

Probiotics and its Implication in Oral Health

Apexa B Patel¹, Patel Advaita B.², Baldev V. Patel³

1- BDS, College of dental sciences and research centre, Ahmedabad, India. 2- Assistanat Professor Kalol Institute of pharmacy, Kalol, India. 3- Professor Department of Microbiology, Gujarat University, India.

Correspondence to:
Dr. Apexa B Patel BDS, College of Dental Sciences
And Research Centre, Ahmedabad, India.
Contact Us: www.ijohmr.com

ABSTRACT

For some years now, bacteria known as probiotics have been added to various food items because they have shown beneficial effects for human health. Probiotics are micro-organisms, principally bacteria, which provide health benefits beyond basic nutrition when ingested. The mechanism of action of probiotics is in their ability to compete with pathogenic microorganisms for adhesion sites, to antagonize the pathogens or to modulate the host's immune response. The main field of research has been focused on the gastro-intestinal tract. However, recently potential application of probiotics for oral health has attracted the attention of researchers. Although only a few clinical studies have been conducted so far. This review article summarizes their composition, characteristics, mechanism of action and their potential implication in oral health.

KEYWORDS: Probiotics, Oral health, Streptococcus mutans

INTRODUCTION

Universally the role of diet in health and well-being is acknowledged. With the evolution of the science of nutrition, research is recently being carried towards improvement of the understanding of physiologic effects of the diet beyond its nutritional effect. In this aspect, probiotics are the subject of intense and widespread research in food and nutritional science and in oral health.¹

According to FAO/WHO, Probiotics are defined as: "living micro-organisms, principally bacteria, safe for human consumption and when ingested in sufficient quantities, have beneficial effects on human health, beyond basic nutrition".² The term prebiotic was given by Gibson and Roberfroid.³ A Prebiotic is a non-digestible food ingredient conferring benefits on the host by selectively stimulating the growth and/or activity of one species of bacteria or group of bacteria in the colon, thus improving the host's health. In the oral cavity probiotics can create a biofilm which act as a protective lining for oral tissues against oral diseases. Such a biofilm keeps bacterial pathogens away from oral tissues, by filling a space which pathogens would otherwise invade, and by competing with cariogenic bacteria and growth of periodontal pathogens. The term synbiotic is used when a product contains both probiotics and prebiotics.⁴ Probiotics are generally used as dietary supplements and act indirectly in preventing colonisation by pathogens.⁵

PROBIOTICS DERIVATIVES

Probiotics are primarily derived from:

- A culture concentrate added to a beverage such as fruit juice.
- Inoculated into prebiotic fibres.
- Inoculated into a milk-based food e.g. dairy products such as milk, milk drink, yogurt,

- cheese, kefir, biodrink
- As concentrated and dried cells packaged as dietary supplements e.g. powder, capsule, gelatin tablets^{6,7}

COMPOSITION OF PROBIOTICS

Probiotics can be yeast, bacteria or moulds. Most commonly they are bacteria.

Microorganisms considered to be probiotics are shown in Table no 1.

Lactobacillus spp.	Bifidobacterium pp. Others	Streptomyces species	Yeasts and Molds	Others
L. acidophilus L. casei L. crispatus L. delbrueckii subsp. bulgaricus L. fermentum L. gasseri L. johnsonii L. paracasei L. plantarum L. reuteri L. rhamnosus	B. bifidum B. breve B. infantis B. longum B. lactis B. adolescentis, Bifidobacterium DN-173 010 B. animalis, B. thermophilum.	Streptococcus faecium, Streptococcus Thermophilus	C. albicans, Saccharomyces boulardii, A. niger, A. oryzae, c. pintolopesii,	Saccharomyces boulardii Lactococcus lactis subsp. cremoris Enterococcus faecium S. diaacetilactis S. intermedius S. salivarius, W. sibiria, Leuconostoc, Pediococcus, Propionibacterium

Table 1: Examples of microorganisms considered to be probiotics.^{5,8,9}

CHARACTERISTICS OF IDEAL PROBIOTIC MICRO-ORGANISM

Characteristics of ideal probiotic micro-organism are as follows:^{5,9,10}

- Should have beneficial effect on the host animal.
- Should be non-pathogenic, nontoxic.
- Should replace and resist the intestinal micro-flora.
- Should be capable of surviving and metabolizing in the gut environment e.g. resistant to low pH.

How to cite this article:

Patel AB, Patel AB, Patel BV. Probiotics and its Implication in Oral Health. Int J Oral Health Med Res 2015;2(3):100-104.

- Should be safe for human consumption and beneficial physiological effects should be scientifically demonstratable.
- Should be stable in acidic and alkaline environments.
- Should be microbiologically characterized
- Should have been subjected to randomised clinical trials;
- Should be able to adhere to the intestinal mucosa or the target tissue.
- Should demonstrate high stability at room temperature, either separately or when mixed with other ingredients.
- Should have no potential to develop diseases.

MECHANISM OF ACTION

In oral health probiotics act by two mechanisms: direct and indirect.⁵⁻⁹ shown in table 2.

Direct	Indirect
<p>Direct interactions in dental plaque:</p> <ul style="list-style-type: none"> • Involvement in binding of oral micro-organisms to proteins (biofilm formation). • Action on plaque formation and on its complex ecosystem by competing and intervening with bacteria-to-bacteria attachments. • Involvement in metabolism of substrates (competing with oral micro-organisms of substrates available). • Production of chemicals that inhibit oral bacteria (antimicrobial substances). 	<p>Indirect probiotic actions in the oral cavity:</p> <ul style="list-style-type: none"> • Prevent plaque formation by neutralizing free electrons. • Modulating the mucosal immune system by reducing pathogen induced production of proinflammatory cytokines. • Affects nonimmunological defence mechanism. • Affecting local immunity. • Regulation of mucosal permeability. • Produces antioxidants or act as antioxidants • Upregulation of intestinal barrier integrity of mucin production • Selection pressure on developing oral microflora towards colonization by less pathogenic species.

Table 2 : Mechanism of action of probiotics in oral health.⁵⁻⁹

PROBIOTICS AND DENTAL CARIES

- Dental caries is a multifactorial disease of bacterial origin which is characterized by acid demineralization of the tooth enamel. *Streptococcus mutans* is among the most common causative organism for dental caries. Elevated levels of streptococcus are strong indicator of increased risk of dental caries.^{9,11}
- To remove cariogenic bacteria from the teeth surface to prevent dental caries:
 - probiotic must be able to adhere to dental surfaces and integrate into the bacterial communities making up the dental biofilm.

- they must become a part of the biofilm that develops on teeth.
- they must compete with cariogenic bacteria.

All these effects of probiotics help in the reduction of the levels of cariogenic bacterial growth.^{9,12}

- Probiotics incorporated into dairy products neutralize acidic conditions. For example, it has been reported that cheese prevents demineralization of the enamel and promotes its remineralization.^{13,14}
- In other reports, one strain of *L. rhamnosus* and the species *L. casei* inhibited in vitro growth of two important cariogenic streptococci, *S. mutans* and *S. sobrinus*.^{15,16}
- More recently, Petti and colleagues reported that yogurt containing *S. thermophilus* and *L. bulgaricus* had selective bactericidal effects on streptococci of the mutans group. Recent clinical studies have shown that regular consumption of yogurt, milk or cheese containing probiotics led to a decrease in the number of cariogenic streptococci in the saliva and a reduction in dental plaque.^{15,17-20}
- More specifically, Nikawa and colleagues reported that consumption of yogurt containing *Lactobacillus reuteri* over a period of 2 weeks have shown reduction in the concentration of *S. mutans* in the saliva by up to 80%. Comparable results were also obtained by incorporating probiotics into chewing gum or lozenges.^{19,21}
- In 2001, Nase and colleagues¹² published the results of a 17-month study on 594 children of 1 to 6 years of age that evaluated the effects on dental caries of consuming milk supplemented with a strain of *L. rhamnosus*. They concluded that children consuming milk containing this probiotic, particularly those 3-4 years of age, had shown significantly lower incidence of dental caries and lower salivary counts of *S. mutans* than controls. With the heterogeneousness of the oral microflora and the mechanisms of action of beneficial bacteria, it seems believable that probiotics would have a favourable effect on the reduction of dental caries.¹⁵

PROBIOTICS AND PERIODONTAL DISEASE

- Periodontal disease is classified into two types: gingivitis and periodontitis. Gingivitis is characterized by inflammation confined to the unattached gingiva and periodontitis is a progressive, destructive disease involving all the supporting tissues of the teeth, including the alveolar bone. The main pathogenic organism associated with periodontitis include *P. gingivalis*, *Treponema denticola*, *Tannerella forsythia* and *Aggregatibacter actinomycetemcomitans*.²²
- The primary etiological factors for the development of periodontal diseases are bacteria in supragingival and subgingival biofilms. Mucosal immune

responses may be induced by probiotic immunisation. The possible mechanism of action of probiotics is the strengthening of the mucosal barrier via topical effects on the epithelium, and the stimulation of both the innate and adaptive immune systems. Reduction in gingival bleeding and reduced gingivitis has been observed by Krasse *et al.* with the ingestion of *L. reuteri*.²³

- According to Koll – Klais *et al.* probiotics containing *Lactobacillus* effected an 82% and 65% inhibition in growth in, respectively, *Porphyromonas gingivalis* and *Prevotella intermedia*.²⁴
- Twetman *et al.* used *L. reuteri*-containing chewing gum in 42 healthy patients and assessed the effects on crevicular fluid volume, cytokine e.g. interleukin-1 β , interleukin-6, interleukin-10, and TNF- α levels and bleeding on probing. The study showed reduction in crevicular fluid volume, the levels of TNF- α and interleukin-8 and bleeding.²⁵
- Riccia *et al.* used lozenges into which *L. brevis* was incorporated to study its anti-inflammatory effects in a group of patients with chronic periodontitis. The study showed significant improvement in the plaque index, gingival index and bleeding on probing for all patients and also a significant reduction in gingival inflammation.²⁴
- Probiotic strains included in periodontal dressings at optimal concentrations of 10⁸ CFU mL⁻¹ were shown to diminish the number of the most frequently isolated periodontal pathogens: *Bacteroides spp.*, *Actinomyces spp.* and *S. intermedius*, and also *C. Albicans*.²⁶
- Probiotic bacteria may favour periodontal health and may even recolonise a gingival pocket after scaling and root planing if they are able to establish themselves in the oral biofilm. However, further longitudinal studies are required to confirm these findings.^{5,22-26}

PROBIOTICS AND HALITOSIS

- Halitosis is a common problem with multiple local and systemic etiological factors. The main oral causes include periodontitis, poor plaque control, deep dental caries, tongue coating and faulty restorations, along with gastrointestinal and lung infections.
- Etiological factors for Halitosis include sulphur containing gases such as hydrogen sulfide, methyl mercaptan and dimethyl sulfide, which are derived from the bacterial degradation of sulfur containing amino acids in the oropharynx predominantly from gram negative anaerobes.^{5,9}
- *L. salivarius TI2711* bacteria have been shown to reduce the count of the oral black pigmented bacteroides, the bacteria strongly associated with production of the VSC's responsible for halitosis.²³
- Halitosis is a condition normally attributed to disturbed commensal microflora equilibrium. Recently it has been positively affected by regular administration of probiotics. Kang *et al.* have shown

a definite inhibitory effect on the production of volatile sulphur compounds (VSC's) by *Fusobacterium nucleatum* after ingestion of *W. cibaria* both *in vitro* and *in vivo*.²⁷

- However, the few studies published do not confirm any evidence based conclusions on the role of probiotics in the treatment of halitosis. It may be that this is where probiotic therapy could indeed bring something new, if there is confirmation of preliminary observations on the "balancing" effect of probiotics on the oral microflora which generate volatile sulphur compounds. Randomised, blinded, and placebocontrolled studies with large enough sample sizes are also needed in this endeavour.^{5,27}

PROBIOTICS AND ORAL CANDIDIASIS

- *Candida albicans* is one of the the most common infectious agents present in the oral cavity. Consumption of probiotic cheese containing *L. rhamnosus* GG and *Propionibacterium freudenreichii ssp. Shermanii* JS shown reduction in *C albicans* count.^{5,9}
- It is important to carry out further research on yeast infections with respect to probiotics. Analysing the molecular mechanisms of probiotic activity might further widen the field of their potential applications.⁵

PROBIOTICS AND HIV

- The role of probiotics to slow down the progression of AIDS (Acquired immunodeficiency syndrome) has been researched by Lin Tao and colleagues (2008). A screening of saliva taken from hundreds of volunteers showed that some *Lactobacillus* strains produced proteins which are capable of binding to a particular type of sugar, called mannose, found on HIV envelope.⁸⁻¹¹
- The binding of the sugar enables the bacteria to stick to the mucosal lining of the mouth and digestive tract and colonize them. One of the strain showed abundant mannose-binding protein particles into its surroundings which binded to the sugar coating and hence neutralized HIV.
- They also observed that immune cells trapped by *lactobacilli* would lead to formation of a clump. This configuration would prevent any immune cells harboring HIV from infecting other cells.⁸

PROBIOTICS AND VOICE PROSTHESIS

- There is no research regarding the relationship between dental restorative materials and probiotics. However in the larynx, the second barrier after oropharynx, probiotics strongly reduce the occurrence of pathogenic bacteria in voice prosthetic biofilms.^{1,7}

- Research studies among patients in the Netherlands have shown that the consumption of buttermilk, which contains *Lactococcus cremoris*, *Lactococcus lactis spp.* can produce antimycotics and other substances, prolongs the lifetime of indwelling voice prostheses.
- Recent research has suggested that consumption of 2 kg/day of Turkish yogurt effectively eliminates biofilm formation on indwelling voice prostheses. It might be possibly related to the presence of *Streptococcus thermophilus* and *Lactobacillus bulgaricus* in Turkish yogurt. *Lactobacilli* have been known for their capacity to interfere with the adhesion of uropathogens to epithelial cells and catheter materials, while *S. thermophilus* can effectively compete with yeasts in their adhesion to substratum surfaces, like silicone rubber. Further research needs to be carried out to determine if it will be possible to treat other infections of the upper digestive tract, like esophagitis, with probiotic containing dairy products rather than with antibiotics.^{1,28}

ROLE OF PROBIOTICS IN GENERAL HEALTH

Research studies have shown that probiotics are used to treat various health problems such as inflammatory bowel disease, gastrointestinal disorders, in treatment of antibiotic associated and traveller's diarrhea, in delaying the onset of cancer, for treatment of lactose intolerance and elevated cholesterol. Furthermore, probiotics are used to treat alcoholic liver diseases, ulcerative colitis, asthma, hepatic encephalopathy, juvenile chronic arthritis, hypertension, in individuals with an allergy to milk protein, to treat urogenital infections and to aid in calcium absorption.^{9,29}

ADMINISTRATION OF PROBIOTICS

Milk products, supplemented with probiotics, are a natural means of oral administration and can be easily adopted in most dietary regimens. However, for the purposes of prevention or treatment of oral diseases, it is specifically targeted applications, formulas, devices, or carriers with slow release of probiotics, which will be needed. Montalto *et al.* administered probiotic mixtures, both in capsules and in liquid form, without observing statistically significant differences in the *S. mutans* counts between the two test groups.^{22,30-31}

The different vehicles used to administer probiotics are as Shown in Fig 1.⁵

SAFETY CONCERNS REGARDING PROBIOTICS

Safety measures are of a major concern due to increased probiotics supplementation of different food products

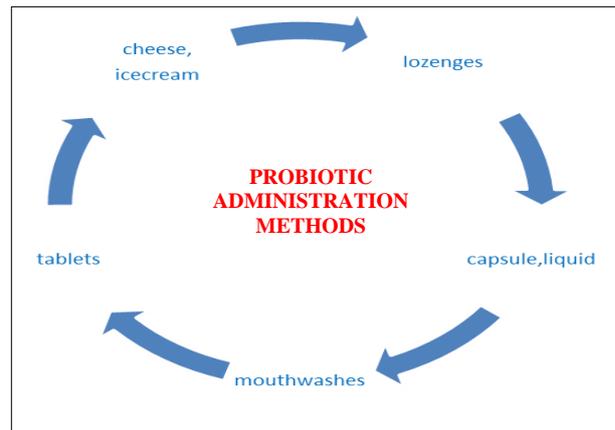


Figure 1: .Probiotic administration methods.

products. Probiotics are often regulated as dietary supplements rather than as pharmaceutical or biological products. Probiotic microorganisms should not be pathogenic, should not have any growth stimulating effects on bacteria causing diarrhoea, and should not have an ability to transfer antibiotic resistance genes, and should not cause sepsis or bacteremia, should maintain genetic stability in oral micro-flora.^{9,29,32}

Lactobacillus induced bacteraemia is a relatively rare condition, with approximately 180 cases reported over the last 30 years. Clinical characteristics of Lactobacillus-induced bacteraemia are highly variable, ranging from asymptomatic to serious septic conditions. However, these symptoms are particularly seen in individuals who have severe underlying diseases, or who are immunocompromised. Careful monitoring of patients is mandatory for this potentially serious condition.^{5,29-32}

FUTURE PROSPECTIVES

Many researchers have reported significant benefits in oral health on the administration of Probiotics. Genetic engineering and the recombinant DNA technology can further improve the probiotic characteristics. Lactic acid production by acidogenic bacteria has been considered to be the major cause for the production of caries lesion. The probiotic acidogenic bacteria can be engineered genetically to prevent dental caries.^{8,9} Mutations can be induced to create the mutants with increased bacteriocin production. Such mutant strains displace the indigenous strains and colonize the oral cavity. Still many *in vitro* and *in vivo* tests for the presence of the desirable characteristics must be carried out and various random trials need to be performed to find out the most potent probiotics organisms for oral health and the most effective ways of their administration. Probiotics application can be extended to treat many health related problems in future. The critical steps in the wider application will be to make products available that are safer and clinically proven in a specific formulation, which should be easily accessible to health care professionals and consumers. In India, sporolac, i.e., *Sporolactobacilli* is commonly used probiotic. Recently *Bacillus mesentericus* is used as an alternate to B-complex

and genetically modified lactic acid bacteria have been used as a vehicle to deliver vaccines in the gastrointestinal tract.^{8,9}

CONCLUSION

Probiotics represent a new area of research in oral health. Preliminary data obtained by various research have been encouraging, but still numerous randomized clinical studies will be required to clearly establish the potential of probiotics in preventing and treating oral diseases. Such clinical studies will allow identification of the probiotics that are best suited to for oral health as well as the most appropriate administration methods such as food products (cheese, milk, yogurt) or supplements (chewing gum, lozenges).¹³⁻³²

REFERENCES

- Reddy JJ, Sampathkumar N, Aradhya S. Probiotics in dentistry: review of the current status. *Rev. Clín. Pesq. Odontol* 2010;6(3):261-67.
- Ross RP, Desmond C, Fitzgerald GF, Stanton C. Overcoming the technological hurdles in the development of probiotic foods. *J. Appl. Microbiol.* 2005; 98: 1410-17.
- Gibson GR, Roberfroid MB. Dietary modulation of the human colonic microbiota: introducing the concept of prebiotics. *Jnl. Nutr.* 1995; 125:1401-12.
- Schrezenmeir J, de Vresne M. Probiotics, prebiotics, and synbiotics - approaching a definition. *Am. J. Clin. Nutr.* 2001; 73:361-64.
- Pradeep K, Kuttappa MA, Prasana KR. Probiotics and oral health: an update. *SADJ: journal of the South African Dental Association.* 2014; 69 (1):20-4.
- Singh T, Majumdar S, Ghosh AK, Pal SP, Waghle SR, Dakchiyani MB. Probiotics in Oral Health- A Review. *J. Adv. Med Dent. Sci. Res.* 2014;2(3):62-5.
- Caglar E, Kargul B, Tanboga I. Bacteriotherapy and probiotics role on oral health. *Oral Dis.* 2005;11(3):131-7
- Jain P, Sharma P. Probiotics and Their Efficacy in Improving Oral Health: A Review. *J. of Appl. Pharma. Sci.* 2012;2(11):151-63.
- Babaji P, Keswani K, Lau H, Lau M, Sharma N, Punga R. Role of probiotics in oral health: A review of the literature. *J. Educ. Ethics. Dent.* 2012;2:52-5.
- Parvez S, Malik K.A, Kang Ah, Kim H.Y. Probiotics and their fermented food products are beneficial for health. *J. of App. Micro.* 2006;100: 1171-85.
- Stamatova I, Meurmann JH. Probiotics: Health benefits in the mouth. *Am. J. Dent.* 2009;22: 329-38.
- Reddy RS, Swapna LA, Ramesh T, Singh TR, Vijayalaxmi N, Lavanya R. Bacteria in Oral Health – Probiotics and Prebiotics A Review. *Int. J. Biol. Med. Res.* 2011;2: 1226-33.
- Gedalia I, Ionat-Bendat D, Ben-Mosheh S, Shapira L. Tooth enamel softening with a cola type drink and rehardening with hard cheese or stimulated saliva in situ. *J Oral Rehabil.* 1991;18(6):501-6.
- Jensen ME, Wefel JS. Effects of processed cheese on human plaque pH and demineralization and remineralization. *Am J Dent.* 1990;3(5):217-23.
- Näse L, Hatakka K, Savilahti E, Saxelin M, Pönkä A, Poussa T, et al. Effect of long-term consumption of a probiotic bacterium, *Lactobacillus rhamnosus* GG, in milk on dental caries and caries risk in children. *Caries Res.* 2001;35(6):412-20.
- Meurman JH, Antila H, Korhonen A, Salminen S. Effect of *Lactobacillus rhamnosus* strain GG (ATCC 53103) on the growth of *Streptococcus sobrinus* in vitro. *Eur J Oral Sci.* 1995;103(4):253-8.
- Petti S, Tarsitani G, Simonetti D'Arca A. Antibacterial activity of yoghurt against viridans streptococci in vitro. *Arch Oral Biol.* 2008;53(10):985-90.
- Ahola AJ, Yli-Knuutila H, Suomalainen T, Poussa T, Ahlström A, Meurman JH, et al. Short-term consumption of probiotic-containing cheese and its effect on dental caries risk factors. *Arch Oral Biol.* 2002;47(11):799-804.
- Caglar E, Kavaloglu SC, Kuscü OO, Sandalli N, Holgerson PL, Twetman S. Effect of chewing gums containing xylitol or probiotic bacteria on salivary mutans streptococci and lactobacilli. *Clin Oral Investig.* 2007;11(4):425-9.
- Nikawa H, Makihira S, Fukushima H, Nishimura H, Ozaki K, Darmawan S, et al. *Lactobacillus reuteri* in bovine milk fermented decreases the oral carriage of mutans streptococci. *Int J Food Microbiol.* 2004;95(2):219-23.
- Caglar E, Cildir SK, Ergeneli S, Sandalli N, Twetman S. Salivary mutans streptococci and lactobacilli levels after ingestion of the probiotic bacterium *Lactobacillus reuteri* ATCC 55730 by straws or tablets. *Acta Odontol Scand.* 2006;64(5):314-8.
- Montalto M, Vastola M, Marigo L et al. Probiotics treatment increases salivary counts of lactobacilli: a double-blind, randomized, controlled study. *Digestion* 2004; 69:53-6.
- Flichy-Fernández AJ, Alegre-Domingo T, Peñarrocha-Oltra D, Peñarrocha-Diago M. Probiotic treatment in the oral cavity: an update. *Medicina Oral Patologia Oral Cirugia Bucal.* 2010 ;15 (5):677-680.
- Riccia DN, Bizzini F, Perilli MG, Polimeni A, Trinchieri V, Amicosante G et al. Anti-inflammatory effects of *Lactobacillus brevis* (CD2) on periodontal disease. *Oral Dis.* 2007; 13(4):376-85.
- Persson RG. Immune responses and vaccination against periodontal infections. *J Clin Periodontol.* 2005; 32:39-53.
- Volozhin AI, Il'in VK, Maksimovskii IM et al. Development and use of periodontal dressing of collagen and *Lactobacillus casei* 37 cell suspension in combined treatment of periodontal disease of inflammatory origin (a microbiological study). *Stomatologiia* 2004; 83:6.
- Kang MS, Na HS, Oh LS. Co-aggregation ability of *Weissella cibaria* isolates with *Fusobacterium nucleatum* and their adhesiveness to epithelial cells. *Federation of European Microbiological Societies Microbiol Lett.* 2005; 253:323-9.
- Busscher HJ, Free RH, Weissenbruch RV, Albers FWJ, Van Der Mei HC. Preliminary observations on influence of dairy products on biofilm removal from silicone rubber voice prostheses in vitro. *J Dairy Sci.* 2000;83(4):641-7.
- Narang S, Gupta R, Narang A. Probiotics in oral health care- A review. *Int J Sci Eng Res* 2011;2:1-5.
- Vanderhoof JA. Probiotics: future directions. *Am J Clin Nutr.* 2001;73(6): 1152S-55S
- Hatakka K, Ahola AJ, Yli-Knuutila H, Richardson M, Poussa T, Meurman JK, et al. Probiotics reduce the prevalence of oral *Candida* in the elderly – a randomized controlled trial. *J Dent Res.* 2007; 86:125-30.
- Grajek W, Olejnik A, Sip A. Probiotics, 'Prebiotics and antioxidants as functional foods. *Acta Biochim Pol* 2005;52:665-71.

Source of Support: Nil
Conflict of Interest: Nil