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Are Probiotics Effective in Preventing Dental Caries? – A Narrative Review

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Review Article

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ABSTRACT

Changing lifestyle has resulted in worsening of oral health in people of all age groups. One such common oral health disease is said to be dental caries. There are various modalities in the prevention of dental caries which include proper maintenance of oral hygiene, fluoride application, chemoprophylactic agents, antimicrobial peptides and sugar substitutes. The increasing global problems with the traditional disease management and prevention strategies have prompted the

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investigators to be in constant search of alternatives for managing the oral health issues. Recently probiotics have been used as an alternative for caries prevention that has gained a lot of importance in improving oral health. The effect of probiotics on dental caries and its related risk factors is gaining momentum in the current era. This narrative review summarised the available literature on different probiotic strains and their mechanism of action and future scope of probiotics in caries prevention.

Keywords: Bifidobacterium; dental caries; oral health; probiotics; lactobacillus; streptococcus.

1. INTRODUCTION

Dental caries is still one of the most frequent diseases in the world, despite a decrease in prevalence in the Western world [1]. The interplay of cariogenic bacteria (mostly *Streptococcus Mutans and Lactobacilli*), a high-fermentable-carbohydrate diet, and host variables such as saliva secretion rate and buffering capacity over time causes the condition [2]. Acidogenic and aciduric strains increase selectively in the oral environment when sugared food/drinks are often provided. Caries lesions occur as a result of these changes, which shift the demineralization/remineralization balance toward net mineral loss over time [3]. The microbial community of caries is diverse and contains many facultative and obligate-anaerobic bacteria [4]. *Streptococcus mutans* have been considered for a long time the major pathogens involved in caries development [5]. The main characteristics of virulence of the *Streptococcus mutans* are their acidogenicity, ability to survive in acidic environments, the ability of biofilm formation and adherence to the tooth. The role of probiotics is the prevention of dental caries by acting as an antagonistic agent on the mutans streptococci. They ultimately decrease the count of the caustic bacteria that are responsible for the development of dental caries [5]. It has been expressed in recent years as a shift in the microflora's preponderance from *Streptococcus mutans* and *Actinomyces* to other bacteria such as *Lactobacillus* and *Bifidobacterium* [6].

2. TRADITIONAL METHODS FOR CARIES PREVENTION

Prevention of dental caries is based on the reduction in the number of cariogenic bacteria which leads to the environment that facilitates remineralization. There are several conventional methods available to prevent development of dental caries. There are many agents that have anti-cariogenic effects. They are divided into three categories based on their mechanisms of action: those that affect plaque and plaque bacteria, those that affect tooth enamel chemistry, and those that buffer oral pH [7]. Based on previous studies, the most commonly used agents are chemoprophylactic agents, antimicrobial peptides, sugar substitutes like xylitol, fluoride therapy and casein phosphopeptides [8-11].

To manage caries risk factors, preventive methods are needed and advised, which are primarily centered on dietary changes, such as reducing sugar intake and increasing host resistance [12]. Antibacterial treatments are occasionally used to suppress cariogenic microflora, although total eradication of caries-associated microbes has proven difficult, if not impossible [13]. Rather it might eradicate the entire oral flora that leads to undesirable effects. In order to overcome this drawback of conventional methods, selective inhibition methods of pathogens responsible for dental caries are being studied at recent times [14]. One such approach is the use of probiotics against dental caries.

3. DEFINING THE TERM PROBIOTICS

Probiotics are "live microorganisms that, when administered in adequate amounts, confer a health benefit on the host," according to the World Health Organization [15]. These microorganisms belong to the natural human flora in order to survive in the acid environment during transit to the intestines. One of the main probiotic health claims is the positive change in microbiota composition traditionally investigated in regard to intestinal health [16]. Probiotics are known to have a number of functions in the digestive system, including preventing cellular adhesion and harmful bacteria invasion. It also changes the environment in the intestine and affects the local and systemic inflammatory immune response [17]. In the last decade, the use of probiotics has generated interest within the dental community with the development of studies focused on reducing caries incidence [18].

Several experimental studies using different strains of Lactobacillus rhamnosus GG, Lactobacillus casei, Lactobacillus reuteri, Lactobacillus plantarum, Lactobacillus brevis CD2, Bifidobacterium, etc. were proposed and Caries incidence decrease, changes in Streptococcus mutans and Lactobacillus counts, plaque pH management, and root caries lesions reversal were all achieved using this method [19-22]. Several options for delivering probiotic strains have been presented. However, specifically formulated devices with slow release of the microbial strain might be needed in order to treat oral diseases.

4. MECHANISM OF ACTION OF PROBIOTICS

Probiotic bacteria include a broad spectrum of harmless and physiologically distinct strains, primarily belonging to the genera Lactobacillus and Bifidobacterium. Research into the health-promoting effects of probiotics has mainly focused on alleviating medical conditions, such as infections of the gastrointestinal tract [23]. The possible positive effect of probiotics has been linked to a number of pathways. These can be divided into four categories:

1. Production of antimicrobials (bacteriocins) or acids that can stop germs from multiplying 2. Pathogens and/or co-aggregation to biofilm compete for cell adhesion sites (competitive inhibition or replacement therapy) 3. Immune function modulation on a local and systemic level. 4. Toxicological degradation [24].

All available data show that the effects of probiotics are species- and strain-specific [25-27]. There are studies which show the effect of probiotics on reducing the incidence of cavities, in which the reduction took *Streptococcus mutans* in the oral cavity mainly with the probiotic *Lactobacillus reuteri* ATCC 55730. Except for *Candida albicans* growth, *Lactobacillus salivarius* BGHO1, *Lactobacillus fermentum* BGHO36 and BGHO 64, *Lactobacillus gasseri* and *Lactobacillus delbrueckii* BGHO89 had antagonistic action on *Ataphylococcus aureus*, *Enterococcus faecalis, Micrococcus flavus, Salmonella enteriti* are identified from samples in the tooth surface and healthy oral mucosa. They also discovered that L. gasseri and L. salivarius BGHO89 strains were resistant to low pH and high bile salt concentrations [28-31].

Streptococcus salivarius strain JH is a potential probiotic candidate which produces multiple proteinaceous antimicrobials (bacteriocins), the inhibitory spectrum that includes *Streptococcus mutans*, one of the principle causative agents for the development of dental caries. The biosynthetic loci for the bacteriocins salivaricin A3, streptin, and streptococcin SA-FF22 were discovered in the genome of strain JH earlier. Thus, strain JH also produces salivaricin E, antibiotic with a mass of 3565.9 Da, which is responsible for the inhibition of *Streptococcus mutans* growth [27].

On literature search, there are different functions for different strains of probiotic like *Lactobacillus* change the regulation of genes that are encoding adherence junction proteins and *Streptococcus salivarius* produce acids that can inhibit the growth pathogens. So, with these actions of probiotic strains, the metabolic activity of biofilm in the oral cavity and composition can be altered which leads to the prevention of dental caries. However, there are between 75 and 100 bacterial species in the oral cavity of each patient, with different combinations of species. So, if that's the case, we might require a mixture of beneficial strains rather than a single strain as oral bacteriotherapy [32].

5. PROBIOTIC STRAINS

Based on the literature search, there are wide range of strains which include *Streptococcus salivarius, Lactobacillus paracasei, Lactobacillus caseii, Lactobacillus rhamnosus, Lactobacillus acidophilus, Lactobacillus reuteri, Lactobacillus plantarum, Lactobacillus brevis* and *Bifidobacterium lactis*. *In vitro* studies on monocultures of different probiotic Lactobacillus strains have shown a varied acid production, while clinical trials have not revealed an impact on plaque acidogenicity [33,34].

A Randomised clinical trial has been done to evaluate the effects of the lactic acid bacterium *Lactobacillus salivarius* on caries risk factors and it was concluded that oral consumption of *Lactobacillus salivarius* WB21 and TI 2711 provided better resistance to caries risk factors compared to the xylitol tablet with no side effects related to advance of caries in the oral cavity [35]. A double-blinded, randomized, placebo-controlled study evaluated the efficacy of the probiotic *Lactobacillus paracasei* GMNL-33 for reducing caries-associated salivary microbial counts in healthy adults. And concluded that a 2-

weeks period of medication was needed for L. paracaseiGMNL-33 via oral administration route to become effective in the probiotic action. After the intervention, a shorter-term probiotic intervention seems to strengthen its inhibitory efficacy against Streptococcus mutans [36]. Another double-blind, randomized, placebo-controlled trial was conducted to provide a preliminary evaluation of *Streptococcus salivarius* M18 for its probiotic application to the prevention, or reduction in the risk of dental caries, and it was discovered that *Streptococcus salivarius* M18 has oral health benefits when it is administered regularly [37]. *Lactobacillus* can secrete intermediates that is capable of inhibiting the formation of cariogenic *Streptococcus mutans* and *Candida albicans* biofilm; and also inhibits fungal morphological transformation thus reducing the pathogenicity of *Candida albicans*; ultimately weakens its pathogenic potential [38]. A shorter-term daily ingestion of lactobacilli-derived probiotics which was a prepared straws or lozenges has been delivered and it reduced the levels of salivary *Streptococcus mutans* in young adults [39]. Lactobacillus GG (LGG) in yoghurt has an inhibitory effect on oral pathogenic bacteria and is beneficial in caries prevention on its daily consumption [40]. An *in-vitro* study investigated the effect of *Lactobacillus lactis* HY 449 on cariogenic biofilm and concluded that it possessed inhibitory mechanisms and effective probiotics for the prevention of dental caries [41]. A randomized double-blinded clinical trial demonstrated that *Streptococcus salivarius* K12 over a 28-day period does not adversely affect the human host on daily ingestion and supports the safety of its oral delivery in a food-based carrier [42]. It has been proved that levels of microorganisms in saliva which is responsible for development of dental caries and it was reduced with probiotic Bifidobacteria in yogurt [43]. *Lactobacillus rhamnosus*has been concluded as a candidate for preventing the incidence of dental caries since it inhibits oral biofilm formation by decreasing glucan production of *S. mutans* and has antibacterial activity and did not integrate into oral biofilm [44].

6. AVAILABLE FORMS OF PROBIOTICS

There are various forms of probiotics available that can be used on a daily basis. Lactobacillus and Bifidobacterium species are common probiotic bacteria utilised in clinical trials focusing on oral health. They are administered in vehicles such as milk, yogurt, cheese, drops, gum, ice cream, lozenges and tablets [45]. The number of *Streptococcus mutans* have been reduced by using the milk form of *Lactobacillus rhamnosus* GG strain, Cheese form of *Lactobacillus* mix and Yoghurt form of *Lactobacillus reuteri* ATCC 55730, *Bifidobacterium* DN-173010 [46-48]. In addition to these results, chewing gum, tablet and Lozenge forms of *Lactobacillus reuteri* ATCC 55730 and ice cream form of *Bifidobacterium lactics* Bb-12 have shown to decrease the count of *Streptococcus mutans* on wide range of age groups [49-51].

Milk, Cereals, drops forms of *Lactobacillus rhamnosus*, *Lactobacillus paracasei*, *Lactobacillus reuteri* are present and they are found to decrease the outcome of dental caries [22,52]. *Streptococcus uberis, Streptococcus oralis, Streptococcus rattus* are available as Tablet form and have an inhibitory action on dental caries [53]. The distribution should ideally be appropriate for people of all ages, particularly small children, because it has been suggested that early exposure to probiotic strains leads to persistent colonisation [54-57]. However, still research goes on the identification of ideal administration methods [58].

7. PROSPECTS FOR PROBIOTICS IN CARIES PREVENTION

The main goal of probiotics is to destroy or reduce the bacteria which is cariogenic, mainly *Streptococcus mutans* and replace it with non-cariogenic bacteria [59]. In order to prevent the occurrence of dental caries, probiotic bacteria should adhere to the oral mucosa and dental tissues as part of the biofilm and compete with the growth of dental pathogens [60]. Probiotics had shown quite a few promising results in prevention of caries, but there are only few clear clinical outcomes pertaining to prevention of caries. So, the proper scientific evidence is still in search. A regular continuous daily intake of probiotic is probably required through vehicles like toothpaste or mouth rinses. For all the anti-carious products to be effective in its action, almost daily usage is needed, therefore probiotics should be incorporated in our daily preventive products like toothpaste. In spite of this, probiotics can also be administered in daily dietary supplements, and it is considered effective to some extent in the prevention of caries [5].

8. FURTHER RESEARCH AND EMERGING PROBIOTC STRAIN

Caries management strategies have come across through various paths and are now witnessing a paradigm shift towards the prevention approach. Bacteriotherapy is one of the most potential concepts to prevent dental caries [61]. There are previous studies on reduction of *Streptococcus mutans* count with the help of available probiotic strains such as *Lactobacillus rhamnosus* GG, *Lactobacillus reuteri,* and *Bifidobacterium.* However, these strains possess certain limitations in their mechanism of action against biofilm and their evidence is still insufficient. In order to overcome those drawbacks of previously available strains, new probiotic strains are under search. *Streptococcus thermophilus* is one such developing strain that has been discovered to be a beneficial probiotic for dental health [30,62]. A Gram-positive bacterium called *Streptococcus salivarius* is now being utilised as an oral probiotic [63]. The most commonly used probiotic *S. salivarius* strains are K12 and M18. In addition to the above strains, *S. salivarius* strain JH has also been found to possess a potent anti-MS activity [59]. And future research on probiotics for caries prevention should be based on new strains, method of administration, prescription methods of probiotics for patients [5].

9. CONCLUSION

Bacteriotherapy plays a significant role in prevention of dental caries [37]. Hence probiotics is one of the evolving preventive strategies for balancing the oral microflora and maintaining the oral health [5,62]. Though probiotic strains are effective in promoting oral hygiene, more information about mechanisms of action on each micro-organism and vehicle by which it is administered are needed.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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