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REVIEW ARTICLE

Bacteriotherapy and probiotics' role on oral health

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Oral infections constitute some of the most common and costly forms of infections in humans. The concept of microbial ecological change as a mechanism for preventing dental disease is an important one while altered microbial ecology may lead to dental disease. New methods such as probiotic approaches (i.e. whole bacteria replacement therapy) to eliminate pathogenic members of the microbiota can be investigated. Bacteriotherapy is an alternative and promising way to combat infections by using harmless bacteria to displace pathogenic microorganisms. Probiotics are one of these new agents which are widely used for their therapeutic action. Limited research is available showing that some probiotic cultures may help dental improvement. Present paper focuses on possible oral benefits of probiotics.
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A new caries prevention method: Bacteriotherapy

Oral infections constitute some of the most common and costly forms of infections in humans. Dental caries and periodontal diseases occur in nearly 95% of the general public. Although fluoride and other preventive efforts have led to a dramatic decline in dental caries, the ability to control the actual infection has been limited (Rolla and Ogaard, 1991; Reich, 2001; Kargul *et al*, 2003).

The concept of microbial ecological change as a mechanism for preventing dental change is an important one. The oral cavity is a complex ecosystem in which a rich and diverse micro biota has evolved. 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, behavior, diet, or medications disturb the homeostasis and lead to endogenous infections or susceptibility to exogenous infections. The resident oral microflora is diverse, being comprised of species with differing nutritional (saccharolytic, proteolytic, secondary feeders), atmospheric (aerobic, anaerobic, facultative, micro-aerophilic, capnophilic) and physico-chemical (pH, co-factors) requirements (Cassell *et al*, 1997). Dental disease may be a consequence of changes in the ecology stated above. If the local environment is perturbed, then potential pathogens may gain a competitive advantage and, under appropriate conditions, reach numbers that predispose a site to disease. Regarding elimination of pathogenic members of the oral cavity a new method such as probiotic approach (i.e. whole bacteria replacement therapy) can be investigated.

Bacteriotherapy is an alternative and promising way to combat infections by using harmless bacteria to displace pathogenic micro organism. Saliva and gastrointestinal secretions, as well as flora (probiotics) and supplied fibers (prebiotics) are important for optimal function. Prebiotics and probiotics offer both protection against and cure of a variety of endemic and acute diseases (Bengmark, 2001). Actually, there is limited research available showing that some probiotic cultures may help dental improvement.

Probiotics

A 'probiotic', by the generally accepted definition, is a 'live microbial feed supplement which beneficially affects the host animal by improving its intestinal microbial balance' (Rasic, 1983). The belief that such bacteria can influence health dates back to the beginning of the 20th century, when the Russian Nobel Prize laureate Elie Metchnikoff reported that Bulgarians lived longer than other nations and supposed that this was because of their consumption of fermented milk products containing viable bacteria. The idea was that the bacteria in the

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fermented products competed with microorganisms that are injurious to health (Metchnikoff, 1907). The term *probiotic*, as an antonym to the term *antibiotic*, was originally proposed in 1965 by Lilley and Stillwell. 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 (Tanboga *et al*, 2003).

Probiotics and general health

The human body lives in a heavily contaminated bacterial environment, and symbiosis with these microorganisms seems to be a condition for survival. A human individual has more prokaryotic organisms associated with skin, lung, and gut surfaces than human eukaryotic cells. A logical management approach to situations that alter our microbial ecology (e.g. diet, environment, antibiotics) would be to deliberately increase our association with specific non-pathogenic organisms to counter that alteration. Probiotics exert a wide spectrum of different effects ranging from direct antagonism against pathogens to influence upon intestinal epithelium and immune system of the host's organism.

Thus conceptually, the use of probiotics constitutes a purposeful attempt to modify the relationship with our immediate microbial environment in ways that may benefit general health (Golledge and Riley, 1996). Probiotic bacteria have been shown to influence the immune system through several molecular mechanisms (Gibson, 1998). A number of potential benefits arising from the use of probiotics have been proposed, including

- increased resistance to infectious diseases (Perdigon *et al*, 1995; Arunachalam *et al*, 2000),
- alleviate lactose intolerance (McDonough *et al*, 1987),
- prevention from gut (Naidu *et al*, 1999), diarrhea (Vanderhoof *et al*, 1999), gastritis (Elmer *et al*, 1996), vaginal and urogenital infections (Hilton *et al*, 1992),
- reduction in blood pressure and regulation of hypertension (Fuller, 1997), serum cholesterol concentration (Fuller, 1997),
- reduction in allergy (Bengmark, 2000), respiratory infections (Hatakka *et al*, 2001) and
- resistance to cancer chemotherapy and decreasing risk of colon cancer (Von Bultzingslowen *et al*, 2003).

Prebiotic

The bacterial population of the human gastrointestinal tract constitutes an enormously complex ecosystem. Most of these organisms are beneficial (e.g. *bifidobacterium* and *lactobacillus*) but some are harmful (e.g. *Salmonella* species, *Helicobacter pylori*, *Clostridium perfringens*). Some dietary substances, the so-called 'prebiotics' can favor the growth of these beneficial bacteria over that of harmful ones. At this point, one should undermine the term concept 'prebiotics' for misunderstandings. Prebiotics are non-digestible food ingredients. Thus these include inulin, fructo-oligosaccharides (FOS), galactooligosaccharide and lactulose (Gibson *et al*, 1995; Guigoz *et al*, 2002). FOS are naturally occurring carbohydrates that cannot be digested or absorbed by humans. They support the growth of *bifidobacteria*. As a result of this effect, it was recommend that patients taking *bifidobacteria* also supplement with FOS (Williams *et al*, 1994).

Generally prebiotic ingestion is characterized by changes in microbial population density (Bertelsen, 2001). Main benefits of prebiotics can be stated as the reduction of harmful or potentially harmful bacteria in the intestine (Salvini *et al*, 2004). This reduces the risk of conditions such as infectious diarrhea and general intestinal malaise. A second one is the increase in large bowel motility and decrease in transit time improves stool quality and bowel regularity as well as increases stool mass. This improves or maintains healthy intestinal functions and reduces the likelihood of constipation.

Probiotic bacteria

Today, research regarding probiotics concentrates essentially on *L. acidophilus*, *L. casei*, *L. reuteri* and *Bifidobacterium bifidum* while practically ignoring the vast array of other species that inhabit the oral tract of humans. Some microorganisms are beneficial to the human body. In the gut microflora of newborn, breast fed children, *bifidobacteria* represents one of the predominant groups of intestinal bacteria. However the presence of *bifidobacteria* decreases after weaning, and potentially pathogenicbacteria begin to predominate. Some *bifidobacteria* are recognized today as probiotic, that is to say, bacteria, which improve the properties of the intestinal flora and contribute to better health (Haschke *et al*, 1998).

The growth in the production of probiotics by the dairy industry in some countries means that it is now increasingly difficult to purchase yogurts that do not contain 'probiotic' bacteria such as *L. acidophilus*. Culture manufacturers recommend formulation of these products at 10^6 probiotic bacteria per gram or milliliter of dairy products, but viable counts may fall below these levels, especially at the end of shelf life.

While defined in term as 'medical probiotics' (microbial preparation) and 'other probiotics '(functional food), probiotics are provided in products in one of four basic ways:

- as a culture concentrate added to a beverage or food (such as fruit juice),
- inoculated into prebiotic fibers,
- inoculated into a milk-based food (dairy products such as milk, milk drink, yoghurt, yoghurt drink, cheese, kefir, biodrink) and
- as concentrated and dried cells packaged as dietary supplements (non-dairy products such as powder, capsule, gelatin tablets).

Probiotics that are present in the world were evaluated in Table 1.

Table 1 Major probiotic products in the world

Strain	*Present in product*	*Country produced in*
Bifidobecterium bifidum	Infant formula	Turkey
B. breve	Drink	Japan
B. lactis	Infant formula	Israel
	Research	Switzerland
	Drink	South Africa, Chile
B. lactis HN019	Research	New Zealand
B. longum	Infant formula	Turkey
B. longum SBT-2928	Milk	Japan
B. longum BB536	Milk	Japan
B. sp	Drink	UK
L. acidophilus	Yogurt	Chile, USA
	Drink	UK
	Yogurt drink	Austria
Lactobacillus acidophilus 5	Yogurt	UK
L. acidophilus 7	Drink	Austria
L. acidophilus Lat 11/83	Research	Russia
L. acidophilus NCFB 1748	Yogurt	Denmark
L. acidophilus SBT-2062	Milk	Japan
L. bulgaricus	Drink	France, Austria
L. casei DN-114 001	Drink	France, Austria
L. casei Shirota	Drink	Argentina, Australia, Belgium, Brazil, Brunei, China, Germany, France, Hong Kong, Indonesia, Japan, Korea, Luxembourg, Mexico, Netherlands, Philippines, Singapore, Taiwan, Thailand, Uruguay, UK, NewYork/USA
L. casei	Drink	USA
	Yogurt	France, Colorado-Arizona/USA
	Kefir	Illinois/USA, Austria
L. helveticus	Milk drink	Finland
	Drink	Iceland
L. johnsonii La1	Yogurt	Switzerland, Germany, Japan, Austria
L. lactis L1A	Yogurt	Sweden
L. plantarum	Kefir	Illinois/USA
L. plantarum 299v	Fruit drink	Sweden
	Ice cream	Sweden
	Recovery drink	Sweden
	Oat mixture	Sweden
L. plantarum JI:1	Research	Sweden
L. reuteri	Infant formula	Israel
	Cheese	Spain, Portugal, Finland
	Milk	Japan, Finland
	Yogurt	USA, Finland
	Yogurt drink	UK
	Ice cream	Finland
	Fruit drink	Finland
L. rhamnosus ATCC53103 (*L. bacillus GG*)	Yogurt	Australia, Papua New Guinea, Indonesia, Finland, Latvia, Estonia, Croatia, Bosnia-Herzegovina, Slovenia, Ecuador, Israel, Italy, Netherlands, South Korea, Japan, Norway, Switzerland
	Yogurt drink	Australia, Finland, Sweden, Croatia, Bosnia-Herzegovina, Slovenia, Ecuador, Uruguay, Netherlands, Taiwan, Norway
	Fruit yogurt	Finland, Sweden
	Milk	UAE, Israel, Italy
	Milk drink	Germany, Portugal, Japan, Iceland, Greenland, Spain, Estonia, Ireland, Israel, South Korea
	Fruit drink	Finland
	Cheese	Finland
	Kefir	Latvia
	Drink	Finland, Estonia, Sweden, Switzerland
	Buttermilk	Finland
	Whey-based drink	Finland
	Quark	Switzerland
L. rhamnosus	Drink	Finland, Sweden, Chile, South Africa
L. rhamnosus LB21	Yogurt	Sweden
L. rhamnosus 271	Drink	Sweden

Table 1 (continued)

Strain	*Present in product*	*Country produced in*
L. salivarius U CC 118	Research	Ireland
L. rhamnosus VTTE-97800	Research	Finland
S. salivarius K12	Lozenge	New Zealand
S. thermophilus	Drink	France, Austria
	Yogurt drink	Austria
	Infant formula	Turkey
Enterococcus faecium	Yogurt	Denmark
Enterococcus faecium Fargo 688	Research	USA

Please note that market and producer names are not demonstrated while non-dairy products are not evaluated.

The question today is what can currently be said about the impact of probiotic bacteria on oral microbial balance? Research about probiotics' effect on oral tissues and microorganisms is still neglected.

Possible effects of probiotics on oral health

As a result of their cariogenic properties, lactobacilli have been of great interest to dental researchers for several decades. They are associated more with carious dentine and the advancing front of caries lesions rather than with the initiation of the dental caries process. However little information has been reported on the beneficial effect of lactobacilli on oral health. Lactobacilli are the most common probiotic bacteria associated with the human gastrointestinal tract, therefore it may also play an important role in the eco physiology of oral micro biota. Various lactobacilli species (*L. paracasei*, *L. gasseri* and *L. fermentum* widely found, *L. salivarius*, *L. plantarum*, *L. crispatus*, and *L. rhamnosus* isolated) were shown to inhabit healthy mouths, although no species was specific to the mouths of healthy subjects (Hojo *et al*, in press).

Development of new ways to block the pathogenesis of oral infections can reduce tissue destruction associated with oral infection and chronic inflammation. Effect of probiotics on the induction and maintenance of oral tolerance has been recently studied through *Lactobacillus paracasei* (NCC 2461), *Lactobacillus johnsonii* (NCC 533) and *Bifidobacterium lactis* Bb12 (NCC 362) on to bovine beta-lactoglobulin (BLG) that was investigated in mice. This study had provided evidence that probiotics modulate the oral tolerance to BLG in gnotobiotic mice (Prioult *et al*, 2003).

From a view, probiotics with lactobacilli that hydrolyse proteins to amino acids and dipeptides, stimulate growth of streptococci: the streptococci produce low pH conditions in the oral environment (Robinson and Tamine, 1981). Also untreated caries cavities should also be questioned at this point. Conversely, in recent studies, it was stated that probiotic might reduce the risk of the highest level of *Streptococcus mutans* (Kashket *et al*, 1991; Ahola *et al*, 2002). Recently, it was evaluated whether the oral administration of lactobacilli could change the salivary counts of these bacteria compared with placebo. Lactobacilli were administered in liquid and in capsule form to volunteer subjects to determine the role of direct contact with the oral cavity. It was found that the oral administration of probiotics, both in capsules and in liquid form, significantly increases salivary counts of lactobacilli while *S. mutans* levels were not modified (Montalto *et al*, 2004).

It should be noted that as most probiotics are in dairy-form containing high Ca, possible demineralization of teeth would be reduced.

There is a concept where these 'beneficial' microorganisms can inhabit a bio-film and actually protect oral tissue from disease. It is possible that one of these biofilm's mechanisms to keep pathogens out is to occupy a space that might otherwise be occupied by a pathogen. An *in vitro* study suggests that *L. rhamnosus GG* (LGG) can inhibit the colonization of streptococci caries pathogens, thus reducing the incidence of caries in children (Meurman *et al*, 1995).

In a Swiss study, bacterial strains with potential properties as oral probiotics, were searched namely for the prevention of dental caries. From 23 dairy microorganisms studied, two were identified; which were able to adhere to saliva-coated hydroxyapatite beads to the same extent as *Streptococcus sobrinus* OMZ176. *Streptococcus thermophilus* NCC1561 and *Lactococcus lactis* NCC2211, were successfully incorporated into a bio-film mimicking the dental plaque. Furthermore, they could grow in such a biofilm together with five strains of oral bacterial species, representative of supragingival plaque. In this system, *Lactococcus lactis* NCC2211 was able to modulate the growth of the oral bacteria, and in particular to diminish the colonization of *Streptococcus oralis* OMZ607, *Veillonella dispar* OMZ493, *Actinomyces naeslundii* OMZ745 and of the cariogenic *Streptococcus sobrinus* OMZ176. These findings encourage further research with selected non-pathogenic dairy bacterial strains with the aim to decrease the cariogenic potential of dental plaque (Comelli *et al*, 2002).

From a periodontal view, a Russian study examined probiotic tablets in complex treatment of gingivitis and different degrees of periodontitis. The treatment of the patients of control group was provided by drug 'Tantum Verde'. The effect of probiotics to the normalization of microflora was found to be higher in comparison with Tantum Verde, particularly in the cases of gingivitis and periodontitis (Grudianov *et al*, 2002).

It should be noted that there is no research regarding relationship between dental restorative materials and probiotics. However in larynx, the second barrier after oropharynx, probiotics strongly reduce the occurrence

of pathogenic bacteria in voice prosthetic bio-films (Free *et al*, 2001).

Installation of probiotics in the oral cavity

Probiotics should adhere to dental tissue for them to establish a cariostatic effect and thus should be a part of the bio-film to fight with cariogenic bacteria (Grudianov *et al*, 2002). For this action, installation of probiotics in oral environment seems important. However the contact time between probiotics and plaque would be short, that the activity will be weak. This activity increases if probiotics could be installed in the oral environment for longer duration. At this point, ideal vehicles of probiotic installation should be determined.

Yoghurt

Dental research revealed results for the oral installation that lactobacilli cannot be installed by the consumption of a probiotic yoghurt. Studies concluded that yoghurt microorganisms did not have some activity against salivary microorganisms, with no relation thought to be found with the installation mechanism (Busscher *et al*, 1999; Petti *et al*, 2001). Conversely, in a research paper, it was concluded that subjects consuming daily bio-yoghurt with *L rhamnosus GG*, harbored this microorganism in their saliva up to 2 weeks after discontinuing consumption of probiotics (Meurman *et al*, 1994). Up to date, it could be assumed that it is questionable if probiotics can colonize in the mouth. Regular consumption of probiotics (dairy products) can decrease the numbers of salivary *Streptococcus mutans* and lactobacilli, however do not have any residual antibacterial activity after discontinuation. However it must be recognised that there may be different activities in other forms of probiotics such as milk, juice or cheese.

Milk and cheese

Milk and cheese are known to contain compounds that reduce the risk of dental caries (Jenkins and Hargreaves, 1989; Bowen and Pearson, 1993; Nase *et al*, 2001). Regarding milk and cheese, one should also recognize the large body of evidence relating to casein phosphopeptides and other milk-derived materials and their role in bio-mineralization and other processes. At this point, research focusing beneficial effects of probiotic milk and cheese seems to be further investigated.

In a recent study, it was examined whether milk containing LGG has an effect on caries and the risk of caries in children when compared with normal milk. LGG was found to reduce the risk of caries significantly Thus, milk containing the probiotic LGG bacteria may have beneficial effects on children's dental health (Nase *et al*, 2001).

It was also examined whether short-term consumption of cheese containing LGG and *Lactobacillus rhamnosus* LC 705 would diminish caries-associated salivary microbial counts in young adults. In this double-blinded, randomized, placebo-controlled study, during the 3-week intervention, the subjects ate 5×15 g cheese per day. The results showed no statistically significant difference between the groups in *Streptococcus mutans* counts after the intervention, but during the post-treatment period there was a significantly greater reduction in these counts in the intervention group compared to the control group. However, *Streptococcus mutans* counts decreased in 20% of all the subjects, regardless of the intervention group. Authors stated that probiotic intervention might reduce the risk of the highest level of *Streptococcus mutans* (Ahola *et al*, 2002). However there is no evidence of a longer term effect of selected strain on oral tissue.

Future

Probiotic consumption has become a life long tradition in Scandinavia and seems to be improving slowly in Turkey.

In field of oral immunology, probiotics are being used as passive local immunization vehicles against dental caries. Recently, by means of systemic immunization with a multivalent vaccine, *L. rhamnosus GG* was chosen as the vehicle to harbor IgG because of its widely known health benefits in humans and animals. High titers of antibodies against human cariogenic bacteria, *S. mutans* and *S. sobrinus*, were produced in bovine colostrum by a vehicle of fermented milk (Wei *et al*, 2002). In a previous study, the development of levels of secretory immunoglobulins in newborns' saliva was examined under physiological conditions and after artificial colonization with non-pathogenic, probiotic bacterial strain *Escherichia coli* O83. It was found that early mucosal colonization with *E. coli* bacteria stimulates the mucosal immune system to produce specific antibodies as well as non-specific secretory immunoglobulins. Regarding both studies, probiotics seems to improve of oral immune response (Vancikova *et al*, 2003).

In food technology, dairy products containing probiotic lactobacilli in combination with prebiotics are currently developed, which may be useful as symbiotic functional food (Corcoran *et al*, 2004).

In oncology field, serious systemic infections may occur during cancer chemotherapy because of disturbances in the oropharyngeal and gastrointestinal microflora, impaired mucosal barrier functions and immunosuppression. Regarding the present condition, treatment with probiotics (*L. plantarum* 299v) improves food intake and body weight in chemotherapized animals. Selected probiotic strain reinforces the oral cavity, along with the gastrointestinal tract, as a source for bacterial dissemination (Von Bultzingslowen *et al*, 2003). The potential benefit may nourish other medical fields.

In Aeronautics and Space technology, one of the most important health problems during space travel is that astronauts' intestinal problems during space travel. Today NASA, USA carries out research into probiotic food products aimed at enabling humans to live in space. The project is known under the name of 'Lacmos.' 'Lac' is Latin for milk and 'Mos' for 'Cosmos.'

Bacteriotherapy in the form of probiotics seems to be a new alternative for oral health giving a new research field for dental science to proceed.

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