ISSN NO. 2320-5407

Journal homepage: http://www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH

RESEARCH ARTICLE

PROBIOTICS: "A new horizon in oral health promotion".

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Manuscript Info

Manuscript History:

Received: 11 January 2015
Final Accepted: 25 February 2015
Published Online: March 2015

Key words:

Probiotic, oral health.

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Abstract

Probiotics are live microrganisms administered in adequate amounts with beneficial health effects on the host.The mechanism of action of probiotics is related to their ability to compete with pathogenic microorganisms for adhesion sites, to antagonize these pathogens or to modulate the host's immune response.The use of probiotic plays an important aspect in dentistry too ever since the oral infections occupied the prime space among the other infections effecting the humans. Probiotic approach has shown promising results in oral cavity with respect to control of chronic disease such as dental caries, periodontitis, and recurring problems like halitosis and candidial infections. The aim of this review is to examine potential mechanisms of probiotic bacteria in the oral cavity and to observe the effects of probiotics with respect to oral health.

INTRODUCTION

The oral cavity is a complex ecosystem which harbours an astonishing variety of microbial species.[1]The wide range in pH, nutrient availability, shedding and non-shedding surfaces, salivary and crevicular fluids select localized, discrete microbial climax communities to fluctuate in composition and metabolic activity but reach a kind of homeostasis in balance with the host. Changes in the environment whether imposed by illness, debility, behaviour, diet, or medications disturb the homeostasis and lead to endogenous infections or susceptibility to exogenous infections. Antimicrobial therapy is the most effective way to combat infections, but side effects like diarrhoea, dermatitis and antimicrobial resistance, are associated with the use of these therapeutic agents. These are some reasons that make researchers to search for some other possibility in the treatment of infection. Bacteriotherapy and Probiosis is an alternate and promising way to fight infections by using harmless bacteria to displace pathogenic microorganisms.[2]

The term Probiotic, meaning "for life," is derived from the Greek language.[3] Probiotics can be defined as living microbes, or as food ingredients containing living microbes, that beneficially influence the health of the host when used in adequate numbers[4]. Marteau *et al*, in 2002, defined them as "microbial preparations or components of microbial cells that have a beneficial effect on health and well-being"[5]. FAO (Food and Agriculture Organisation) of the United Nation and the WHO defined probiotics as "live microorganisms", which, when administered in adequate amounts confer a health benefit on the host.

COMPOSITION OF PROBIOTICS

Probiotics, which are regulated as dietary supplements and foods, consist of yeast or bacteria. They are available as capsules, gels, pastes, tablets, packets, liquids, or powders, and are contained in various fermented foods, most

commonly yogurt or dairy drinks. Probiotic products may contain a single microorganism or a mixture of several species. Probiotics can be bacteria, moulds, yeast. But most probiotics are bacteria. Among bacteria, lactic acid bacteria are more popular.[6]

HISTORY OF PROBIOCTICS

The idea of probiotics dates back when Elie Metchnikoff, the Ukrainian born Nobel prize winner working at the Pasteur Institute at the beginning of the last century proposed, in 1907, that the lactic acid producing strain Lactobacillus bulgaricus (contained in Bulgarian yoghurt) is able to displace pathological intestinal micro biota. Metchnikoff himself introduced in his diet sour milk fermented with the bacteria called "Bulgarian Bacillus" and found his health benefited (Metchnikoff E.1907). Lilley and Stillwell (1965) introduced the term probiotics. In 1984 Hull identified the first probiotic species, the lactobacillus acidophilus. Later in 1991, Holcombh identified bifidobacterium bifidum. WHO in 1994 described the probiotics as next most important in immune defense system following antibiotic resistance. These incidences paved way for a new concept of probiotics in medicine and dentistry.[7]

PROBIOTICS AND ORAL HEALTH

Given the widespread emergence of bacterial resistance to antibiotics, the concept of probiotic therapy has been considered for application in oral health.[8]More than 700 species of oral microbiota have been detected in the human mouth and the resident microbiota of one individual may consist of 30-100 species.[1]An essential requirement for a microorganism to be an oral probiotic is its ability to adhere to and colonize surfaces in the oral cavity[9].

MECHANISM OF PROBIOTIC ACTION ON ORAL HEALTH

Microorganisms generally considered as probiotics may not have oral cavity as their inherent habitat, so their possibility to confer benefit on oral health is then questionable. The suggested mechanisms of probiotic action are drawn entirely from gastrointestinal studies. Since, mouth is the gateway of the Gastro Intestinal tract, there is every reason to believe that atleast some probiotic mechanisms may play a role in the oral cavity.

Some of the hypothetical mechanisms of probiotic action in the oral cavity are:
- Lactobacilli play an important role in maintaining the microecological balance in the oral cavity.
- Direct interaction in dental plaque.
- Involvement in binding of oral micro-organisms to proteins [interference in formation of acquired pellicle].
- Action on plaque formation and on its complex ecosystem by competing and intervening with bacterial attachments.
- Involvement in metabolism of substrate and production of chemicals that inhibit oral bacteria.

Indirect probiotic actions are also featured such as
- Modulating systemic immune function.
- Effect on local immunity.
- Effect on non-immunologic defense mechanisms.
- Regulation of mucosal permeability.
- Probiotics as an antioxidants and produce antioxidants.
- Prevent plaque formation by neutralizing the free electrons.

Immune inductive sites in the oral cavity are within the diffuse lymphoid aggregates of the Waldeyer's ring. Lingual and pharyngeal tonsils and adenoids contain most of the lymphatic tissue. Dentritic cells in the mucosal surfaces play vital role in antigen presentation and in activating T-cell responses. Depending on the signals from dendritic cells either immune tolerance or active immune response toward a specific antigen may occur.However, more studies investigating the role probiotics on activation of the oral immune inductive sites are required before further conclusions are drawn.

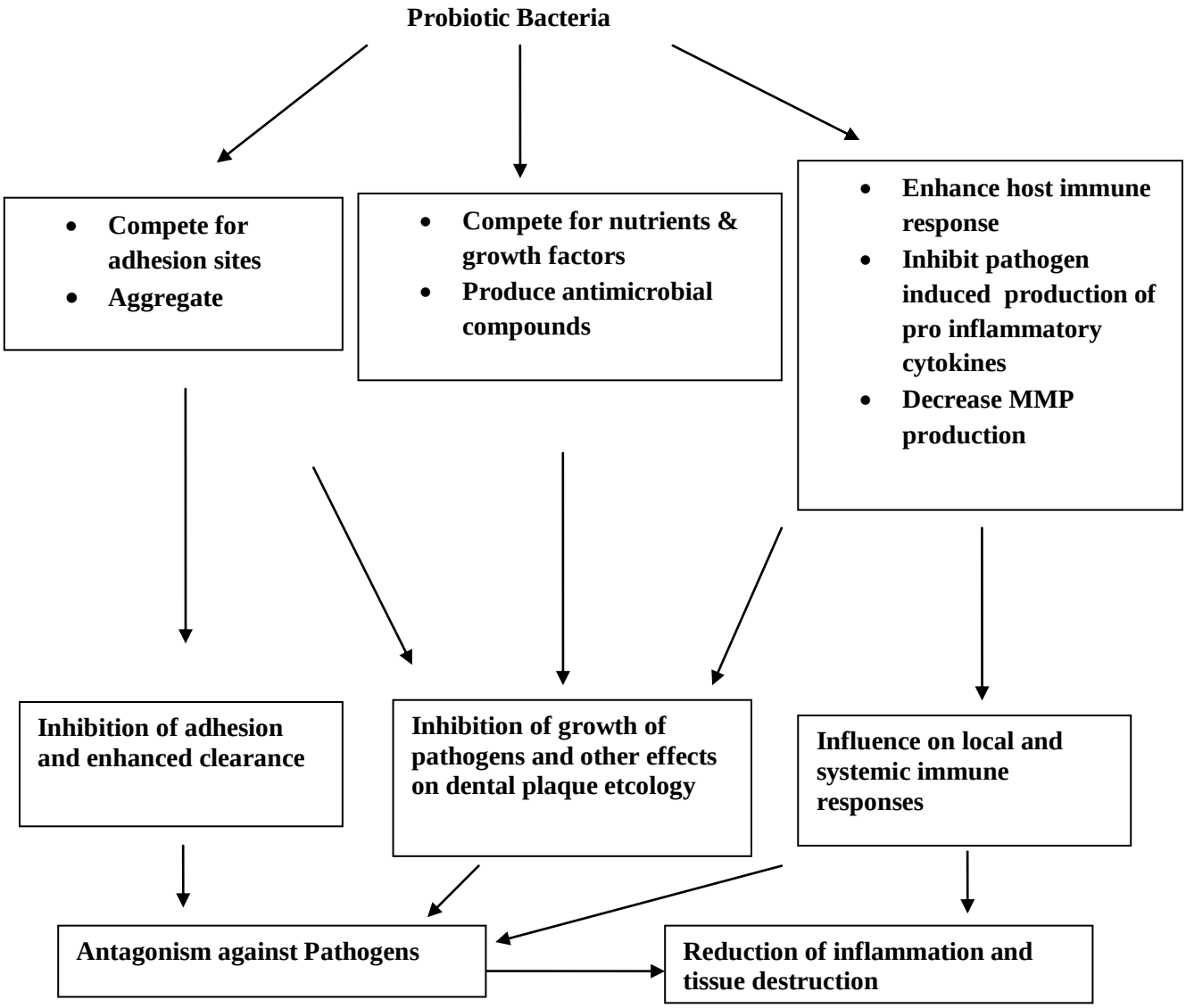

Figure1. Possible Mechanisms of Probiotic Action in the Oral Cavity [10].

APPLICATION OF PROBIOTICS TO ORAL HEALTH

Probiotics and Dental Caries

A number of researchers are developing 'probiotic' methods to treat the caries causing pathogens. 'Probiotic', as used here, means that mechanisms are employed to selectively remove only the (odonto) pathogen while leaving the remainder of the oral ecosystem intact.[11] One of the replacement therapy options entails the application of a genetically engineered 'effector strain' of *S. mutans* that will replace the cariogenic or 'wild strain' to prevent or arrest caries and to promote optimal remineralization of tooth surfaces that have been demineralized but that have not become cavitated. 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 noncariogenic bacteria has shown promising results. These studies have employed different approaches[12]

- Early studies concentrated on utilizing bacteria that expressed bacteriocins or bacteriocin-like inhibitory substances (BLIS) that specifically prevented the growth of cariogenic bacteria.
- One approach has been to identify food grade and probiotic bacteria, which have ability to colonize teeth and influence the supragingival plaque.
- Also, strains have been screened for suitable antagonistic activity against relevant oral bacteria.
- Another approach utilized recombinant strain of *S. mutans* expressing urease, which was shown to reduce the cariogenicity of plaque in an animal model.
- 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.
- A different way of accomplishing the removal of the pathogens is to develop 'targeted antimicrobials'.The basic idea is to develop an inexpensive targeting molecule that will reliably attach to only the organism of interest, in this case *S. mutans*, *S. sobrinus* or other chosen pathogen. Once the targeting molecule is perfected, then a 'killer' molecule is optimized and chained to the targeting molecule. The combined unit then selectively eliminates the infection of interest. In the case of the oral cavity and dental caries, this system is attractive from the perspective of eliminating all the pathogens thereby precluding the regrowth of the original infection. There is also compelling evidence from clinical trials and laboratory efforts demonstrating that once the bacterial ecosystem is free of *S. mutans*, it is difficult to reintroduce the organisms.[11,12]

Probiotics and Periodontal Disease

Taking into account the two major treatment strategies against periodontal diseases, namely the elimination of specific pathogens and the suppression of a destructive host response, the probiotic approach may add value in achieving these treatment goals.Fig 2 outlines the possible mechanisms whereby probiotic species might positively affect periodontal health.[13] The effect of probiotics tablets on gingivitis and different grades of periodontitis was studied by Grudianov *et al*. and it found that probiotics treatment resulted in better microbiota normalization than control group[14]. Krasse *et al*. showed a significantly reduced gingival index and bacterial plaque amount in patients treated with *L. reuteri* than in a placebo group and concluded that this probiotic was effective to reduce gingivitis and bacterial plaque deposition in patients with moderate-to-severe gingivitis[15]. According to Koll-Klais *et al*. high levels of *Lactobacillus* in microbiota caused an 82% and 65% inhibition in *Porphyromonas gingivalis* and *Prevotella intermedia* growth, respectively [16]. Twetman *et al*. used *L. reuteri* containing chewing gum in 42 healthy patients and assessed its effects on crevicular fluid volume, cytokine (interleukin-10, interleukin-6, interleukin-10, and TNF-α) levels, and bleeding on probing. Crevicular fluid volume, as well as TNF-α and interleukin-8 levels, and bleeding were significantly reduced[17]. Shimauchi *et al*. described a beneficial effect of probiotics tablets, containing *lactobacillus salivarius* WB21, in the treatment of periodontitis patients[18].

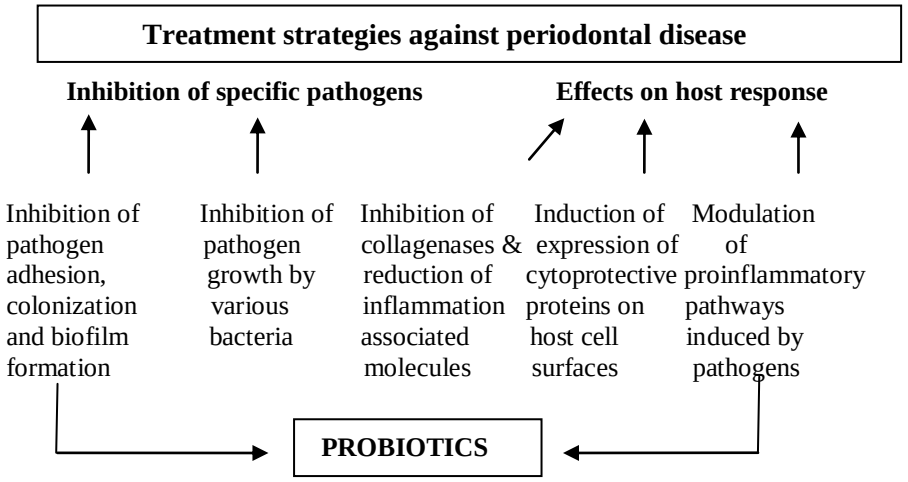

Figure 2: Theoretical possibilities for probiotics to affect periodontal health.[13]

Probiotics and Halitosis

Halitosis has many causes (including consumption of particular foods, metabolic disorders, respiratory tract infections), but in most cases it is associated with an imbalance of the commensal microflora of the oral cavity[19]. More specifically, halitosis results from the action of anaerobic bacteria that degrade salivary and food proteins to generate amino acids, which are in turn transformed into volatile sulphur compounds, including hydrogen sulphide and methanethiol.[19] Kang and colleagues reported the capacity of various strains of *W. cibaria* to inhibit the production of volatile sulphur compounds by *F. nucleatum*. They concluded that this beneficial effect resulted from the production of hydrogen peroxide by *W. cibaria*, which inhibited the proliferation of *F. nucleatum*.[20] These authors also found that gargling with a solution containing *W. cibaria* was associated with a net reduction in the production of hydrogen sulphide and methanethiol and consequently a reduction in bad breath.[20]

Probiotics and Candidiasis

Candida albicans is among the most common infectious agents in the oral cavity. The incidence of yeast infections is higher at older age and under conditions of impaired immunity. Testing the pattern of colonisation of *L. acidophilus* and *L. fermentum*, Elahi *et al* showed a rapid decline in *C. albicans* in mice after the intake of probiotic strains. Continuous consumption of probiotics led to almost undetectable numbers of fungi in the oral cavity, maintaining the protective effect for a prolonged period after cessation of application.The capacity of different *lactobacilli* to stimulate cellular and humoral factors of mucosal protection varies particularly in terms of salivary nitrous oxide and c-interferon levels. Elahi *et al* have observed a correlation between the highest peak of interleukin-4 secretion and complete eradication of *C. Albicans*.[21]

Probiotics and cancer

Oral cancer accounts for the second most common malignancy in our country. The five year survival disease free rate remains at around 50% only for oral cancer. More than 80% of the oral cancers are due to the usage of tobacco related products. Several attempts have been made by researchers to find out methods to keep this disease under control.On persuing the literature, several in vivo studies have demonstrated encouraging outcomes, mainly attributed to its antimicrobial effects against carcinogen-producing microorganisms, antimutagenic properties, and alteration of the tumor differentiation processes. Further, in humans it has been observed that the ingestion of probiotics has lead to a reduction in the genotoxic components and products which induce DNA damage.However conclusive evidence on the role of probiotics in oral cancer is lacking at the moment.[22]

FUTURE PROSPECTIVES OF PROBIOTICS

Many researchers have reported significant benefits in oral health on administration of Probiotics. Recently, oral lactic acid bacteria and bifidobacteria have been isolated and characterized for various oral health purposes, including caries, periodontal diseases, and halitosis. The new probiotic products targeted for oral health purposes do not necessarily comprise the same species as products now in market. Genetically modified microbes bring a new dimension to the concept of probiotics. Their main thrush is on reducing the harmful properties of pathogenic strains naturally colonizing the oral cavity. The modified strain could then be used to replace the original pathogen. Also they could be used to enhance the properties of a potentially beneficial strain. In field of oral immunology, probiotics are being used as passive local immunization vehicles against dental caries. Bacteriophages, viruses that kill bacteria, have been detected in oral pathogens, such as Actinobacillus actinomycetem comitans, and they may play a role in the pathogenicity.

Subsequently, future studies should be conducted to investigate if phage therapy might be applied for oral and dental diseases in the same way as has been attempted for systemic infections. The selection of the best probiotic for oral health is also an issue that calls for further study.[23]

CONCLUSION

Probiotics are a new and interesting field of research in oral microbiology. Bacteriotherapy in the form of probiotics seems to be a natural way to maintain health and protect oral tissues from diseases.The existence of probiotics in the indigenous oral microflora of humans warrants exploration because these bacteria offer the advantage of being perfectly adapted to the human oral ecosystem. Knowledege of probiotics on the host immune system has entered a new and fascinating phase of research and progression in this field is likely to offer novel and useful means to modulate host immunity for protection from, or treatment of a wide variety of oral diseases and disorders. Thus probiotics have turned out to be very promising in ensuring oral health and wellbeing.

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