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Probiotic Supplementation: A Promising Preventive Strategy for Dental Caries

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ABSTRACT

Dental diseases are widespread health problems encountered globally. Tooth decay is one of the most widespread oral health issues globally. Key factors contributing to the development of dental caries include inadequate oral hygiene, the presence of specific carbohydrates in the diet, dental biofilm formation, high levels of cariogenic microbes, reduced salivary flow, insufficient fluoride exposure, gingival recession, genetic predispositions, and neglect of personal dental care. Various preventive strategies have been employed to lower the risk of developing dental caries. Probiotics are live microorganisms that, when taken in appropriate quantities, provide health benefits to the host. They are acknowledged as potential supplementary treatments for various diseases. This manuscript reviews recent research on the role of probiotics in preventing dental caries and explores the potential mechanisms behind their effects. Literature reviews show that regular consumption of probiotic products significantly lowers the risk of dental caries by inhibiting cariogenic bacteria and promoting beneficial microbes in the oral cavity. The beneficial effects of probiotics are likely due to their ability to buffer salivary pH, produce bacteriocins and enzymes (such as dextranase, mutanase, and urease), and compete for adhesion and colonization on tooth surfaces. Additional research is needed to evaluate the effectiveness of long-term probiotic supplementation in controlling dental diseases and to assess how probiotic use during childhood affects the risk of developing caries.

Keywords: Dental caries, Bacteriocin, Microbiota, Probiotics.

1 Introduction

The mouth hosts a wide range of microorganisms that play a role in the host's health and disease condition. Bacteria are the primary inhabitants of the oral cavity. The composition of oral microbiota varies based on the surfaces colonized, nutrient availability, oral hygiene habits, and environmental influences [1]. Disruption of the normal balance of resident microbes (healthy oral microbiota) leads to the onset of oral conditions such as dental caries (tooth decay), periodontitis, gingivitis, infections related to endodontics and orthodontics, and periimplantitis [2]. Dental diseases, especially dental caries, are the most prevalent health issue affecting a larger number of people in developing nations [3]. In 2015, global expenditures on dental disease treatment were estimated at approximately $544.41 billion, with costs varying depending on the specific treatment procedures and interventions [4,5].

Dental caries is a complex, chronic condition where cariogenic bacteria cause destruction and demineralization of the hard tissues of the teeth, leading to an imbalance between tooth minerals and oral microbial biofilms. Numerous factors contribute to the development of dental caries [6–9]. Dental caries begins when resident microbes produce organic acids from carbohydrate metabolism, leading to pH reduction and subsequent demineralization of teeth. Prolonged demineralization ultimately results in the formation of a cavity on the tooth surface. Nevertheless, demineralization can be reversed through the application of fluoride supplements. An imbalance in the oral microbial community may also contribute to cavity formation due to the release of bacterial enzymes such as glucan sucrases [9].

Various alternative and effective therapeutic approaches, aside from antimicrobial agents, are now utilized for the treatment of oral diseases. Microbial enzymes like glucanase (including dextranase and mutanase), deoxyribonucleases (DNases), and ionic detergents are employed to eradicate plaque biofilms. Other potential treatments for oral infections include light-activated microbial cell destruction and the use of microbial protease inhibitors [2]. Likewise, probiotics are acknowledged as a powerful treatment option for dental conditions. Probiotics are living microorganisms that, when taken in appropriate quantities, provide health benefits to the host and have been demonstrated to serve as alternative or complementary therapeutic options for various diseases and conditions [10–17]. Probiotic treatments beneficially alter the microbial balance in the gut, actively combat the formation of dental plaque biofilms, and enhance the host's immune response to cariogenic microbes [18].

This manuscript reviews the efficacy of probiotics in preventing or treating dental caries. The manuscript also explores the potential mechanisms responsible for the positive impact of probiotics on oral microbial composition. The literature was searched across multiple databases such as Scopus, Web of Science, PubMed, and Google Scholar, using keywords like "probiotics," "dental caries," and "oral microbiome." Relevant articles were chosen for the manuscript without limiting by publication date.

2 Dental Microbiota

The microbiota plays a crucial role in the physiological, immunological, and psychological aspects of its host. In general, the microbiota maintains a beneficial relationship with the host system, particularly influencing host metabolism and immune function. However, disruptions caused by external factors such as pathogenic infections or immunosuppressive drugs, as well as internal factors like autoimmune disorders, can lead to mild to severe health problems. Age, method of delivery at birth, genetic predisposition, dietary habits, antibiotic usage, and the consumption of probiotics and prebiotics are key factors influencing the composition of the gut microbiota [19]. The mouth serves as the primary gateway for microbial entry into the host system, and each part of the body harbors a distinct, site-specific microbial community. The oral mucosa, tongue, tooth surfaces, and gingival regions host specific microbial communities, while saliva contains a diverse mixture of oral microorganisms [20].

The oral microbiota comprises approximately 700-1000 species and around 19,000 distinct genotypes within the microbial community. The diversity of the oral microbiota differs among individuals. Oral microbial diversity is significantly influenced by diet, age, genetics, hygiene practices, and living conditions. The overuse of antibiotics, cytotoxic drugs, and immunodeficiency conditions also disrupt permanent oral microbial habitats [21, 22]. Studies of the oral microbiome using metagenomic methods have unveiled the composition, complexity, and functional aspects of oral microbes in both health and disease [23].

Streptococcus mutans is closely linked to dental caries and is recognized as a key cariogenic bacterium because of its capacity to thrive in acidic environments and produce antigens that enable it to survive in both saliva and the extracellular matrix [24–26]. In addition to mutans streptococci, streptococcal strains and Candida species are frequently found in 40 to 60% of caries cases in both adults and children, and are regarded as significant secondary cariogenic agents [17, 27]. Candida species are considered potent opportunistic cariogenic yeasts due to their capability to produce short-chain carboxylic acids and proteinases, as well as their capacity to adhere to non-living surfaces and form biofilms [28, 29]. Lactobacilli are commonly found in caries lesions as well. Similar to Candida species, lactobacilli are acid-resistant organisms linked to the progression of dental caries [30].

The microbial composition of caries lesions and plaque biofilms is influenced by factors such as the presence of easily digestible carbohydrates, acidity levels, and the prevalence of acid-resistant species. Nevertheless, mutans streptococci, Candida species, and lactobacilli are typical cariogenic microbes. However, recent advancements in molecular detection and high-throughput sequencing have uncovered several less common novel microbial species in oral plaques and biofilms. Scardovia wiggsiae, Slackia exigua, Firmicutes, Granulicatella elegans, Bifidobacterium, Corynebacterium matruchotii, Streptococcus cristatus, Streptococcus gordonii, Neisseria flavescens, N. mucosa, and N. pharynges are among the newly identified species and phylotypes of microorganisms detected in dental caries and plaque biofilms in both adults and children [31–40]. In general, the literature suggests that the oral microbiota is distinctive and varied. Until recently, mutans streptococci were thought to be the primary cause of dental caries, but S. mutans has been found absent in some instances of dental caries [24]; it has also been observed in biofilms on tooth surfaces [41]. While advanced techniques and research methods have shed light on some aspects of the oral microbiota in relation to both health and disease, additional studies are necessary to fully uncover the mechanisms and main contributors to the development of dental caries.

2.1 Probiotic Use's Impact on Dental Caries in People

Numerous studies in chidren and adults have investigated the impact of probiotics on dental caries Table 1.

Table 1. The questions of survey that send to dentists.

Probiotics	Dose	Subjects	Effects	Ref
		Children		
Lactobacillus rhamnosus GG containing milk	5-10×10^5 CFU perml	Children (1-6 years old; n=594)	To decrease the risk of caries	[42]
Probiotic juice containing L. rhamnosus GG	5×10^6 CFU per ml (200 ml per day)	Children (3-6 years old; n=530)	To decrease the risk of caries, the need for dental care & Streptococcus mutans count	[43]
Probiora3 tablet (S. uberis KJ2TM, S. oralis KJ3TM, and S. rattus JH145TM)	-	Children (4-6 years old; n=40)	To decrease Cariogenic bacteria count	[44]
Probiora3 tablet (S. uberis KJ2TM, S. oralis KJ3TM, and S. rattus JH145TM)	1 tablet per day	Children (2-3 years old; n=138)	To decrease Dental caries, Caries increment & Risk reduction	[45]
L. rhamnosus, Bifidobacterium longum, and Saccharomyces cerevisiae (or) Bacillus coagulans	1.25×10^9 CFU of each strain (or) 150×10^6 CFU of B. coagulans	Children (7-14 years old; n=150)	To decrease S. mutans count	[46]
Streptococcus salivarius M18	3.6×10^9 CFU	Children (5-10 years old; n=100)	To decrease Plaque scores & S. mutans count	[47]
Lactobacilli reuteri	2×10^8 CFU per day	Children (6-12 years old; n=60)	To decrease S. mutans count & Lactobacilli count	[48]
S. uberis KJ2, S. oralis KJ3, S. rattus JH145	10^8 CFU per day	Children (6-12 years old; n=60)	To decrease S. mutans count & Lactobacilli count	[48]
L. reuteri ATCC 55730	10^8 CFU per day	Children (n=113)	To decrease Caries lesions & Gingivitis	[49]
Lactobacillus rhamnosus LB21 and fluoride	10^7 CFU/ml (150 ml per day); 2.5mg of fluoride per liter	Children (1-15 years old; n=248)	To decrease Dental caries & Antibiotic treatment	[50]
Streptococcus salivarius M18	10^9 CFU/tablet (1 tablet per day)	Children (6-17 years old; n=76)	Prevent the development of caries	[51]
Milk containing L. rhamnosus SP1	10^7 CFU/ml (150 ml per day)	Children (2-3 years old; n=261)	To decrease Caries increment & Dental caries	[52]
Yakult (milk containing L. casei Shirota)	-	Children (7-11 years old; n=18)	To increase Minimum pH To decrease pH recovery time	[53]
BioGaia (L. reuteri DSM 17938 and L. reuteri ATCC PTA 5289) Orbit Gum (Xylitol)	-	Children (7-12 years old; n=200)	To decrease Plaque and gingival scores & Salivary mutans streptococci count	[54]
Milk containing L. paracasei SD1	10^7 CFU/g (5g per day)	Children (12-14 years old; n=122)	To increase Lactobacilli load To decrease Salivary mutans streptococci count, Caries lesions & Caries risk	[55]
Milk containing L. paracasei SD1	10^7 CFU/g (5g per day)	Children (1.5-5 years old; n=124)	To decrease Salivary mutans streptococci count Delayed the caries development	[56]
Milk containing L. paracasei SD1	10^7 CFU/g (5 g per day)	Children (12-14 years old; n=40)	To increase Total lactobacilli and L. casei/L. paracasei & Salivary IgA level To decrease Total Streptococci and S. mutans	[57]
L. rhamnosus and Bifidobacterium longum	Lacto:5×10^6 CFU Bifido:3×10^6 CFU	Children (3-4 years old; n=363)	S. mutans and Lactobacillus species count To increase Salivary buffering capacity	[58]
L. rhamnosus SD11 (milk powder or fermented milk)	7.5±0.20×10^7 CFU/g (5 g per day) or 5×1010 CFU/ml (100 ml per day)	Children (13-14 years old; n=458)	To increase Lactobacilli load To decrease S. mutans, % of caries progression & Caries lesions	[59]
		Adults		
L. rhamnosus LC705 and Lactobacillus rhamnosus GG containing cheese	LC705:1.2×10^7 CFU/g GG:1.9×10^7 CFU/g	Adults (18-35 years old; n=74)	To decrease S. mutans and yeast count	[60]
Bifidobacterium DN-173010	7×10^7 CFU/g	Adults (21-24 years old; n=21)	To decrease Salivary mutans streptococci count	[61]
Probiotic mouthwash:ProBiora3 (Streptococcus oralis KJ3sm, S. uberis KJ2sm, and S. rattus JH145)	10^6 or 10^8 CFU of each strain	Adults (21-35 years old; n=20)	To decrease Harmful bacterial count & the risk of development of caries	[62]
Fermented milk containing Lactobacillus casei Shirota	10^8 CFU per ml (65 ml per day)	Adults (20-35 years old; n=28)	To decrease Gingival crevicular fluid volume, Bleeding on probing & Gingival inflammation	[63]
L. paracasei GMNL-33	3×10^8 cells/tablet (thrice a day)	Adults (20-26 years old; n=78)	To decrease S. mutans count No change in Lactobacilli counts and salivary buffer capacity	[64]
Heat-killed L.paracasei DSMZ16671	1 or 2mg of cells	Adults (n=78)	To decrease Salivary mutans streptococci count	[65]
L. paracasei SD1	7.5±0.20×10^8 CFU/g (10 g per day)	Adults (18-25 years old; n=40)	To decrease Salivary mutans streptococci count To increase Lactobacilli count	[66]
L. salivarius WB21, or L. salivarius TI2711	WB21:6.7×10^8 CFU/tablet TI2711:2.8×10^8 CFU/tablet	Adults (24.8±2.3 years; n=64)	To decrease Salivary mutans streptococci count No change in salivary flow and salivary pH To increase Salivary buffering capacity & Lactobacilli levels	[67]
Probiotic milk containing L. rhamnosus LB21 or fluoride	10^7 CFU/ml (200 ml per day); 5.0 mg of fluoride per liter	Elder adults (58-84 years old; n=408)	No change in microbial load To increase ECM score & RCI reversal rate	[68]
Probiotic lozenges (Hyperbiotics Pro-Dental, U.S.A)	-	High-risk of developing caries patients (n=36)	To decrease Plaque accumulation & Calculus formation	[69]

A significant body of evidence suggests that regular consumption of probiotic products can reduce the incidence of dental caries.

In children, the regular intake of probiotic milk containing Lactobacillus rhamnosus GG (5–10 × 10^5 CFU/ml) over a period of 7 months (5 days a week) notably decreased the incidence of dental cavities. Specifically, the use of probiotic milk decreased the number of Streptococcus mutans bacteria and lowered the cumulative score for dental cavities in 3–4-year-old children compared to those receiving a placebo. The study suggested that probiotic milk could be viewed as a beneficial dietary supplement for enhancing the oral health of children attending daycare [42]. Likewise, extended consumption of carrot-pineapple juice (Gefilus®) enriched with L. rhamnosus GG and calcium decreased the count of S. mutans and lowered the likelihood of dental cavities in children [43].

The administration of Probiora3® tablets decreased the count of cariogenic bacteria in children at high risk of dental cavities. A 15-day course of probiotic tablets resulted in a significant reduction in cariogenic bacteria count compared to the initial measurement, and the protective benefits of probiotics persisted during the 15-day follow-up period [60]. Over a period of one year, daily supplementation with Probiora3® tablets reduced the advancement and occurrence of dental cavities. Furthermore, probiotic supplementation lowered the likelihood of children developing dental cavities [61]. The use of a blend of probiotic supplements (1.25×10^9 CFU each of L. rhamnosus, Bifidobacterium longum, and Saccharomyces cerevisiae) or a single strain (Bacillus coagulans; 1.5×10^8 CFU) for 14 days notably decreased the number of S. mutans bacteria in children compared to a placebo. Both probiotic supplements enhanced children's oral hygiene by lowering the count of cariogenic microbes. The research indicated that employing B. coagulans is cost-effective and enhances oral health, thereby helping to prevent dental cavities in children [62]. Giving Streptococcus salivarius M18 (3.6×10^9 CFU per day) for 3 months notably decreased the plaque score in children compared to the placebo control. The M18 strain demonstrated extensive antimicrobial activity against various cariogenic bacteria. There were no reported adverse effects from using M18 among the participants throughout the study period. The treatment group showed a decrease in S. mutans count, which was linked to the enhanced colonization of the M18 strain. There were no notable variations in the counts of S. salivarius, Lactobacillus, Streptococcus, and Candida species between the groups receiving treatment and those receiving a placebo. The study proposed that consistent use of S. salivarius M18 could potentially lower the risk of plaque buildup by inhibiting the growth of cariogenic bacteria, specifically S. mutans, in children [44].

The use of PerioBalance (probiotic lozenges containing 2×10^8 CFU of Lactobacilli reuteri) for 28 days and EvoraKids (chewing tablets containing 10^8 cells of S. uberis KJ2, S. oralis KJ3, S. rattus JH145) for 30 days resulted in a significant decrease in S. mutans and Lactobacillus counts in children. The study concluded that both PerioBalance and EvoraKids are sufficiently effective in reducing dental cavities caused by bacterial species [45].

Providing L. reuteri ATCC 55730 (10^8 CFU per day) to mothers during the final month of pregnancy and to newborns for one year resulted in a decreased occurrence of dental issues such as cavities and gingivitis, persisting up to nine years after treatment. The incidence of dental cavities was lower in the group receiving probiotics compared to the placebo group. There were no differences observed among the subjects in terms of salivary levels of mutans streptococci and lactobacilli, salivary secretory IgA, plaque index, and gingival bleeding index. The research indicated that administering L. reuteri ATCC 55730 in early childhood resulted in lower rates of dental cavities and gingivitis scores, even at the age of 9 years. The protective effect was attributed to the successful transmission of L. reuteri from mothers to their children [63].

Stecksén-Blicks et al. According to [68], providing preschool children with probiotic milk containing L. rhamnosus LB21 (10^7 CFU/ml; 150 ml per day) and fluoride (2.5 mg per liter) for 21 months significantly decreased dental cavities by up to 75% and reduced the necessity for antibiotic treatment compared to a placebo control. Initially and after treatment, there were no notable discrepancies in the counts of Lactobacilli and mutans streptococci between the treatment and control groups. The findings suggest that regular use of probiotics and fluoride could potentially lower the occurrence of dental cavities in preschool-aged children.

Children who took daily supplements of Streptococcus salivarius M18 tablets (1 billion CFU per day) for 90 days experienced a decreased risk of developing dental cavities. More specifically, the likelihood of preventing new cavities, susceptibility, and bacterial load was significantly reduced following probiotic treatment compared to both the initial condition and the placebo [46]. The administration of 150 ml of probiotic milk containing L. rhamnosus SP1 (10^7 CFU/ml) over 40 weeks notably decreased the advancement and severity of dental cavities in children compared to the placebo control. No negative effects were noted. The findings indicate that consistent long-term intake of L. rhamnosus SP1 could potentially decrease the occurrence of dental cavities in children [64].

The intake of L. casei Shirota-fortified milk (Yakult) for 7 days demonstrated beneficial effects on the risk of dental cavities in children. The group that received probiotic supplementation experienced a rise in the lowest salivary pH levels, along with decreased acidity of oral biofilm and shorter pH recovery times. There was no alteration observed in the counts of lactobacilli and mutans streptococci, as well as in the risk factors for dental cavities. The findings suggested that brief supplementation with L. casei Shirota has the ability to lower the functional acidity of oral biofilms in children, indicating that Yakult could be utilized for preventing and treating dental cavities [47]. Kaur et al. (2018) investigated the effectiveness of probiotics and xylitol chewing gums on children's oral health. The children were given either BioGaia™ (containing L. reuteri DSM 17938 and L. reuteri ATCC PTA 5289) or Orbit® Gum (with Xylitol) once a day for 3 weeks, and the study measured alterations in S. mutans count, plaque, and gingival indexes. There was no notable distinction in S. mutans count and plaque index between the probiotic and xylitol groups. However, the probiotic group exhibited a significant reduction in the gingival index. When

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comparing within each group, both probiotics and xylitol chewing gums notably decreased plaque and gingival indexes, as well as reduced the S. mutans count in children compared to their initial baseline measurements. The findings showed that BioGaia™ effectively lowered the likelihood of dental cavities in children compared to Orbit® Gum, suggesting that probiotic-based chewing gums are a promising adjunct therapy in treating cavities [48].

Teanpaisan et al. According to [65], consuming milk enriched with L. paracasei SD1 (10^7 CFU/g; 5 g per day) significantly boosted lactobacilli levels and decreased salivary mutans streptococci counts. Overall, the probiotic intervention lowered the risk of developing cavities and prevented the worsening of caries lesions in children aged 12-14 years. The study demonstrated that long-term consumption of the probiotic strain L. paracasei SD1 enhanced resistance to dental caries in children. These findings are supported by the research of Pahumunto et al. which found that consuming probiotic milk with L. paracasei SD1 (10^7 CFU/g; 5 g per day) for 3 months reduced both caries development and mutans streptococci count in preschool children compared to a placebo [66]. The probiotic group experienced a reduction in caries progression, and there was also a regression of caries lesions observed within this group. Consuming probiotic milk decreased tooth decay in children compared to the placebo and baseline values. The results suggested that L. paracasei SD1 could lower the risk of caries in children by promoting the regression of caries lesions, reducing tooth decay, and slowing caries progression [66]. Consuming L. paracasei SD1-enriched milk for 6 months significantly reduced total streptococci and S. mutans levels while increasing total lactobacilli and L. casei/L. paracasei levels in children. Ingesting L. paracasei SD1 raised salivary IgA levels, which showed a positive correlation with L. casei/L. paracasei counts. The findings indicated that milk containing L. paracasei SD1 might help prevent caries [67]. Conversely, providing probiotic supplementation with L. paracasei F19 during early life did not influence the occurrence of dental caries. The intervention had no impact on the count of cariogenic bacteria in later life stages, and the probiotic strain was not found in the saliva samples of the participants after a 9-year follow-up period. The findings indicated that the intervention with L. paracasei F19 does not provide long-term benefits for oral health [49].

Approximately 363 preschool children were given 200 ml (once daily) of probiotics (containing 5×10^6 CFU of L. rhamnosus and 3×10^6 CFU of Bifidobacterium longum) or standard milk over a period of 9 months. Next, the study compared the changes in S. mutans and Lactobacillus species counts, salivary pH, salivary buffer capacity, and dental plaque between the baseline and the placebo control group. The findings demonstrated that after 9 months, probiotic milk consumption effectively decreased the Lactobacillus species count and enhanced the salivary buffer capacity in preschool children. There were no notable changes observed in the count of S. mutans, pH levels, or plaque index. The findings indicated that milk containing L. rhamnosus and B. longum reduced the lactobacilli levels in children. Further research is necessary before recommending this probiotic milk for managing caries in preschool children [50].

Probiotic supplementation, whether through fermented milk with 5×10^{1010} CFU/ml of L. rhamnosus SD11 or condensed milk powder containing $7.5\pm0.20\times10^7$ CFU/g of L. rhamnosus SD11, led to significant reductions in caries lesions, the percentage of caries progression, and S. mutans count in children. Both the fermented milk and condensed milk powder demonstrated beneficial effects compared to their respective baseline measures and placebo controls [51]. However, Angarita-Diaz et al. (2019) found that providing probiotic milk containing 7.5×105 CFU/ml of L. rhamnosus GG and 4.5×10^5 CFU/ml of B. longum for 3 months did not demonstrate positive effects on the oral health status of children. The consumption of probiotic milk led to increased salivary acidity and decreased remineralization of dental caries, yet it did not reduce the count of S. mutans. The findings suggested negative impacts on the oral health of children, emphasizing the critical importance of selecting effective probiotic strains when developing dental care products [52].

The brief intervention (3 weeks) using probiotic cheese enriched with L. rhamnosus GG (1.9×10^7 CFU/g) and L. rhamnosus LC705 (1.2×10^7 CFU/g) decreased salivary counts of S. mutans and yeast. However, no substantial changes were noted after the intervention period. The count of cariogenic microbes decreased in all participants, regardless of the treatment received, indicating that consuming cheese may potentially lower the risk of developing cavities [53]. Consuming probiotic yogurt with Bifidobacterium DN 173010 (7×10^7 CFU/g) for 2 weeks (200 g per day) notably decreased the count of mutans streptococci compared to the placebo group. However, there was a reduction in lactobacilli levels among healthy participants consuming probiotic yogurt, although this decrease did not show statistical significance compared to the control group. The main research confirmed that supplementing with Bifidobacterium DN-173010 reduces cariogenic bacteria in saliva among adults [54].

The application of mouthwash containing probiotics decreased the likelihood of dental caries formation. Healthy individuals were instructed to use ProBiora3®, a blend of Streptococcus oralis KJ3sm, Strep. uberis KJ2sm, and Strep. rattus JH145, twice daily for a period of 4 weeks as a mouthwash (Dosage: 10^6 and 10^8 CFU per day). The findings indicated that the utilization of ProBiora3® did not cause any negative effects on the participants, and there was no impact observed on the oral microbial community. A four-week application of ProBiora3® decreased the presence of detrimental bacteria in both the oral cavity and periodontal sulcus. The research suggested that ProBiora3™ could be beneficial for promoting oral cleanliness [55].

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Over a period of 4 weeks, daily intake of 65 ml of fermented milk containing Lactobacillus casei Shirota (10^8 CFU per ml) decreased biomarkers associated with gingival inflammation in healthy adults. Specifically, the volume of gingival crevicular fluid and the scores for bleeding on probing were notably decreased following the treatment compared to the placebo control. The study suggested that daily intake of probiotic milk could mitigate the impacts of gingival inflammation induced by plaque [56].

Consuming probiotic tablets with Lactobacillus paracasei GMNL 33 (3×10^8 cells/tablet; three times daily for 2 weeks) notably decreased the salivary count of Streptococcus mutans in adults following the 2-week treatment period. The assessments conducted before, immediately after treatment, and two weeks post-treatment showed that consuming Lactobacillus paracasei GMNL-33 did not impact the count of Lactobacillus species or salivary buffer capacity. The findings suggested that it takes at least two weeks for Lactobacillus paracasei GMNL-33 administration to effectively reduce cariogenic S. mutans levels in adults [57].

Consuming condensed milk with L. paracasei strain SD1 for four weeks notably decreased the number of mutans streptococci in saliva and slightly lowered lactobacilli levels in adult participants [69]. These findings suggest that incorporating L. paracasei-infused candy and milk could be an efficient method for controlling dental cavities and maintaining oral health.

Young adults received L. salivarius WB21 (6.7×10^8 CFU per tablet), L. salivarius TI2711 (2.8×10^8 CFU per tablet), Ovalgen DC, or xylitol daily for a duration of 2 weeks. The levels of mutans streptococci and lactobacilli, salivary pH, salivary flow rate, and buffering capacity were assessed before and after the intervention to analyze changes. Supplementing with L. salivarius, particularly the WB21 strain, notably decreased mutans streptococci levels and enhanced lactobacilli counts, with no observed alterations in salivary flow rate and pH. The group supplemented with TI2711 showed an increase in salivary buffering capacity. The findings demonstrated that using L. salivarius tablets can lower the risk of developing dental cavities [58].

Elderly adult volunteers were given probiotics (L. rhamnosus LB21; 10^7 CFU/ml) and/or fluoride (5 mg per liter) in milk daily for 15 months (200 ml per day). The study assessed changes in S. mutans and Lactobacillus levels in dental plaque from before treatment to after treatment. The findings indicated minimal changes in microbial levels, with no statistically significant differences observed. The groups consuming probiotic and probiotic + fluoride milk showed higher rates of reversal in the root caries index and increased electric caries measurement scores compared to the placebo group. The electric caries measurement showed that consuming milk with probiotic + fluoride increased dental mineralization in elderly participants. In particular, milk containing fluoride improved primary root caries lesions (PRCL) in elderly individuals. The findings indicated that regularly consuming milk with probiotic and/or fluoride could potentially decrease primary root caries lesions (PRCL) in elderly adults [59].

Using probiotic lozenges (Hyperbiotics Pro-Dental, U.S.A) for 60 days decreased plaque buildup and calculus formation in patients at high risk of developing cavities. In particular, the application of probiotic lozenges influences the debris, plaque, and calculus indices, OHI-S (Oral Hygiene Index-Simplified), DMF-T (decayed, missing, and filled teeth), saliva buffering capacity, saliva pH, and salivary flow rate in patients at high risk of developing cavities. The findings indicated that regular use of probiotic lozenges could help prevent dental caries in patients at high risk of developing cavities [70].

3 Potential Mechanisms of Action for Probiotics

The reasons why probiotics benefit dental health, such as reducing caries and plaque, vary for each strain and involve a combination of competing actions. The probiotic strain Streptococcus A12 competes against cariogenic S. mutans by raising plaque pH through the arginolytic pathway, adhering to tooth surfaces, and secreting a challisin-like protease that inhibits the bacteriocin production of S. mutans [71]. Likewise, Streptococcus dentisani produces bacteriocin that eliminates cariogenic bacteria and regulates dental plaque pH through the arginolytic pathway [72]. These results stem from initial in vitro studies; additional clinical assessments are needed to validate the efficacy of these strains as therapeutic agents against dental cavities.

Streptococcus salivarius strains are acknowledged as probiotics for dental plaque. S. salivarius competes with cariogenic bacteria through its capability to colonize soft tissues. Children who were supplemented with S. salivarius strain M18 exhibited notably reduced plaque scores and S. mutans counts. The decrease in plaque scores and cariogenic bacteria count was associated with the greater colonization of S. salivarius M18 [44]. The bacteriocin produced by S. salivarius M18 inhibits microorganisms in dental plaque. Additionally, S. salivarius M18 generates urease and dextranase enzymes, which help neutralize saliva acidity and reduce plaque formation, respectively [46]. S. salivarius JH is recognized as a highly effective probiotic strain against plaque, attributed to its bacteriocins such as streptin, salivaricin A3, streptococcin SA-FF22, and salivaricin E, along with its dextranase enzyme [73]. Supplementing with L. paracasei SD1 raised salivary levels of human neutrophil peptide 1-3 (HNP1-3), increased lactobacilli counts, and decreased mutans streptococci counts. While SD1 increased HNP1-3 levels, the beneficial probiotic effects were not linked to HNP1-3. The results indicated that microbial competition was responsible for the decrease in new pit and fissure caries [74]. In summary, research indicates that probiotics act against caries and plaque through mechanisms such as competing for colonization in the oral cavity, buffering saliva and plaque pH, and producing bacteriocins and enzymes (like dextranase and urease). Additional research is needed to explore these aspects and determine the effectiveness of probiotic strains as potential therapeutic options.

4 Future Research Directions

While current research indicates promising results regarding the short-term benefits of probiotic supplementation in reducing dental caries, long-term studies are essential to comprehensively understand their sustained effectiveness. Future research should focus on extended clinical trials that monitor the oral health of participants over several years. These studies should aim to determine whether continuous consumption of probiotics can maintain a reduced incidence of dental caries or if their effects diminish over time. Long-term studies will also help identify any potential adverse effects of prolonged probiotic use, ensuring their safety for extended consumption. Additionally, research should explore the optimal dosage and frequency of probiotic intake required for long-term benefits. Determining the right balance is crucial, as excessive consumption might not only be economically impractical but could also disrupt the natural microbial balance in the mouth. Understanding the duration for which probiotics need to be consumed to achieve a lasting reduction in caries incidence is another critical aspect that requires investigation. This will help in developing guidelines for probiotic use in dental care. Childhood is a critical period for establishing long-term oral health. The early colonization of the oral microbiome significantly influences the future risk of developing dental caries. Therefore, studying the impact of probiotic supplementation during childhood is paramount. Future research should focus on conducting longitudinal studies that begin in early childhood and extend into adulthood. These studies should aim to determine whether early probiotic intervention can result in a permanent shift towards a healthier oral microbiome, thereby reducing the lifetime risk of dental caries.

Investigating the best timing for probiotic intervention is also important. Research should explore whether introducing probiotics at specific stages of dental development, such as during tooth eruption or the establishment of the primary dentition, is more effective. Additionally, studies should evaluate whether maternal probiotic intake during pregnancy and lactation can influence the oral microbiome of infants, thereby providing an early protective effect against dental caries.

While several probiotic strains have shown potential in reducing dental caries, not all strains are equally effective. Future research should focus on identifying and characterizing the most effective probiotic strains for oral health. This includes understanding the specific mechanisms through which different strains exert their beneficial effects, such as their ability to produce bacteriocins, compete for adhesion sites, or modulate the immune response in the oral cavity. Genomic and proteomic analyses can provide insights into the functional capabilities of various probiotic strains. These advanced techniques can help identify genes and proteins involved in cariogenic inhibition and biofilm disruption. By pinpointing the most effective strains, researchers can develop targeted probiotic formulations that offer maximum protection against dental caries.

Combining probiotics with other preventive measures, such as fluoride treatments, dental sealants, and antimicrobial agents, could enhance their effectiveness in preventing dental caries. Future research should investigate the synergistic effects of such combinations. Studies should explore whether the concurrent use of probiotics and fluoride, for example, can provide superior protection against caries compared to either intervention alone. Research should also examine the timing and sequence of these combined interventions. Understanding whether probiotics should be administered before, after, or alongside other treatments will help in developing comprehensive caries prevention protocols. Additionally, exploring the potential interactions between probiotics and common oral care products, such as toothpaste and mouthwash, will provide valuable insights into how to integrate probiotics into daily oral hygiene routines.

The method of delivering probiotics to the oral cavity is a critical factor influencing their effectiveness. Future research should focus on developing and optimizing various delivery systems to ensure maximum retention and activity of probiotics in the mouth. Traditional delivery methods, such as dairy products, may not provide prolonged contact with the oral tissues. Innovative delivery systems, such as probiotic-infused chewing gums, lozenges, mouth rinses, and toothpaste, offer the potential for extended interaction with the oral microbiome.

Studies should investigate the stability and viability of probiotics in different delivery formats. Ensuring that probiotics remain active throughout the shelf life of the product and during their passage through the oral cavity is crucial for their efficacy. Research should also explore consumer acceptance and compliance with different delivery systems, as these factors significantly influence the success of probiotic interventions in real-world settings. Oral health disparities exist across different populations, influenced by socioeconomic status, geographic location, and access to dental care. Future research should examine the potential of probiotic supplementation to address these disparities. Studies should investigate whether probiotics can provide an affordable and accessible means of caries prevention in underserved communities with limited access to traditional dental care.

Research should also explore the cultural and dietary preferences of different populations to develop probiotic products that are acceptable and appealing to diverse groups.

Understanding the barriers to probiotic adoption in various settings will help in designing effective public health interventions aimed at reducing oral health inequalities.

The oral microbiome is not isolated from the rest of the body; it interacts with and influences overall health. Future research should explore the broader health benefits of probiotic supplementation beyond dental caries prevention. Studies should investigate whether maintaining a healthy oral microbiome through probiotic use can reduce the risk of systemic conditions linked to oral health, such as cardiovascular disease, diabetes, and respiratory infections. Interdisciplinary research involving oral health experts, microbiologists, and medical professionals can provide a holistic understanding of the interconnectedness between oral and systemic health. By elucidating the broader health impacts of probiotics, researchers can strengthen the case for their inclusion in general health promotion strategies.

5 Conclusion

Some probiotic interventions did not demonstrate a positive effect on the oral health of the participants in the studies. Certain studies found no beneficial or even unfavorable effects of probiotic supplementation on managing caries [49–52]. For example, providing Bifidobacterium animalis subsp. lactis BB-12 to infants aged 1-2 months at a dosage of 10^{10} CFU per day for up to 2 years did not affect oral hygiene status or mutans streptococci counts observed four years after the intervention. The presence of dental plaque and cavities correlated with the lifestyle of children. The research indicated that administering BB-12 in early life did not have a lasting impact on oral health later in life [75]. Providing lozenges containing L. reuteri DSM 17938 and L. reuteri ATCC PTA 5289 (10^9 CFU per strain) for nearly 17 months did not result in significant improvement in the oral health of orthodontic patients. Specifically, there were no alterations in mutans streptococci and lactobacilli counts, and there was no disparity in the occurrence of white spot lesions between the groups receiving treatment and those receiving a placebo [76]. Novel methods for preventing dental caries are emphasizing early detection and monitoring techniques such as DIAGNOdent, Electronic Caries Monitor, Digital Imaging Fiber Optic Transillumination, and quantitative light-induced fluorescence. Caries prevention measures include the utilization of xylitol, pit and fissure sealants, and the development of vaccines against dental caries [77]. Based on the literature review, the majority of studies indicated that probiotics effectively prevent the development of dental caries, suggesting controlled use for beneficial outcomes. Alternatively, using genetically modified S. mutans mutants and engineered microbes with biosynthetic gene clusters has been suggested as a method to prevent cavities.

These methods need additional research to determine their practicality and dependability [78]. In addition to probiotics and microbial treatments, various unconventional approaches have been applied to enhance oral health [2], but these methods require further study regarding their specificity, safety, acceptability, and economic viability. Recently, Nascimento et al. (2019) found that analyzing arginine metabolism with the arginine deiminase system could help identify the risk of caries in children [79].

Based on the current literature review, it is concluded that employing effective probiotics aids in preventing dental caries and lowering the risk of caries development in both children and adults. Most studies focused on evaluating the anticariogenic potential of Lactobacillus and Streptococcus species. Hence, additional research is necessary on different probiotic strains to enhance the overall oral health of individuals. Identifying effective probiotic strains, determining their formulation, dosage, intervention duration, and understanding the interaction between host and microbes are crucial factors influencing the beneficial effects of probiotic supplementation in preventing dental caries.

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