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Probiotics and Oral Health

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1. Introduction

All great thoughts have already been thought; what is necessary is only to try to think them again....

Johann Wolfgang

Man is the most intelligent animal on the earth, as he is the only species gifted with the power of thinking and reasoning. He always manages to come up with solutions for *most problems* on earth. Ironically, most problems on earth are directly or indirectly created by Man himself. That's the reason he is most often referred to as an *intelligent fool*.

The man-made problem prevailing across the field of medicine is the development of *antibiotic resistance*, largely contributed by us, the health professionals. The indiscriminate and reckless use of antibiotics has led to the emergence of multi-resistant strains of bacteria. This unfortunate development has led scientists to seek other means of fighting infections. [1]

The good-old but forgotten concept of *bacteriotherapy* seem to offer innovative tools for the treatment of infectious diseases. Hence, rightly quoted "All great thoughts have already been thought; what is necessary is only to try to think them again".

Bacteriotherapy is the administration of naturally occurring bacteria of human origin as a therapeutic manipulation of the bacterial microenvironment in the patient's body. [1] The Basic principle is to use good bacteria to compete against pathogenic bacteria. Bacteriotherapy has been studied and tested to control infectious diseases, particularly in the GI tract. Recent studies have shown that this therapeutic method may be used to influence body function in other systems too, beyond the intestine. [1, 2, 3]

2. History

It was in the first decade of 1900, the beginning of the 20th century when the Ukrainian-born Nobel prize laureate Elie Metchnikoff observed the positive beneficial effect of some bacteria on the human health and suggested that these beneficial bacteria can be used to replace harmful microbes in the body. He reported that Bulgarians lived longer than other population which was due to their consumption of Bulgarian yoghurt which contained lactic acid bacteria.[4] Metchnikoff worked at the Pasteur Institute in Paris and had discovered *Lactobacillus bulgarius*, a strain he later introduced into commercial production of sour-milk products in France and throughout Europe. He devoted the last decade of his life to the study of lactic-acid producing bacteria as a means of increasing human longevity. [5] He developed a theory stating that senility is caused by poisoning of

the body by the products of some of the bacteria for which he proposed a diet containing milk fermented by lactobacilli producing lactic acid to prevent the multiplication of these organisms. [6] The concept of probiotics was thus born and a new field of microbiology came into light.

The first clinical trials were performed in the 1930s on the effect of probiotics on constipation. Ever since then, different microorganisms have been used for their ability to prevent and cure diseases. [7]

In 1994, the WHO deemed probiotics to be the next-most important immune defence system when commonly prescribed antibiotics are rendered useless by antibiotic resistance. The use of probiotics in antibiotic resistance is termed as *microbial interference therapy*. [7]

The literature on the possible role of probiotics on oral and dental health is scarce and the studies on probiotics v/s oral health are still in their cradle. [6]

3. What are Probiotics?

The term probiotic means ‘for life’, was first coined by Lilly and Stillwell. [8]

4. Definition

[Adopted by the International Scientific Association for Probiotics and Prebiotics term]

Probiotics are defined as “Live microorganisms, which when administered in adequate amounts, confer a health benefit on the host” (Guarner et al 2005) [9]

5. Oral probiotic organisms [7]

The most common probiotic strains belong to the genera Lactobacillus and Bifidobacterium. Bacterial strains that have been tested for probiotic action in the oral cavity include:

LACTOBACILLI SPECIES	BIFIDOBACTERIUM SPECIES	OTHERS
<ul style="list-style-type: none">• L. acidophilus• L. rhamnosus GG• L. johnsonii• L. casei• L. rhamnosus• L. gasseri• L. reuteri• L. paracasei	<ul style="list-style-type: none">• B. bifidum• B. longum• B. infantis• Bifidobacterium DN-173 010	<ul style="list-style-type: none">• S. salivarius• W. cibaria•

Table 1.

L. rhamnosus GG, ATCC 53103 (LGG) is the most widely studied probiotic bacterium. Named after the discoverers, Sherwood Gorbach and Barry Goldin, produces a substance

with potential inhibitory activity against different bacterial species including cariogenic *Streptococcus* species. [1]

6. Vehicles for probiotic administration for oral health purpose

The various means of administration of probiotics for oral health purpose that has been studies are:

- Lozenges
- Tablets
- Cheese
- Yoghurt
- Mouth rinse
- Capsule, Liquid

7. Mechanisms of probiotic action on oral health

An essential requirement for an organism to be “an oral probiotic” is its ability to adhere to and colonize surfaces in the oral cavity. 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. [6]The suggested mechanisms of probiotic action are drawn entirely from gastrointestinal studies. Since, mouth is the gateway of the GI tract, there is every reason to believe that atleast some probiotic mechanisms may play a role in the oral cavity. [1] 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.[11]
- 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.[12, 13]

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 antioxidants and produce antioxidants.
- Prevent plaque formation by neutralizing the free electrons. [14, 15, 16]

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. Dendritic 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. [6] However, more studies investigating the role probiotics on activation of the oral immune inductive sites are required before further conclusions are drawn.

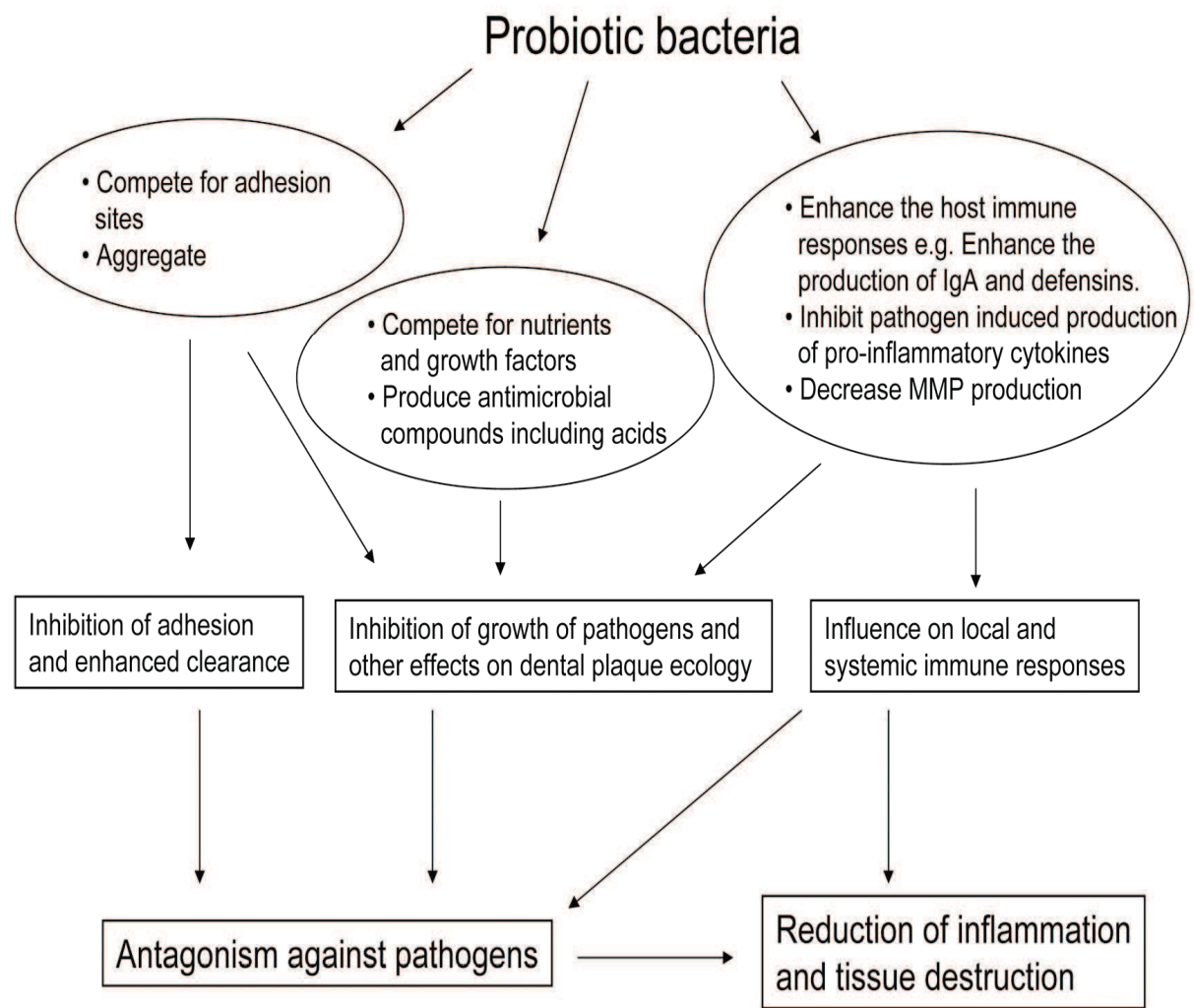


Fig. Possible Mechanisms of Probiotic Action in the Oral Cavity [10]

8. Action of probiotics on oral health

8.1 Action on organisms associated with dental caries

Several investigations have shown reduction in the number of mutans streptococci in saliva after consumption of various probiotic products, [17 – 25] however such an effect has not been observed in all studies. [26]

Náse et al, 2001 showed that supplementing 1-6 year old children with *L. rhamnosus* for 7 months significantly reduced the risk of dental caries. [17]

Comelli EM et al (2002) studied 23 dairy bacterial strains for the prevention of dental caries and reported that only two strains namely *Streptococcus thermophilus* and *Lactococcus lactis* were able to adhere to saliva-coated hydroxyapatite and were further successfully incorporated into a biofilm similar to the dental plaque. Furthermore, they could grow together with five strains of oral bacterial species commonly found in supragingival plaque. In this system, *Lactobacillus lactis* was able to modulate the growth of the oral bacteria, and in particular to diminish the colonization of *Streptococcus oralis*, *Veillonella dispar*, *Actinomyces naeslundii* and of the cariogenic *Strep.sobrinus*. [27]

Chung et al, 2004 showed that the probiotic strain *L. fermentum* found in the saliva of healthy children significantly inhibited the formation of the insoluble glucan produced by *S. mutans*. It did not affect the multiplication of this pathogenic strain, but it completely inhibited the adherence onto cuvette walls. [28]

Koll-Klais et al (2005) used various lactobacilli strains in their study and stated that 69% of these strains inhibited *S. mutans*, 82% inhibited *P. gingivalis*. [29]

An increase in the number of salivary lactobacilli has also been seen in some studies. [18, 26]

The products containing probiotic LGG bacteria may have beneficial effects on the dental health. The LGG bacteria had been shown not to ferment lactose or sucrose. [30]

Stamatova et al, in their study that was conducted in 2007 stated that *L. rhamnosus* & *Lactobacillus bulgaricus* produced inhibitory effects against *P. gingivalis*, *Fusobacterium nucleatum* & streptococcal species. [31]

Strahnic et al, 2007 conducted a study using probiotic strains *L. salivarius* & *L. fermentum* and both strains showed antagonistic activity on the growth of *S. mutans* and *Streptococcus pneumoniae*. *L. salivarius* was able to survive an environment of low pH as that produced by a high number of *S. mutans*. [32]

N.S.H. Mehanna et al (2009) investigated the effect of plant meswak and some probiotic bacteria on *Streptococcus mutans* and *Porphyromonas gingivalis* isolated from human oral cavity as most common oral pathogenic strains. The results of the study indicated that *Lactobacillus rhamnosus* had a marked decreasing effect on the colonization of both *Streptococcus mutans* and *Porphyromonas gingivalis*. [33]

A recently published review article by Anna Haukioja in 2010 does not give a conclusive statement about the effect of probiotics on dental caries or caries related organisms since the study groups have been relatively small and of fairly shorter duration. [10]

8.2 Action on periodontal diseases

Encouraging results have been obtained in studies investigating the role of probiotics for the treatment of various periodontal diseases, gingivitis, plaque levels, and periodontitis.

Reduction in the number of periodontopathogens in the plaque has also been observed. Again, most studies have been fairly short. [10]

Koll-Klais and team (2005) found a prevalence of *Lactobacillus gasseri* and *L. fermentum* in the oral cavity of healthy individuals compared to those with chronic periodontitis. Further to this, the same researchers have found that lactobacilli inhibit the growth of periodontopathogens, demonstrating the influence of lactobacilli in the oral cavity of a healthy individual. [29]

Riccia, et al (2007) recently studied the anti-inflammatory effects of *Lactobacillus brevis* in a group of patients with chronic periodontitis. The treatment, which involved sucking on lozenges containing *L. brevis* over a period of 4 days, led to improvements in the targeted clinical parameters (plaque index, gingival index, bleeding on probing) for all patients. In that study, a significant reduction in salivary levels of prostaglandin E2 (PGE2) and matrix metalloproteinases (MMPs) was also observed. The authors suggested that the beneficial anti-inflammatory effects of *L. brevis* could be attributed to its capacity to prevent the production of nitric oxide and, consequently, the release of PGE2 and the activation of MMPs induced by the nitric oxide. However, *L. brevis* may also be antagonistic, leading to a reduction in the quantity of plaque and therefore an improvement in the gingival index. [34]

Shimazaki and colleagues (2008) used epidemiological data to assess the relationship between periodontal health and the consumption of dairy products such as cheese, milk and yogurt. The authors found that individuals, particularly nonsmokers, who regularly consumed yogurt or beverages containing lactic acid exhibited lower probing depths and less loss of clinical attachment than individuals who consumed few of these dairy products. A similar effect was not observed with milk or cheese. By controlling the growth of the pathogens responsible for periodontitis, the lactic acid bacteria present in yogurt would be in part responsible for the beneficial effects observed. [35]

Harini PM and Anegundi RT 2010 found that probiotic mouth rinse was effective in reducing plaque accumulation and gingival inflammation in 6-8 year old children. [36]

8.3 Halitosis

There are a number of reasons for the onset of halitosis (bad smelling breath) –consumption of particular foods, metabolic disorders and respiratory tract infections – but commonly it is associated with an imbalance of the commensal microflora of the oral cavity. [37]

An unbalanced oral microflora has been associated with the production of malodorous substances called volatile sulphur compounds (VSCs). These are by-products of microbial degradation of proteins, blood, mucins found in saliva, and traces of food retained on oral surfaces. Kazor and team (2003) looked at the species of bacteria found on the tongue of patients suffering from halitosis and compared the findings with subjects who were considered healthy. The species found to be most associated with halitosis were *Atopobium parvulum*, *Eubacterium sulci*, *Fusobacterium periodonticum*. In the same study, *Streptococcus salivarius* was found to be the most prevalent in the healthy subjects, and this is thought to be due to the capability of *S. salivarius* to produce bacteriocins which could contribute to reducing the number of bacteria that produce VSCs. [38]

Probiotics are marketed for the treatment of both mouth and gut associated halitosis.

8.4 Probiotics and *Candida albicans*

C. albicans is a leading cause of infection in oral cavity; it is particularly common in the elderly and in immunocompromised patients. Hatakka et al (2007) showed a reduced prevalence of *C. albicans* after taking probiotics in cheese containing *L. rhamnosus* GG and *Propionibacterium freudenreichii*. [39]

Results obtained by Koll et al (2008) when assessing the effects of various *Lactobacillus* strains in oral cavity were markedly different; most strains suppressed growth of periodontal pathogens, including *actinomyces comitans* (60 out of 67 tested strains); *Porphyromona gingivalis* (35 out of 42 strains), *P. intermedia* (26 out of 42 strains), and cariogenic *S. mutans* (37 out of 67 strains). No inhibition was found, however, for *C. albicans* growth. [40]

Hasslöf P et al (2010) investigated the ability of a selection of lactobacilli strains, used in commercially available probiotic products, to inhibit growth of oral mutans streptococci and *C. albicans* in vitro by agar overlay method. At concentrations ranging from 10⁹ to 10⁵ CFU/ml, all lactobacilli strains inhibited the growth of the mutans streptococci completely with the exception of *L. acidophilus* La5 that executed only a slight inhibition of some strains at concentrations corresponding to 10⁷ and 10⁵ CFU/ml. All the tested lactobacilli strains reduced candida growth but the effect was generally weaker than for mutans streptococci. The two *L. plantarum* strains and *L. reuteri* ATCC 55730 displayed the strongest inhibition on *Candida albicans*. [41]

8.5 Probiotics and HIV

Recently it has been postulated that the probiotic bacteria may slow down AIDS progression. Lin Tao and his colleagues (2008) screened hundreds of bacteria taken from the saliva of volunteers. The results showed that some *Lactobacillus* strains had produced proteins capable of binding a particular type of sugar found on HIV envelope, called mannose. The binding of the sugar enables the bacteria to stick to the mucosal lining of the mouth and digestive tract, forming colonization. One strain secreted abundant mannose-binding protein particles into its surroundings, neutralizing HIV by binding to its sugar coating. They also observed that immune cells trapped by lactobacilli formed a clump. This configuration would immobilize any immune cells harboring HIV and prevent them from infecting other cells. [42]

9. Residence time of probiotics in oral cavity

Residence time of probiotics in oral cavity after treatment withdrawal was studied by Çağlar et al (2006) A reduced *S. mutans* level was shown after a two-week use of a *L. reuteri*-enriched yogurt; effects were observed during use and for a few days after discontinuation. [43]

A loss of *L. reuteri* colonization was observed by Wolf et al (1995) two months after having discontinued probiotic use. [44] *L. rhamnosus* GG administration and oral cavity colonization was studied by Yli-Knuuttila et al in 2006. The authors concluded that permanent colonization in oral cavity was unlikely (although possible in some cases) and suggested the probiotic to be used on a regular basis. [45]

Binding strength of 17 *Lactobacillus* strains and 7 bifidobacteria strains to saliva and oral mucous membrane was variable in different strains, according to a study by Haukioja et al in 2006, such a strength variation caused an increased residence time of probiotic in oral cavity.[46] Latency time of probiotic *S. salivarius* K12, 4 tablets/day for 3 days, was assessed in several oral cavity areas in a 35-day follow-up, by Horz et al (2007) probiotic could be found on oral mucous membrane, tongue and in stimulated saliva for more than 3 weeks, with a gradually reduced *S. salivarius* K12 level being detected beginning 8 days after treatment withdrawal. [47]

The findings of the studies on oral colonization of probiotics did not suggest that a permanent installation can take place. However, one needs to bear in mind that most studies were conducted in adults and it may be questioned if a permanent installation readily can occur in persons with an already established microflora.[1] Therefore, it seems especially important that further research needs to be carried on infants because it is very likely that the chance of a permanent colonization of probiotics increases with a regular exposure from early childhood. [3]

10. Conclusion

The oral cavity with its diversity of microbial species has been shown to harbor strains also distinguished as probiotics as such. Further studies identifying resident probiotics in the mouth, and their eventual effect on the oral environment are required.

Probiotics are a new and interesting field of research in oral microbiology and oral medicine. Bacteriotherapy in the form of probiotics seems to be a natural way to maintain health and protect oral tissues from diseases. But, this area of research in relation to oral health is still in

its infancy and further long term randomized controlled studies are required before definite conclusions are drawn regarding their effective action on oral health.

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Oral Health Care - Pediatric, Research, Epidemiology and Clinical Practices

Edited by Prof. Mandeep Viridi

ISBN 978-953-51-0133-8

Hard cover, 302 pages

Publisher InTech

Published online 29, February, 2012

Published in print edition February, 2012

Oral health care in pediatric dentistry deals with complete oral health, including preventive aspects for children right from their conception to adolescence, encompassing all the spheres of dentistry including various specialties. It also includes planning a preventive program at individual and community levels. The current research interests in oral health care include studies regarding the role of stem cells, tissue culture, and other ground-breaking technologies available to the scientific community in addition to traditional fields such as anatomy, physiology, and pharmaceuticals etc of the oral cavity. Public health and epidemiology in oral health care is about the monitoring of the general oral health of a community, general afflictions they are suffering from, and an overall approach for care and correction of the same. The oral health care-giver undertakes evaluation of conditions affecting individuals for infections, developmental anomalies, habits, etc. and provides corrective action in clinical conditions. The present work is a compendium of articles by internationally renowned and reputed specialists about the current developments in various fields of oral health care.

How to reference

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Harini Priya Vishnu (2012). Probiotics and Oral Health, Oral Health Care - Pediatric, Research, Epidemiology and Clinical Practices, Prof. Mandeep Viridi (Ed.), ISBN: 978-953-51-0133-8, InTech, Available from: <http://www.intechopen.com/books/oral-health-care-pediatric-research-epidemiology-and-clinical-practices/probiotics-oral-health>

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