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Bacteria for Bacteria- ”Defusing the Myths, Defining the Solutions”

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ABSTRACT

Probiotics makes use of natural bacteria to confer health benefits but only when administered in small amounts. Conventional and commercially available probiotic food includes yogurt, fermented and unfermented milk, soya beverages etc., which contain bacteria such as Lactobacillus and Bifidobacterium. Probiotic are known to provide health benefits when consumed and have the ability to prevent and treat various diseases. It has a major role in treating antibiotics and antimicrobial resistance clinical conditions. Current scientific advancement would be the right time to change the way bacteria are treated. Better understanding of the science and further clinical trials of these tiny forms of life and their benefits on human will further broaden the scope of its applications. This article gives an overview about probiotics and its role of prevention in oral health problem.

Keywords: Probiotics, Caries, Immune response, Lactobacillus, prebiotics.

INTRODUCTION

The gastro-intestinal system begins with oral cavity and hence there is a belief that probiotic mechanism will play a role. Oral cavity harbors a diverse array of bacterial species, which could constitute for some of the most common infections in human. Kazor et al in 2003 reported that there are more than 600 species that colonize in oral cavity[1]. The balance of all these microorganisms can be disturbed in to pathogenic flora, which can lead to various oral health problems. Most common among them is dental caries, which is an infectious, microbial disease that causes demineralization of the inorganic component and dissolution of the organic component of the tooth structure and progresses into dentin and pulp, which in turn compromises tooth vitality. Caries formation is mostly due to oral Streptococci especially mutans are involved in caries formation. Earlier caries management was effectively removing the diseased demineralized portion and restoring it with biocompatible restorative materials[2]. Currently, management of caries focus is on prevention strategy, thus infection is treated well before its manifestation. In olden times, the use of beneficial bacteria have gained popularity and have now enabled the researchers to combat the microbial ecological change of dental caries and other oral health problem.

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Authentic Background

Lilly & Stillwell coined the word "probiotic" in 1965. It is derived from the Latin preposition "pro" (for) and Greek adjective "biotics", meaning 'fit for life'. The first positive observation of its role was investigated by Elli Metchnikoff (1907), the Ukraine born Nobel Prize winner who was working at the Pasteur institute in the beginning of last century[3]. He proposed (1907) that Lactobacillus bulgaricus (present in Bulgarian yoghurt), the lactic acid producing strain is capable of displacing the pathological intestinal microbiota. It adopts the measure to replace the pathological bacteria into beneficial bacteria in our body. The first researcher to discover the beneficial properties of fermented dairy products was Elli Metchnikoff[3].

Mann and Spoerring (1974) discovered that fermented yogurt reduce blood serum cholesterol. Hull (1984) identified the first probiotic species, the Lactobacillus acidophilus and later in 1991, Bifidobacterium bifi was discovered by Holcombh[4].

Definitions

Numerous definitions by various authors was proposed for probiotics and they are listed in Table I below[5-7,4]:

A common definition for the term 'probiotics' was put forward by WHO and by Food and agricultural organization (FAO) of United Nation as "live microorganism which when administered in adequate amount confer health benefits on the host."

Relationship Between Prebiotics And Probiotics

According to Gibson and Roberfroid, the term "prebiotic," is a non-digestable food ingredient that improves the host health by specifically stimulating growth as well as the activity of one bacterium or group of bacterium[8]. Prebiotics are found naturally in bananas, asparagus, garlic, tomato, and onion wheal. When a product contains both prebiotics and probiotics it is known as symbiotic. Prebiotics selectively favours the growth of probiotics. The commonly known probiotics includes insulin, fructo-oligosaccharides, galacto-oligosaccharides and lactose and xylo-oligosaccharide[7].

Mechanism Of Probiotics

Probiotics exert their health benefits by the following mechanisms[10,11];

- Normalization of intestinal microbiota
- Creation of antimicrobial substances to cause antagonization of pathogens
- Compete with pathogen for binding to the receptor sites
- Stimulating cells that modulate immune system

Probiotics In Oral Health

Ideal Features Of Probiotic[11,12]

1. Strain should have the ability to exert a favorable response on the host. Eg: increased growth and resistance to disease.
2. It should remain stable and viable for longer

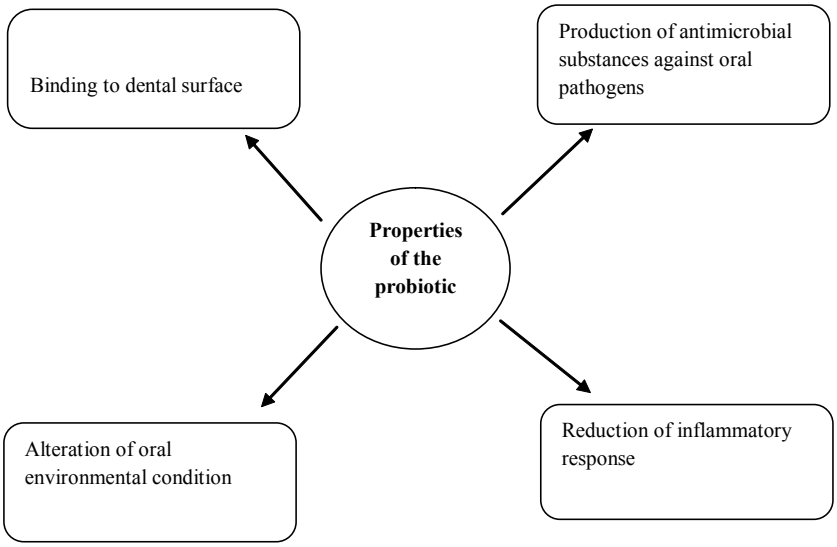


Fig. 1: Properties of Probiotics

duration under suitable storage conditions.

3. It should not cause any type of diseases and should be non-toxic.
4. It should get adapted to the gut environment and survive in it ex: resistance to acidic environment and organic acids and also maintain genetic stability in oral microflora.
5. Its effect is directly related to the presence of viable cells, preferably in large numbers.

Probiotics Microorganisms

Mechanism of Probiotic Action On Oral Health

The bacterial resistance to antibiotics has opened a new avenue to consider the idea of probiotic therapy (bacterial therapy) as an alternative to manage oral health issues. In oral environment, probiotics tends to keeps the deleterious pathogens away by forming a thin film over the tooth surface and filling the space around the tooth[12,11]. It is mainly gaining its importance in treating dental caries, periodontal disease, halitosis, and oral candidiasis.

Probiotics mode of action in oral environment includes:

- Immune modulation
- Modulation of immunological mechanisms in gut
- Production of mucin
- Down regulation of inflammatory responses
- Anti-microbial compounds production
- Competition with pathogens and blockage of adhesion sites
- Stimulation of immunoglobulin A production

Probiotic directly interact with disease-causing organisms and compete with them to reduce its virulence thus reducing their disease causing efficiency, which is achieved by production of antimicrobial substance against pathogenic organisms.

Competitive exclusion

Beneficial microbes interact with disease causing organism for its nutrition or enterocyte adhesion sites. This adhesion helps probiotic to extend their effect on microorganisms[13]. Probiotic strains obtained from dairy products are used to test for adhesion to oral mucosal epithelial cells. The two methods predominantly used to examine this adhesion mechanism includes;

Year	Definition	Author
1965	Substance produced by microorganisms that promote the growth of other microorganisms	Lilly and Stillwell et al
1974	Organism and substances that contribute to intestinal microbial balance.	Parker et al
1989	A live microbial feed supplement that beneficially affects the host and improve the intestinal microbial balance.	Fuller et al
1992	A viable monoculture or mixed-culture of microorganisms upon ingestion by animal or human, beneficially affects the host by improving the properties of the indigenous microflora.	Havenaar and HuisInt Veld *et al*
1996	Living microorganisms that upon ingestion exert health benefits beyond inherent basic nutrition.	Schaafsma et al
1999	A microbial dietary adjuvant that beneficially affects the host physiology by modulating mucosal and systemic immunity as well as by improving nutritional and microbial balance in the intestinal tract.	Naidu et al
2001	A preparation or a product containing viable microorganisms in sufficient numbers can alter the microflora (by implantation/ colonization) of the host and exert beneficial health effects.	Schrezemeir and de Verse *et al*
2001	Live microorganisms when administered in adequate amounts confer health benefits to the host.	FAO/WHO report

- Saliva coated hydroxyapatite
- Hydroxyapatite coated with buffers, proteins and other substances

Modulation Of Host Immune Response

Probiotics interact with immune system and strengthens them, which in turn helps in disease prevention[14]. Modulation of host immune includes the innate as well as the acquired immune system.

Vehicles of administration

Probiotics are commonly supplied in any one of the given four forms[14,13,12]:

- Concentrate of culture added to a food or beverages such as fruit juice.
- Inoculated into prebiotic fibers
- Inoculants into a milk-based food, dairy products such as yoghurt, milk drink, milk.
- As concentrated and dried cells packaged in dietary supplements, non-dairy products.

Probiotics and Dental Caries

Numerous researchers have been reported to treat dental caries using "probiotic" which is considered as a major oral issue. It acts on dental caries by selectively removing only the disease causing pathogen while leaving the oral ecosystem intact. Streptococcus mutans is the main causative microorganisms in the caries development because of its ability to produce water-soluble glucan[15]. Its acidogenic properties and rapid metabolism of glucose, sucrose and fructose generate a low pH that challenges the homeostasis with a shift towards bacteria and induce dental caries.

***Lactobacillus* spp.**	***Bifidobacterium* spp.**	**Others**
L.acidophilus	B.bifidum	Saccharomyces boulardii
L.casei	B.breve	Enterococcus faecium
L.crispatus	B.infantis	Streptococcus
L.delbrueckiisubspp.bulgaricus	B.longum	Salivarius subspp
L.fermentum	B.lactis	Thermophilus
L.gasseri	B.adolescentis	S.diaacetylactitis
L.johnsonii		S.intermedius
L.paracasei		Lactococcus
L.plantarum		Lactissubsp.cremoris
L.reuteri		
L.rhamnosus		

Vehicle	**Strain**	**Outcome**	**Reference**
Lozenge	S.salivarius	Decreases oral Volatile sulphur compounds levels	Burton et al
Straw, tablet	L.reuteri ATCC55730	Reduction of S.mutans count	Caglar et al
Yoghurt	Bifidobacterium DN-173010	Salivary S.mutans counts decreases	Caglar et al
Cheese	L.rhamnosus GG, Propionibacterium JS	Reduced risk of high yeast counts and hypo salivation	Hatakka et al
Rinse solution	W.cibaria	Decrease in Volatile Sulphur Compounds	Kang et al
Capsule liquid	L.sporogenes,L.bifidum, L.bulgarius,L.thermophilus, L.acidophilus,L.casei, L.rhamnosus	Increased salivary counts of lactobacilli without significant decrease in S.mutans counts	Montalto et al
Yogurt drink	L.rhamnosus GG	Temporary oral cavity colonization	Yli-Knuuttila et al

Caries related mechanisms of probiotic activity

- Lactobacilli and Bifidobacteria are both acidogenic and aciduric. The species such as L.rhamnosus GG and B.lactis BB-12 do not ferment sucrose.[16]
- The probiotics generate low pH that is crucial for anti-microbial actions.
- The growth inhibition has been attributed to the generation of low pH either through organic acid production or bacteriocin production active at low pH.
- The adhesion capacity and persistence on the oral mucosa and teeth-Lactobacilli show varying degrees of adhesion to silver-coated hydroxyapetite surface.[17]
- Interactions between oral microorganisms and probiotics: it alter the protein component which in turn prevent colonization of other bacteria.

Probiotics and count of Streptococcus Mutans

Increase in mutans streptococci doesn't correlate with caries risk. However decreasing mutans streptococci will improve the oral microflora of the plaque which in turn can make the bacteria less virulent without affecting the normal flora. In adults, various vehicles of administration have shown decrease in Mutans Streptococci count. Whereas, use of probiotics in infants has its limitations because its effect on unerupted teeth is still not been elicited.

Clinical Case

Case report 1

In a Finnish study, 594 children (1-6 years old) attending a day-care centre received L.rhamnosus GG containing milk for 7 months.[18] It is observed that milk consumed children has reduced caries risk significantly in 3-4 year old children.

Case report 2

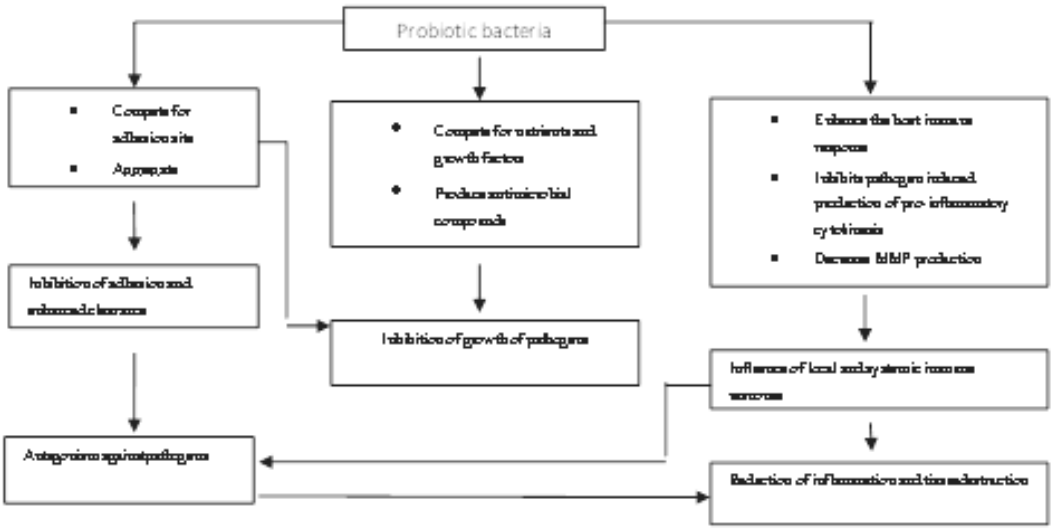
In a Swedish study, 248 preschool children of age group between 1 to 5 years age received either a control milk or tested milk supplemented with fluoride along with L.rhamnosus LB21 for 21 months and was found that caries risk was greatly decreased in test group.[19]

Case report 3

Yli-Knuuttila et al assessed colonization of Lactobacillus rhamnosus in the oral cavity of healthy students after 14 day trial period and reported that the occurrence of L. rhamnosus was has gradually decreased indicating no permanent colonization and its persistence was only temporary.[20]

Case report 4

Haukioja et al defined a mechanism whereby Lactobacillus and B-lactis 6612 affected the composition of salivary pellicle on hydroxyapetite and thereby inhibited Streptococcus mutans adherence in vitro.[21]



Case report 5

Kang MS et al proposed that Weissella cibaria isolates inhibitsthe formation of S. mutans biofilm. Weissella cibariais a water-soluble polymers formed from sucrose.[22]

Case report 6

Calgary et al (2007) proposed that use of chewing gums containing probiotic bacteria or xylitol reduced the levels of salivary mutans streptococci. [23]

Probiotics and Periodontal Disease

Periodontitis is a multifactorial disease that affects the hard and soft tissue components of the periodontium. The complexity of the microbial population and the interaction between the host and bacteria defense mechanism threatens the balance of parasitic organism and the ecological niche.[24] Though antibiotics are prescribed commonly for the treatment of periodontitis, probiotics could be a safer and better alternative mode of treatment.

Periodontal disease related mechanism of probiotics:

1. Inhibition of specific pathogens, inhibition of adhesion and colonization of bacteria and its growth.[25]
2. Effects on host response by inhibition of collagenase
3. Lowering the inflammatory molecules.
4. Induction of cytoprotective proteins on host cell surfaces.
5. Modulation of pro-inflammatory pathways.
6. Prevention of cytokine-induced apoptosis.
7. Modulation of host immune response.

Probiotics have similar response to a pathogen, but doesn't cause periodontal destruction. It protects the epithelial barrier by maintaining tight junction protein expression. L. paracasei and L. rhamnosus has a capacity to antagonize porphyromonas gingivalis and streptococcus mutans. Weissella cibaria, a gram positive anaerobic lactic acid bacterium isolated from humans present in fermented foods found to have high probiotic action, as it secretes hydrogen peroxide and bacteriocins against bacteria. It also has a capacity to co-aggregate with F.nucleatum and epithelial cells.[25] This significant property enable this good bacteria to colonize in the mouth and limit the proliferation of pathogenic bacteria.

Clinical Case

Case report 1

Krause et al observed reduction in gingival bleeding and gingivitis with the application of L. reuteri.[26]

Case report 2

Co-aggregation ability of Fusobacterium nucleatum with Weissella cibaria and their attachment to epithelial cells was tested and it was found that F. nucleatum have an important role as a bridge organism which facilitates the colonization of other bacteria by co-aggregation and this ability enables Lactobacillus spp., to form a barrier which in turn prevents colonization of pathogenic bacteria as it generates some inhibitory substance.[27]

Case report 3

In a study describing the bacterial growth, its survival in saliva and oral cavity, Haukioja et al tested the colonization capability of probiotics that are commercially available and Lactobacillus and Bifidobacterium stains. Results showed that all the strains demonstrated 24 hours survival rate but differing in their binding rapidly to saliva coated surfaces. Lactobacillus strains showed better adhering capacity and they may compete for same binding sites on saliva coated hydroxyapatite with F.nucleatum which showed lower colonization property. This indicates that probiotics affect the biofilm formation and modify microflora.

Risks during Probiotic Treatment

For most people taking a quality probiotic supplement doesn't have any side effects other than high energy and better digestive health. But for some people whose gut bacterial level is imbalance develop certain side effects.[29,30] But they are uncommon and rare. The side effects include:

1. Sepsis: Lactobacillus species are found to be one of the known cause for bacterial endocarditis especially in adults in absence of probiotic supplementation. Several reports have directly linked the lactobacillus cases to ingestion of probiotics. Major risk is considered for immunocompromised patients

and premature infants.

2. Immunosuppression or over immune stimulation: some people are immunosuppressed while others immune system gets over stimulated but they are rarely reported.
3. Deleterious metabolic activities

CONCLUSION

In future, probiotics will gain importance in treating antibiotics overuse and antimicrobial resistant conditions. With the advent in scientific technology, it would be the right moment to change in the way microorganisms are treated. Probiotics helps to maintain good health and protect oral tissues in a more natural way. In future, various clinical trials, are needed to formulate the potent probiotic strains and its perfect route of administration for its enhanced benefits.[31] Scientific research can lead to genetically modify or formulate potential probiotic strains which in turn can offer a new treatment modalities for the present and future generations.

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