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''Role of Probiotics supplementation in prevention of dental caries''

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

﴿وَأَنْ لَيْسَ لِلْإِنسَانِ إِلَّا مَا سَعَى (39) وَأَنَّ سَعْيَهُ سَوْفَ يُرَى (40)﴾

(سورة النجم)

الاهـــــداء...

أهدي هذا البحث باسمي ونيابة عن زملائي في البحث كعربون من الامتنان والاعتراف بالبيئة الأكاديمية الفريدة التي قدمها لنا الكادر التدرسي في كليتنا الموقرة. لقد كان دعمكم وتشجيعكم الكثير من الأثر في نـجاح هذا البحث.

شكرًا للبنية التحتية المتقدمة والموارد الغنية التي وفرتموها، والتي سهلت لنا الجهد المبذول في اكمال هذا البحث . لا يمكننا إلا أن نقدر الجهود المستمرة لتحسين مستوى التعليم والبحث في هذه الكلية المميزة.

نأمل أن يكون هذا الاهداء خطوة صغيرة نحو تقديم شكرنا وامتناننا لكم، ونتطلع إلى المزيد من التعاون والإنـجازات المشتركة في المستقبل.

بكل الاحترام والتقدير.

الشكر والتقدير

اتوجه بالشكروالتقدير الى عمادة وجميع اعضاء الكادر التدرسي في (جامعة بابل / كلية طب الاسنان) على كل ما تقدم من قبلهم للوصول لهذه المرحلة الدراسة المتقدمة

وبوجه الخصوص الى الفروع (المعالجة و الاحياء المجهرية و طب اسنان الاطفال) لاشرافهم ومتابعتهم على انجاز هذا البحث الدراسي

Contents

1. INTRODUCTION

Dental caries is a chronic endogenous infection caused by the normal oral commensal flora. The carious lesion is the result of demineralization of enamel and later of dentine by acids produced by plaque microorganisms as they metabolize dietary carbohydrates. However, the initial process of enamel demineralization is usually followed by remineralization and cavitation occurs when the former process overtakes the latter. [1,2]

Once the surface layer of enamel has been lost, the infection invariably progresses to dentine with the pulp becoming firstly inflamed and then necrotic then caries was is defined as localized destruction of the tissues of the tooth by bacterial fermentation of dietary carbohydrates. always used in the treatment of dental caries is the antibiotic and nowadays the usage of probiotic is more relevant because the probiotic is the new or updated version of antibiotic.[3,4]

"Probiotics" are with us since the time people have been eating fermented milk; however, its relation with health benefits drew attention only when Metchnikoff in 1907 observed that bacteria in the fermented milk competed with the micro-organisms that are injurious to health. Lilley and Stillwell in (1965) described these beneficial micro-organisms in fermented milk using the term. “probiotic." In 1989, Fuller defined them as a live microbial food supplement, which beneficially affects the host animal by improving its microbial balance.[5] The first probiotic species introduced into research were Lactobacillus acidophilus by Hull, et al. in (1984) and Bifidobacterium bifidum by Holcombh, et al. in 1991.[6]

The bacterial population of human gastrointestinal (GI) tract constitutes an enormously complex ecosystem. Most of these organisms are beneficial but some are harmful. The term "prebiotics" and this term can favor the growth of these beneficial bacteria over that of harmful ones. Prebiotics are non-digestible food ingredients such as inulin, fructo-oligosach- harides, and lactulose that cannot be digested by humans but support the growth of beneficial bacteria.[6] The term "synbiotic" is used when a product contains both probiotics and prebiotics because the word alludes to synergism, this term should be reserved for products in which the prebiotic compound selectively favors the probiotic compound.[7].

2 Dental caries

2.1 Classification [8]

Dental caries can be classified with respect to the site of lesion:

- the pit or fissure caries (seen in molars, premolars and the lingual surface of maxillary incisors)
- smooth-surface caries (seen mainly on approximal tooth surfaces just below the contact point)
- root surface caries (seen on cementum or dentine when the root is exposed to the oral environment)
- recurrent caries (associated with an existing restoration)

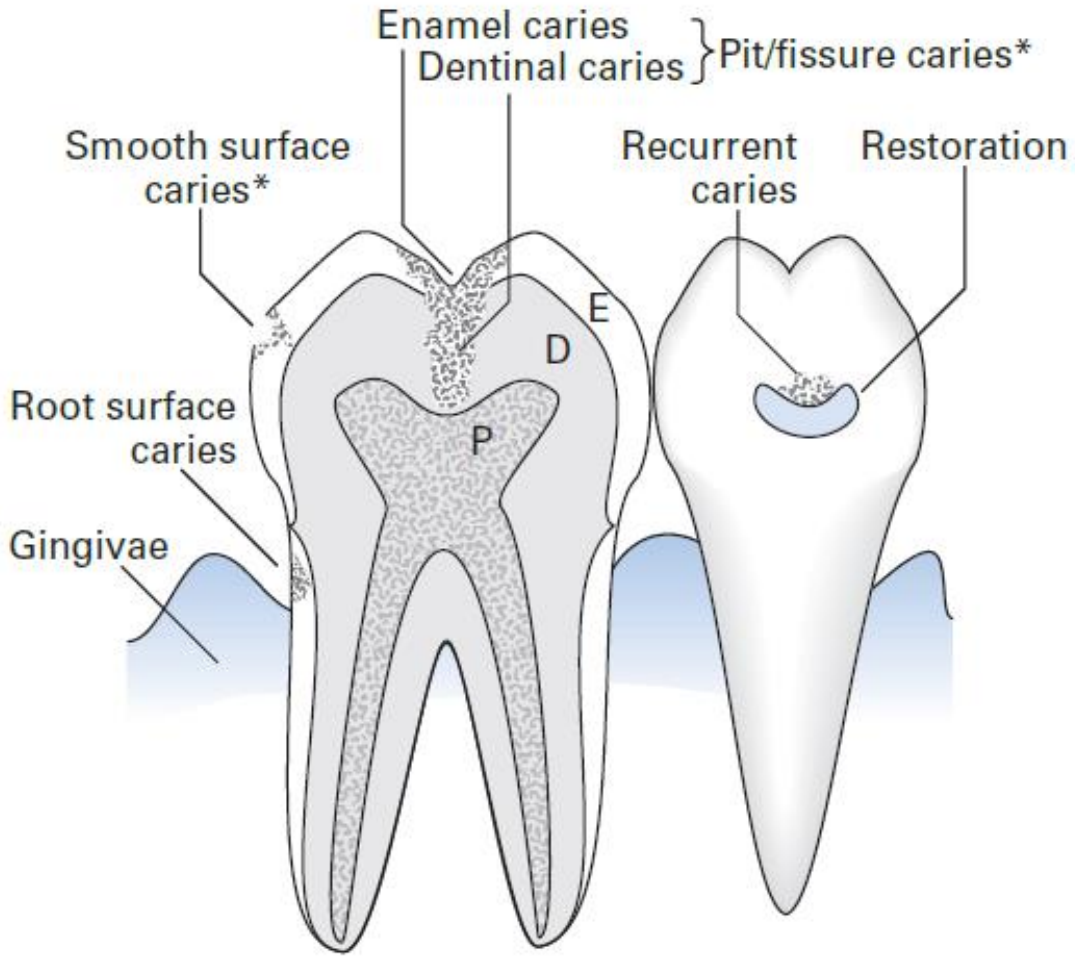

Figure 1.1: dental caries classifications [8]

2.2 Risk factors of dental caries:

Dental caries (with periodontal disease) is one of the most common human diseases and affects the vast majority of individuals. Although caries was not uncommon in the developing world, the recent affluence in these regions has resulted in a remarkable upsurge in caries due to the ready and cheap availability of fermentable carbohydrates [9]. In contrast, caries prevalence is falling overall in the developed world due to the increasing awareness of cariogenic food sources and the general improvement in oral hygiene and the dental care delivery systems. Caries of enamel surfaces is particularly common up to the age of 20 years, after which it tends to stabilize. However, in later life, root surface caries becomes increasingly prevalent, due to gingival recession, exposing the vulnerable cementum to cariogenic bacteria [10].

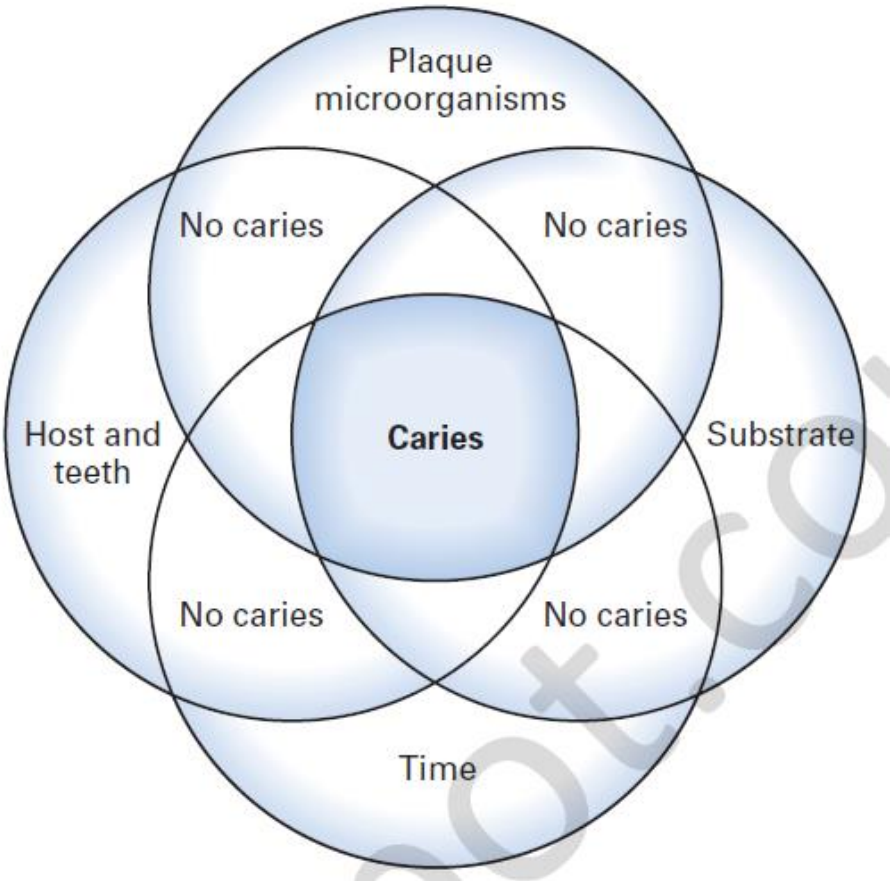

Figure 1.2: factors that influence dental caries [8]

2.3 Diagnosis

Diagnosis is usually by a combination of:

- **Direct observation.**
- **Probing.** Some do not advocate probing as this may create an incipient breach of the enamel and spread the infection from one tooth surface to another.
- **Radiographs.** Early white-spot lesions may easily be missed because they cannot be detected by the eye or by radiography. Similarly, it is possible for large carious lesions to develop in pits and fissures with very little clinical evidence of disease.
- **Experimental methods.** Methods of potential practical
- value include laser fluorescence for diagnosis of buccal
- and lingual caries, and electrical impedance (resistance)
- to detect occlusal caries.
- **Microbiological tests** may be helpful in the assessment of caries

2.4 Treatment:

- Restorative Dentistry: Dentists use various restorative materials (e.g., composite resin, amalgam) to repair cavities. The decayed portion is removed, and the tooth is restored.

- Root Canal Therapy: For deeper cavities affecting the pulp, root canal treatment removes infected tissue and seals the root canals.

- Laser Therapy: Low-intensity lasers can selectively remove carious tissue.

This approach made no attempt to cure the disease, and the patient often returned some months later requiring further fillings due to new or recurrent caries.
In contrast, the modern philosophy in caries management highlights:

• early detection

• the importance of accurate diagnosis

• minimal cavity preparation techniques

• active prevention.

The result of such measures should be less, rather than more, demand for restorative treatment by individual patients.

2.5 Prevention:

I. Oral Hygiene: Regular brushing, flossing, and tongue cleaning help remove plaque and prevent bacterial build up.
II. Fluoride: Fluoridated toothpaste, mouth rinses, and professional fluoride treatments enhance enamel resistance.
III. Dietary Modifications: Limit sugary snacks and acidic beverages. Opt for water or milk instead.
IV. Regular Dental Visits: Professional cleanings, examinations, and early detection are crucial.
V. Caries Risk Assessment: Assessing individual risk helps tailor preventive strategies.
VI. Community Programs: Water fluoridation and school-based sealant programs benefit populations.
VII. Probiotics: Probiotics are live bacteria and yeasts that naturally reside in the body. They are designed to maintain or repopulate the "good" gut bacteria, which play a crucial role in digestive health. Probiotics support a healthy gut microbiome, which includes bacteria, viruses, fungi, and other microscopic organisms in the intestines. A balanced microbiome contributes to immune health and recovery from illnesses.

3 PROBIOTICS

3.1 History OF PROBIOTICS

There is a long history of health claims concerning living microorganisms in food, particularly lactic acid bacteria. In a Persian version of the Old Testament it is stated that “Abraham owed his longevity to the consumption of sour milk”. In 76 BC the Roman historian Plinius recommended the administration of fermented milk products for treating gastroenteritis. [11] Etymologically, the term appears to be a composite of the Latin preposition pro (for) and the Greek adjective biwtikoc (biotic), the latter deriving from the noun bioc (bios, „life“). However, the term probiotic was coined by Lilley and Stillwell (1965). Some definitions of probiotics is given in 1905- Henry Tissier, French paediatrician, observed a low number Bifidobacteria (first isolated probiotic bacteria) in the stools of the breast-fed infants with diarrhea as compared to the healthy infants. [12,13]

1907- Elie Metchnikoff, Russian scientist and Nobel laureate observed that certain rural populations in Europe (Bulgaria and the Russian steppes) who mainly depended on milk fermented by lactic acid bacteria for their sustenance had comparatively longer lives. By that time, it was known that milk fermented with lactic acid bacteria inhibits the growth of proteolytic bacteria because of its low pH which is caused by the

fermentation of lactose. Based on these facts, Metchnikoff proposed that consumption of fermented milk would ‘‘seed‟ the intestine with harmless lactic acid bacteria, decreases the intestinal pH thereby suppressing the growth of proteolytic bacteria. [11,12,13], Alfred Nissle, German professor (1917) isolated Escherichia coli strains from the faeces of an unaffected soldier. Escherichia coli strains were used for the treatment of acute gastrointestinal infections when the antibiotics were not yet available. [12,13], 1930s- Witnessed the first clinical trials on probiotics (strains of E. coli) for their effect on constipation. [12], 1984-The first probiotic species introduced into research was Lactobacillus acidophilus by Hull et al. 1991- Holcombh et al used Bifidibacterium bifidumas probiotic in their research. [11]

3.2 Prebiotics

As described, prebiotics have been an integral part of the human diet for many centuries. However, it is far more recently that their nutritional properties were recognised and this is outlined elsewhere in this book. The use of oligosaccharides to effect increases in gut bacteria seen as beneficial has been in existence in Japan for many years, however the term 'prebiotic' was only first coined in the mid-1990s (Gibson and Roberfroid, 1995). This clearly built upon the success of probiotics for microflora management approaches. The approach targets indigenous beneficial bacteria in the gut and uses nonviable food ingredients to selectively promote them. They are finding increasing use in functional foods, since there are few stability issues and they are resistant to heat. As described elsewhere, some prebiotics can also improve food quality characteristics such as mouthfeel and other textural aspects. They have also been exploited as low calorie fat replacers.

constitute selectively fermented dietary ingredients, which result in alterations in the composition or activity of the gut microbiota, with beneficial effects on host health. In contrast to probiotics, which are viable organisms, prebiotics present non-viable food components [14]. Most data regarding their usefulness are based on food ingredients, belonging mainly to two chemical groups, inulin-type fructans (ITF) and galactooligosaccharides (GOS). These data have demon strated stimulation of Bifidobacteria and Lactobacilli growth, thus conferring important changes in gut microbiota compo sition [15]. Various natural sources of prebiotics exist, such as beans, legumes, starchy fruits, cereals, and soybean [16, 17]. Besides, many substances are suggested to be prebiotics, such as “galacto-oligosacaccharides, inulin-type fructans, arabionoxylan, and arabinoxylan oligosaccharides, chitin glucans from fungi or even several phenolic compounds,” due to their potential to improve gut microbiota composition and thus exert positive health results.

Table (1) that shows the difference between probiotic and prebiotic

Parameters of comparison	Prebiotic	Probiotic
Meaning	Specialized plant fibre that acts as food for beneficial microorganisms	Real bacteria strains that alter the population of healthy bacteria
Health Advantage	Reduction of cancer risk, enhanced absorption of calcium, etc.,	Lowering the risk or advancement of chronic diseases, reducing allergies, etc.,
Compounds	Made up of a complex carbohydrate-fibre	Made up of actual organisms
Consumption	Our digestive system is incapable of breaking down prebiotics	Probiotics sustain in the gut
Found in	Barley, asparagus, beans	Kombucha, yogurt,

3.3 COMPOSITION OF PROBIOTICS

Probiotics can be bacteria, molds or yeast. However, most probiotics are bacteria. Among bacteria, lactic acid bacteria are more popular. Lactobacillus acidophilus, Lactobacillus casei, Lactobacillus lactis, Lactobacillus helviticus, Lactobacillus salivarius, Lactobacillus plantrum, Lactobacillus bulgari- cus, Lactobacillus rhamnosus, Lactobacillus johnsonii, Lactobacillus reuteri, Lactobacillus fermentum, Lactobacillus del-brueckii, Streptococcus thermophilus, Enterococcus faecium, Enterococcus faecalis, B. bifidum, Bifidobacterium breve, B. longum, and Saccharomyces boulardii are commonly used bacterial probiotics [18]. A probiotic may be made out of a single bacterial strain or it may be a consortium as well. Probiotics can be in the form of:

1- powder form
2- liquid form
3- gel
4- paste
5- granules or available in the form of capsules, sachets, etc.

3.4 FEATURE OF PROBIOTICS

A good probiotic agent needs to be:

1- non-pathogenic
2- nontoxic
3- resistant to gastric acid, adhere to gut epithelial tissue and produce antibacterial substances.
4- It should persist, albeit for short periods in the Gl tract influencing metabolic activities such as cholesterol assimilation, lactose activity, and vitamin production.

Probiotics can be available following basic ways:

1. A culture concentrate added to a beverage or food (such as a fruit juice).
2. Inoculated into prebiotic fibres.
3. Inoculants into a milk-based food (dairy products such as milk, yogurt, cheese).
4. As concentrated and dried cells packaged as dietary supplements (non-dairy products) such as powder, capsule, gelatine tablets.

The survival of probiotic organisms in the gut depends on the colonization factors that they possess as well as on the organelles which enable them to resist the antibacterial mechanisms that operate in the gut. In addition to the antibacterial mechanisms, they need to avoid the effects of peristalsis, which tend to flush out bacteria with food. This can be achieved either by immobilizing themselves or by growing at a much faster rate than the rate of removal by peristalsis. The probiotic strain needs to be resistant to the bile acid, e.g., Bifidobacteria strains proved significantly less acid-resistant than the Lactobacillus strains, when exposed to human gastric juice.[8]

3.5 METHODS OF ADMINISTRATION

Milk and milk products are the most popular carriers of probiotics. Milk contains calcium, calcium lactate and other organic and inorganic compounds with known anti-cariogenic properties. **[12]** The most common probiotic strains used orally belong to the genera *lactobacillus* and *Bifidobacteria.* **[19,20,21]** Common probiotic vehicles are: **[5,6,12]**

1- lozenges
2- tablets
3- capsule
4- mouthrinse
5- liquid
6- cheese
7- yoghurt
8- ice-creams

However, for the purposes of prevention or treatment of oral diseases, specifically targeted applications, formulas, devices, or carriers with slow release of probiotics might be needed. **[12]**

Probiotics are introduced into the products in one of the four basic ways. **[5,6]**

- A culture concentrate added to a beverage or food (fruit juice).
- Inoculated into prebiotic fibres.
- As Inoculants into a milk dairy product. As concentrated and dried cells packaged as dietary supplements (powder, capsule, tablets)

3.6 MECHANISMS OF ACTION

The approach with probiotic therapy in the oral cavity relies on the hypothesis that harmless bacteria could occupy a space in a biofilm that otherwise would be colonized by a pathogen [22]. Probiotic bacteria guard the oral health by competing with the oral pathogens for nutrients, growth factors and site of adhesion. [23] the mechanisms of action are still poorly understood and most studies on them are in vitro and on animals [24]. It is hypothesized that both systemic and local mechanisms occur. The suggested mechanisms of probiotic action on oral health are drawn entirely from gastrointestinal studies. Since the mouth represents the first part of the gastrointestinal tract, there is every reason to believe that at least some probiotic mechanisms may also play a role in that part of the system. [11]. For better explanation refer to the figure given below in (figure 1.3)

The mechanisms include [25]:

1. interference with other microorganisms; the ability to exclude or inhibit pathogens,
2. modulation of host immune responses resulting in both local and systemic effects
3. influencing the function of the intestinal epithelial barrier

or in other way can be classified as direct or indirect action

1- Direct actions

- Direct interaction in dental plaque
- Maintains micro ecological balance in oral cavity
- Competing & intervening with bacterial attachments
- Produces chemicals that inhibit oral pathogenic bacteria

2- Indirect actions

- Affects local immunity
- Affects non-immunological defence
- Modulates systemic immune function
- Regulation of mucosal immune system
- Produces antioxidants or act as antioxidants
- Prevention of plaque formation by neutralising free electrons
- Upregulation of intestinal barrier integrity & mucin production

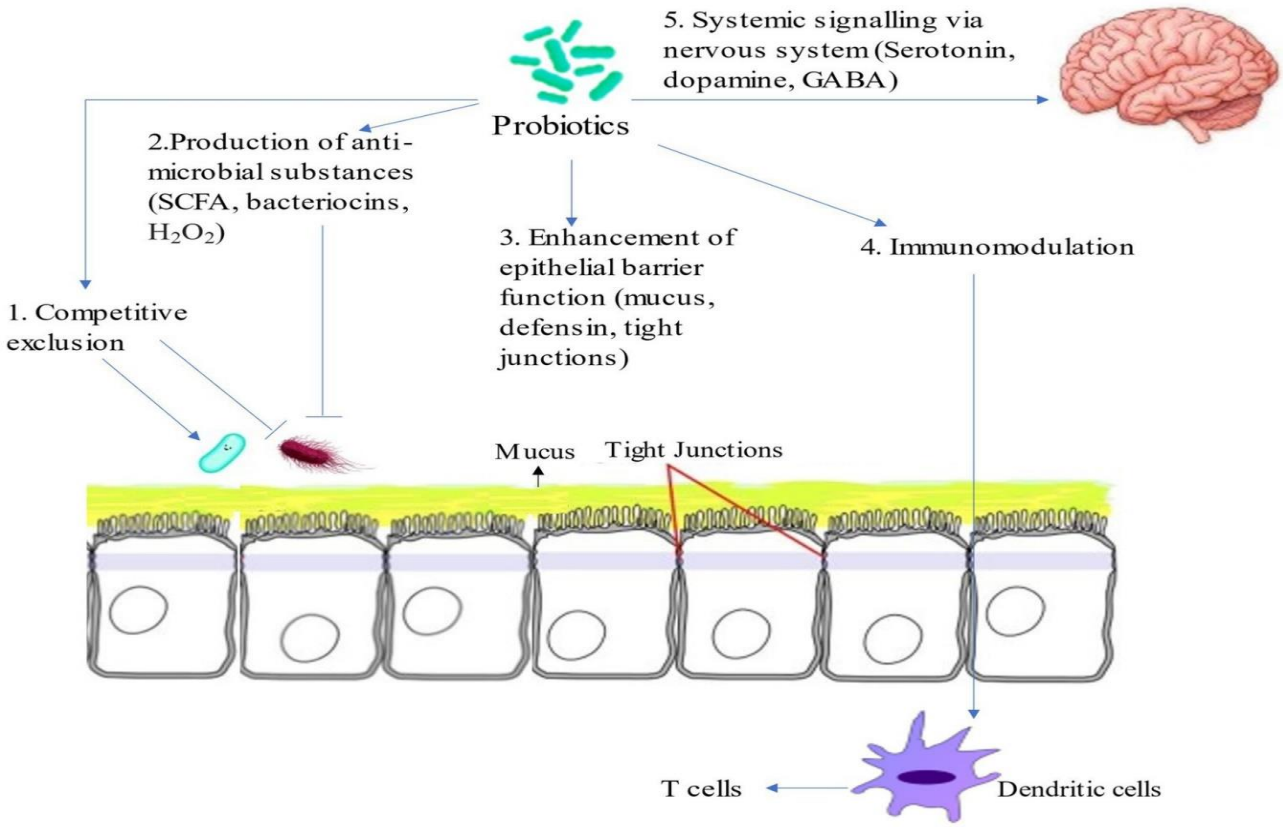

Figure 1.3 : mechanism of action [11]

Explaining beneficial probiotic effects include modulation of host immune response leading to strengthening of the resistance to pathogenic challenge and alteration of the composition and metabolic activity of host micro-flora at the specific location. Among paramount selection criteria for probiotics are:

1. Adhesion and colonization (at least transitory) in the human body. Adhesion may increase the retention time of a probiotic and place bacteria and host surfaces (body fluids and epithelial cells) in close contact, thus facilitating further probiotic activity.

2. Enhancement of the non-specific and specific immune response of the host.

3. Production of antimicrobial substances and competition with pathogens for binding sites.

4. Survival and resistance to human defence mechanisms during the oro-gastro-intestinal transit.

5. Safety to the macro-organism.[9]

3.7 PROBIOTICS AND ORAL CAVITY

In this section we go through the effectiveness of probiotics on different diseases like dental caries, periodontal infection and halitosis.

3.8 Effect on dental caries

To date only 8 well-designed randomized controlled trials with dental caries as primary outcome have been published (Table 2). Probiotic strains, administration, duration of intervention,and target group have varied. In a majority of thestudies (75%), the interventions resulted in caries reduction in the treatment groups. Three studies investigated the long-term effect of an intervention during infancy. Hasslof et al. [26] showed that feeding probiotic L. paracasei subsp. Paracasei strain F19 during weaning (4–13 months of age) had no effect on either counts of MS or on dental caries at follow-up at 9 years of age. In contrast, Stensson et al. [27] showed that an intervention with L. reuteri ATCC 55730 during the first year of life reduced the prevalence of approximal caries lesions in the primary dentition at 9 years of age. Eighty-two percent of the children in the probiotic group and 58% in the placebo group were caries-free. There was no effect on MS counts. Taipale et al. [28] investigated in a low caries population, if an intervention with Bifidobacterium animalis subsp. lactis BB-12 during infancy

In pre-school children attending day care centres, three studies evaluated the caries-preventive effect of daily consumption of milk with added probiotic bacteria. A Finnish report suggested that Lactobacillus rhamnosus GG could reduce the incidence of caries [30] and a Swedish study with L. rhamnosus LB21 suggested similar effects, although a confounding effect from the fluoride, which had been added to the test milk, could not be excluded [31].

Later, a study from Chile showed that regular intake of milk supplemented with L. rhamnosus SP1 reduced the caries development in children aged 2–3 years [34]. Additionally, in a high caries population in Sweden, administration of a probiotic chewing tablet with Streptococcus uberis KJ2, Streptococcus oralis KJ3 and Streptococcus rattus JH145 was effective in preventing caries in 2- to 3-year-old children [35]. In elderly, the effect on primary root caries lesions of interventions with milk supplemented with 5 ppm fluoride and/or probiotic L.rhamnosus LB21 were studied [36]. Results indicated an effect on reversal of the soft and leathery texture of primary root caries lesions. The beneficial effect was strongest when both fluoride and lactobacilli were added to the milk.

In caries, there is an increase in acidogenic and acid-tolerating species such as mutans streptococci and lactobacilli, although other bacteria with similar properties can also be found like Bifidobacteria, nonmutans streptococci, Actinomyces spp., Propionibacterium spp., Veillonella spp. and Atopobium spp. Use of probiotics and molecular genetics to replace and displace cariogenic bacteria with non-cariogenic bacteria has shown promising results. These studies have employed different approaches:[6]

1. Early studies concentrated on utilizing bacteria that expressed bacteriocins or bacteriocin-like inhibitory substances that specifically prevented the growth of cariogenic bacteria.

2. One approach has been to identify food grade and probiotic bacteria which have ability to colonize teeth and influence the supra-gingival plaque.

3. Also, strains have been screened for suitable antagonistic activity against relevant oral bacteria.

4. Another approach utilized recombinant strain of S. mutans expressing urease, which was shown to reduce the cariogenicity of plaque in an animal model.

5. Similarly, genetically modified probiotics with enhanced properties can be developed ("designer probiotics"). For example, a recombinant strain of Lactobacillus that expressed antibodies targeting one of the major adhesions of S. mutans (antigen I/II) was able to reduce both the viable counts of S. mutans and the caries score in a rat model.

3.9 Effect on periodontists

As other example is periodontitis is a multifactorial disease that encompasses the hard- and soft-tissue, microbial colonization (with or without invasion), inflammatory responses and adaptive immune responses. The complexity of the local tissue components, including bacteria and/or their products and virtually all aspects of host response mechanisms, has complicated our ability to elucidate the critical protective functions in the tissues and has continually provided evidence for the potential of host destructive factors as the ultimate causative parameters in the disease. Treatment of periodontal diseases in recent years has moved towards an antibiotic/anti-microbial model of disease management. Probiotics might be a promising area of research in the treatment of periodontitis.

They make excellent maintenance product because they produce antioxidants. Antioxidants prevent plaque formation by neutralizing the free electrons that are needed for the mineral formation. Probiotics are able to breakdown putrescence odors by fixating on the toxic gases (volatile sulfur compounds) and changing them to gases needed for metabolism. Teughels, et al. reported that the subgingival application of a bacterial mixture including Streptococcus sanguis, Streptococcus salivarius, and Streptococcus mitis after scaling and root planning significantly suppressed the re-colonization of Porphyromona gulae (canine P. gingivalis) and P. intermedia in a beagle dog model. This guided pocket re-colonization approach may provide a valuable addition or alternative to the armamentarium of treatment options for periodontitis[37].

Candida species constitute part of the commensal oral flora in about 50% of healthy subjects, but are able to cause a clinically apparent lesion if the immune defenses are breached either on the local or systemic level. One study has shown that the subjects who consumed cheese containing the probiotic L. rhammnosus GG exhibited reduction in the prevalence of oral Candida which subsequently may confer protective effect against oral candidosis. This may be partly explained by the finding of the ex vivo experiment which demonstrated a profound but variable ability of commercially available strain of lactobacilli probiotics to inhibit the growth of C. albicans possibly due to the low pH milieu produced by the lactobacilli [29,31].

Relevant to this is the laboratory study which demonstrated that the Candida-infected mice which were fed with L. acidophilus exhibited accelerated clearance of C. albicans from the mouth. The most common probiotics used are listed in the table below.

Table: 1.1 shows the most common used probiotics in dentistry

Condition	Lactobacillus strains	Bifidobacterium strains	Others
Dental caries and periodontitis	*L. reuteri* DSM 17938 *L. reuteri* ATCC 55730 *L. reuteri* ATCC PTA 5289 *L. paracasei* F19 *L. paracasei* GMNL-33 *L. rhamnosus* GG *L. rhamnosus hct 70* *L. rhamnosus* LB21 *L. salivarius* WB21 *L.casei*	*Bifidobacterium* DN 173010 *Bifidobacterium animalis* subspecies *lactis* BB-12 *Bifidobacterium animalis* subsp. *lactis* DN 173010	S. mutans Ingbritt S. mutans ATCC 25175 S. mutans GS-5 S. sobrinus ATCC 33478
Halitosis	*L. salivarius* WB21 *L. reuteri* DSM 17938 *L.casei* strain *Shirota*		*S.salivaris* K12 *W. Cibaria*
Oral candidiasis	*L. rhamnosus* GG		*Propionibacterium freudenreichii species Shermani JS*

3.10 Indications [38]

Proven indications

1. Rotavirus diarrhea

2. Reduction of antibiotic-associated side effects.

Possible indications

1. Food allergies and lactose intolerance

2. Actopic eczema

3. Prevention of vaginitis

4. Urogenital infections

5. Irritable bowel syndrome

6. Inflammatory bowel syndrome

7. Cystic fibrosis

8. Traveller's diarrhea

9. H. pylori infection

10. Various cancers.

3.11 PRECAUTION AND CONTRAINDICATION

Some live micro-organisms have a long history of use as probiotics without causing illness in people. Probiotics' safety has not been thoroughly studied scientifically. More information is especially needed on how safe they are for young children, elderly people, and people with compromised immune systems.

Side effects of probiotics, if they occur, tend to be

1- mild and digestive (such as gas or bloating). More serious effects have been seen in some people.
2- Probiotics might theoretically cause infections that need to be treated with antibiotics, especially in people with underlying health conditions.
3- They could also cause unhealthy metabolic activities, too much stimulation of the immune system, or gene transfer (insertion of genetic material into a cell).[9]

4- Since Probiotics Contain Live Micro-Organisms, there is a Slight Chance That These Preparations Might Cause
5- Medical Infection, Particularly in Critically Ill or Severely Immunocompromised patients.[10]
6- Probiotic Strains Of Lactobacillus Have Also Been Reported To Cause Bacteremia in patients With Short-Bowel Syndrome, Possibly Due to Altered GUT Integrity.
7- Fungemia has been reported when Saccharomyces Capsules were open and added at the bedside. [39,40]
8- Lactobacillus preparations are contraindicated in persons with a hypersensitivity to lactose or milk.[41]
9- Streptococcus Bouulardii is contraindicated in patients with a yeast allergy. [39,42]
10- However, no contraindications are listed for bifidobacteria, since most species are considered nonpathogenic and Non-toxigenic. [10,39,43]

Probiotic products taken by mouth as a dietary supplement are manufactured and regulated as foods, not drugs. Furthermore, uncertainty about specificity of probiotics effects and their mechanism of action is a cause of concern.

3.12 THE EFFECTS OF PROBIOTICS ON VACCINE EFFICENCY:

Probiotics are live commensal microorganisms that have positive benefits for the host that are generally consumed as a component of fermented foods. They have an impact on both innate and adaptive immune systems and decrease infections [15, 16]. A meta-analysis comprising 1,979 adults showed that probiotics and prebiotics effectively promote immunogenicity by influencing seroconversion and seroprotection rates in adults vaccinated with influenza vaccines [44].

3.13 What is the difference or compression between Probiotic and Vaccine?

Vaccines:

- Definition: Vaccines are biological preparations that stimulate the immune system to recognize and fight specific pathogens (viruses or bacteria). They contain harmless components of the pathogen (antigens) to trigger an immune response.

- Function: Vaccines prime the immune system to produce antibodies and memory cells. If the vaccinated person encounters the actual pathogen later, their immune system can respond rapidly, preventing or reducing the severity of the disease.

- COVID-19 Vaccines: COVID-19 vaccines, such as those developed for SARS-CoV-2, have been crucial in controlling the pandemic. They significantly reduce the risk of infection, severe illness, and transmission.

In summary:

- Probiotics support gut health and may alleviate COVID-19 symptoms but do not replace vaccines.

- Vaccines are essential for preventing infectious diseases and have been effective against COVID-19.

Vaccination is defined as the stimulation and development of the adaptive immune system by administering specific antigens. Vaccines' efficacy, in inducing immunity, varies in different societies due to economic, social, and biological conditions.

4 Conclusions

Probiotics are safe microorganisms that when administered to human subjects in adequate doses and at appropriate periods confer some beneficial effects to the host. The Mechanisms of action of probiotics involve colonization and normalization of perturbed intestinal microbial communities in both children and adults; competitive exclusion of pathogens and bacteriocin production; modulation of enzymatic activities related to metabolization of a number of carcinogens and other toxic substances; and production of volatile fatty acids, namely, SCFAs and BCFAs, which play a role in the maintenance of energy homeostasis and regulation of functionality in peripheral tissues. In addition, probiotics increase intestinal cell adhesion and mucin production and modulate the activity of gut-associated lymphoid tissue and the immune system. Similarly, probiotic metabolites are able to interact with the brain-gut axis and play a role in behaviour. All the aforementioned mechanisms of action should encourage investigators, companies, stakeholders, and consumers to learn about the effects of probiotics as a whole and evaluate those strains that show promising results.

These steps toward establishing good science'' may result in the approval of health claims in the near future.

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