction in the oral cavity, which is one of the factors of caries [10, 13, 25]. The latest discovery is also the use of synbiotics in anti-caries therapy. In 2011 the first statement about positive functionalities of synbiotics against *Streptococcus mutans* was made [10]. The administration of a probiotic for 15 days proved less effective in reducing the level of *Streptococcus mutans* in the saliva of children than a therapy with synbiotics [26].

Caries prophylaxis is connected with the prevention of pH decrease. Arginine (L-arg), which is a prebiotic, is controlled by ADS (arginine deiminase system) and discharges ornithine, citrulline, ammonia, and carbon dioxide, which suppress cariogenic bacteria acid production [10, 13]. L- arg may affect the decrease of adhesion and accumulation of pathogenic bacteria, which is a method of tooth decay reduction [13].

Due to the alkaline nature of L-arg, bacteria such as: *Streptococcus gordonii, Streptococcus parasanguinis, Streptococcus intermedius, Streptococcus australis,* and *Streptococcus cristatus* grow on the medium enriched with this amino acid and inhibit the development of *Streptococcus mutans* [13, 25]. However, the use of Arginine in the form of a prebiotic has also shown negative effects

in the long-term use. It enhances the multiplication of anaerobic bacteria (*Porphyromonas gingivalis*) and is a risk factor for increasing the pH of dental plaque [10].

Lactobacillus rhamnosus GG is an ideal candidate to combat the cariogenic *Streptococcus mutans UA159*. An *in vitro* study showed that the fusion of this probiotic with a prebiotic in the form of a collagen peptide significantly inhibits the development and virulence potential of *Streptococcus mutans*, and thus reduces its ability to secrete acid, thins the three-dimensional structure of the pathogenic biofilm, which is why it is effectively destroyed [42].

Previously conducted *in vitro* tests confirmed the validity of using synbiotics containing *Lactobacillus rhamnosus GG* and L-arginine to compete with caries pathogens. The higher the concentration of L-arginine, the more effectively the probiotic bacteria grew [10].

A solution with a 2% concentration of polysaccharide glucomannan hydrolysate (GMH) simulates the growth of *Lactobacillus acidophilus*, which makes it impossible for *Streptococcus mutans* to progress as opposed to the situation when only a GOS prebiotic is used [10, 13]. However, there is no clear explanation for the effect of GMH on *Lactobacillus acidophilus* [10].

Another prebiotic belonging to carbohydrates compounds (oligosaccharides) is fructooligosachharides (FOS). It has been proven that it effectively reduces the level of bacteria responsible for caries. A high concentration of FOS can be found in red bananas [35]. Recently, two potential candidates that could play a key role as prebiotics have been found: β-methyl-D-galactoside and N-acetyl-D-mannosamine, but studies have not yet confirmed their impact on dental caries prevention. Their action *in vitro* relies on increasing the dominance of commensal bacteria in oral conditions [10].

Conclusions

Despite declining statistics, dental caries remain firmly at the top of oral diseases. This multifactorial condition occurs mainly as a result of a reaction between the cariogenic bacteria that break down dietary carbohydrates and the oral microflora. Fluctuations in oral microbiota homeostasis lead to a state

of dysbiosis that increases the likelihood of the disease. Many methods are used to rebalance the oral microbiota, including: AMPs (antimicrobial peptides), nanoparticle drug delivery systems, EPM disruption techniques, immune response enhancers, and most importantly, good oral hygiene with mouthwashes, fluoridated toothpaste, and the use of dental floss [1]. However, due to the prevalence of high bacteria resistance and side effects, researchers are constantly looking for a suitable alternative method of treating tooth decay. New solutions are needed to help maintain and restore balance in the oral environment. In this review, based on the results found over the last 5 years, it is concluded that one of the newer discoveries are probiotics and synbiotics.

This review presents the effectiveness of these alternative methods in dental caries treatment and demonstrates that despite the need to perform many studies confirming their effectiveness, they seem to be one of the promising therapeutic and preventative solutions.

References

1. Radaic A, Kapila YL. The oralome and its dysbiosis: New insights into oral microbiome-host interactions. Computational and Structural Biotechnology Journal 2021; 19: 1335–1360.
2. Li X, Liu Y, Yang X, Li C, Song Z. The Oral Microbiota: Community Composition, Influencing Factors, Pathogenesis, and Interventions. Frontiers in Microbiology 2022 (Apr 29); 13: 895537. https://doi.org/10.3389/fmicb.2022.895537. PMID: 35572634; PMCID: PMC9100676.
3. Girija ASS, Ganesh PS. Functional biomes beyond the bacteriome in the oral ecosystem. Japanese Dental Science Review 2022; 58: 217–226.
4. López-Valverde N, López-Valverde A, Macedo de Sousa B, Rodríguez C, Suárez A, Aragoneses JM. Role of Probiotics in Halitosis of Oral Origin: A Systematic Review and Meta-Analysis of Randomized Clinical Studies. Frontiers in Nutrition 2022 (Jan 21); 8: 787908. https://doi.org/10.3389/fnut.2021.787908. PMID: 35127785; PMCID: PMC8813778.
5. Twetman S. Prevention of dental caries as a non-communicable disease. Eur J Oral Sci 2018 (Oct 1); 126: 19–25.

6. Sanghvi U, Chhabra T, Sethuraman R. Effect of probiotics on the amount and pH of saliva in edentulous patients: A Prospective study. J Indian Prosthodont Soc 2018; 18(3): 277.
7. Karbalaei M, Keikha M, Kobyliak NM, Khatib Zadeh Z, Yousefi B, Eslami M. Alleviation of halitosis by use of probiotics and their protective mechanisms in the oral cavity. New Microbes and New Infections 2021 (Apr 23); 42:100887. https://doi.org/10.1016/j.nmni.2021.100887. PMID: 34123388; PMCID: PMC8173312.
8. Mokhtari S, Atarbashi-Moghadam S, Motevaseli E, Ghafouri-Fard S, Hesampour A. Lactobacillus fermentum and Lactobacillus crispatus Do Not Have Cytotoxic Effects on HN5 Oral Squamous Cell Carcinoma Cell Line. Int J Dent 2021 (Sep 28): 3034068. https://doi.org/10.1155/2021/3034068. PMID: 34621315; PMCID: PMC8492272.
9. Babina K, Salikhova D, Polyakova M, Svitich O, Samoylikov R, El-Abed SA et al. The Effect of Oral Probiotics (Streptococcus Salivarius k12) on the Salivary Level of Secretory Immunoglobulin A, Salivation Rate, and Oral Biofilm: A Pilot Randomized Clinical Trial. Nutrients 2022 (Mar 1); 14(5).
10. BijleID MN, Ekambaram M, Lo ECM, Yiu CKY. Synbiotics in caries prevention: A scoping review. PLoS ONE 2020 (Aug 12); 15(8): e0237547. https://doi.org/10.1371/journal.pone.0237547. PMID: 32785270; PMCID: PMC7423128.
11. Majanga V, Viriri S. A Survey of Dental Caries Segmentation and Detection Techniques. Scientific World Journal 2022 (Apr 11): 8415705. https://doi.org/10.1155/2022/8415705. PMID: 35450417; PMCID: PMC9017544.
12. Abikshyeet P, Mishra P, Bhuyan L, Kumar V, Mahapatra N, Adhikary T. J Pharm Bioallied Sci 2022;14(Suppl 1): S34-S38. https://doi.org/10.4103/jpbs.jpbs_801_21. Epub 2022 Jul 13. PMID: 36110745; PMCID: PMC9469361.
13. Hernández P, Sánchez MC, Llama-Palacios A, Ciudad MJ, Collado L. Strategies to Combat Caries by Maintaining the Integrity of Biofilm and Homeostasis during the Rapid Phase of Supragingival Plaque Formation. Antibiotics 2022; 11(7): 880. https://doi.org/10.3390/antibiotics.

14. Marsh PD. In Sickness and in Health-What Does the Oral Microbiome Mean to Us? An Ecological Perspective. Advances in Dental Research 2018; 29(1): 60–65.
15. Kouhounde S, Adéoti K, Mounir M, Giusti A, Refinetti P, Otu A et al. Applications of Probiotic-Based Multi-Components to Human, Animal and Ecosystem Health: Concepts, Methodologies, and Action Mechanisms. Microorganisms. MDPI2022 (Aug 24); 10(9): 1700. https://doi.org/10.3390/microorganisms10091700. PMID: 36144301; PMCID: PMC9502345.
16. Zhang Y, Ding Y, Guo Q. Probiotic Species in the Management of Periodontal Diseases: An Overview. Frontiers in Cellular and Infection Microbiology 2022 (Mar 25); 12: 806463. https://doi.org/10.3389/fcimb.2022.806463. PMID: 35402306; PMCID: PMC8990095.
17. Motta P de B, Motta LJ, Costa da Mota AC, Leal Gonçalves ML, Silva T, Momolli M et al. Comparative study between photodynamic therapy with urucum + Led and probiotics in halitosis reduction-protocol for a controlled clinical trial. PLoS One 2021 (May 14);16(5): e0247096.
18. Hasslöf P, Stecksén-Blicks C. Chapter 10: Probiotic bacteria and dental caries. In: Monographs in Oral Science. S. Karger AG; 2019, pp. 99–107.
19. Bustamante M, Oomah BD, Mosi-Roa Y, Rubilar M, Burgos-Díaz C. Probiotics as an Adjunct Therapy for the Treatment of Halitosis, Dental Caries and Periodontitis. Probiotics and Antimicrobial Proteins 2020; 12(2): 325–334.
20. Lin TH, Lin CH, Pan TM. The implication of probiotics in the prevention of dental caries. Applied Microbiology and Biotechnology 2018; 102(2): 577–586. https://doi.org/10.1007/s00253-017-8664.
21. Archambault LS, Dongari-Bagtzoglou A. Probiotics for Oral Candidiasis: Critical Appraisal of the Evidence and a Path Forward. Front Oral Heal 2022 (Apr 14); 3.
22. Kamal Y, Kandil M, Eissa M, Yousef R, Elsaadany B. Probiotics as a prophylaxis to prevent oral candidiasis in patients with Sjogren's syndrome: a double-blinded, placebo-controlled, randomized trial. Rheumatol Int 2020 (Jun); 40(6): 873–879. https://doi.org/10.1007/s00296-020-04558-9.

23. Sudhakaran S., Tom JJ, Shyam A, Mohan S, Ali S, and Raj M. Effect of Chlorhexidine and Probiotics on Halitosis 2021 (Jun); 13(Suppl 1): S807–S811. https://doi.org/10.4103/jpbs.JPBS_768_2 PMCID: PMC8375843PMID: 34447205.
24. Seidel CL, Gerlach RG, Weider M, Wölfel T, Schwarz V, Ströbel A et al. Influence of probiotics on the periodontium, the oral microbiota and the immune response during orthodontic treatment in adolescent and adult patients (ProMB Trial): study protocol for a prospective, double--blind, controlled, randomized clinical trial. BMC Oral Health 2022 (Apr 12); 22(1).
25. Mohd Fuad AS, Amran NA, Nasruddin NS, Burhanudin NA, Dashper S, Arzmi MH. The Mechanisms of Probiotics, Prebiotics, Synbiotics, and Postbiotics in Oral Cancer Management. Probiotics Antimicrob Proteins 2023; 15: 1298–1311. https://doi.org/10.1007/s12602-022-09985-7. Epub 2022 Sep 1. PMID: 36048406; PMCID: PMC9434094.
26. Di Stefano M, Polizzi A, Santonocito S, Romano A, Lombardi T, Isola G. Impact of Oral Microbiome in Periodontal Health and Periodontitis: A Critical Review on Prevention and Treatment. Int J Mol Sci 2022; 23(9): 5142. https://doi.org/10.3390/ijms23095142.
27. Cunningham M, Azcarate-Peril MA, Barnard A, Benoit V, Grimaldi R, Guyonnet D et al. Shaping the Future of Probiotics and Prebiotics. Trends Microbiol 2021; 29(8): 667–685. https://doi.org/10.1016/j.tim.2021.01.003.
28. Haas AN, Furlaneto F, Gaio EJ, Gomes SC, Palioto DB, Castilho RM et al. New tendencies in non-surgical periodontal therapy. Braz Oral Res 2021; 35(Supplement 2): e095. https://doi.org/10.1590/1807--3107bor-2021.vol35.0095.
29. Kim HJ, Yoo HJ. Inhibitory effects of Streptococcus salivarius K12 on formation of cariogenic biofilm. J Dent Sci 2023 (Jan); 18(1): 65–72. https://doi.org/10.1016/j.jds.2022.07.011. Epub 2022 (Aug 5). PMID: 36643262; PMCID: PMC9831821.
30. Sengupta P, Desai PD, Maity I, Mazumdar P, Biswas S, Choudhury SR et al. Comparative evaluation of different probiotic products on salivary

Streptococcus mutans and Lactobacillus level in caries risk population. J Conserv Dent 2020 (Nov – Dec); 23(6): 619–623.

31. Chen Z, Schlafer S, Göstemeyer G, Schwendicke F. Probiotic effects on multispecies biofilm composition, architecture, and caries activity in vitro. Microorganisms 2020 (Aug 21); 8(9): 1272. https://doi.org/10.3390/microorganisms8091272.
32. Hasslöf P, Granqvist L, Stecksén-Blicks C, Twetman S. Prevention of Recurrent Childhood Caries with Probiotic Supplements: A Randomized Controlled Trial with a 12-Month Follow-Up. Probiotics Antimicrob Proteins 2022 (Apr); 14(2): 384–390. https://doi.org/10.1007/s12602--022-09913-9.
33. Wu J, Jiang X, Yang Q, Zhang Y, Wang C, Huang R. Inhibition of Streptococcus mutans Biofilm Formation by the Joint Action of Oxyresveratrol and Lactobacillus casei. Appl Environ Microbiol 2022 (May 10); 88(9): e0243621. https://doi.org/10.1128/aem.02436-21.
34. Kim JH, Jang HJ, Lee NK, Paik HD. Antibacterial and Antibiofilm Effect of Cell-Free Supernatant of Lactobacillus brevis KCCM 202399 Isolated from Korean Fermented Food against Streptococcus mutans KCTC 5458. J Microbiol Biotechnol 2022 (Jan 28); 32(1): 56–63.
35. Martirosyan DM, Singh J. A new definition of functional food by FFC: What makes a new definition unique? Functional Foods in Health and Disease 2022; 5(6): 209–223. https://doi.org/10.31989/ffhd.v5i6.183.
36. Chen LR, Lai CL, Chen JP, Kao CT. The Effect of Probiotics Use on Salivary Cariogenic Bacteria in Orthodontic Patients with Various Caries Risk Status. Nutrients. 2022 (Aug 4); 14(15): 3196. https://doi.org/10.3390/nu14153196.
37. Zhang J, Duan Z. Identification of a new probiotic strain, Lactiplantibacillus plantarum VHProbi® V38, and its use as an oral health agent. Front Microbiol 2022 (Dec 12); 13.
38. Mundula T, Ricci F, Barbetta B, Baccini M, Amedei A. Effect of probiotics on oral candidiasis: A systematic review and meta-analysis. Nutrients 2019; 11(10): 2449. https://doi.org/10.3390/nu11102449. PMID: 31615039; PMCID: PMC6836010.

39. Mokhtar M, Rismayuddin NAR, Mat Yassim AS, Ahmad H, Abdul Wahab R, Dashper S et al. Streptococcus salivarius K12 inhibits Candida albicans aggregation, biofilm formation and dimorphism. Biofouling 2021 (Aug); 37(7): 767–776.
40. Kamble A, Jabin Z, Agarwal N, Anand A. Effectiveness of Oral Probiotics in Reducing S. Mutans Count in Caries-active Children: A Comparison with Chlorhexidine and Herbal Mouthrinse (Hiora®). Int J Clin Pediatr Dent 2022; 15(S2): S207–211.
41. Lordello VB, Meneguin AB, de Annunzio SR, Taranto MP, Chorilli M, Fontana CR et al. Orodispersible film loaded with enterococcus faecium crl183 presents anti-candida albicans biofilm activity in vitro. Pharmaceutics 2021 (Jul); 13(7): 998.
42. Jung HY, Cai JN, Yoo SC, Kim SH, Jeon JG, Kim D. Collagen Peptide in a Combinatorial Treatment with Lactobacillus rhamnosus Inhibits the Cariogenic Properties of Streptococcus mutans: An In Vitro Study. Int J Mol Sci 2022 (Feb 7); 23(3): 1860. https://doi.org/10.3390/ijms23031860.