American Journal of

Food Technology

ISSN 1557-4571

Academic Journals Inc.

www.academicjournals.com

American Journal of Food Technology 7 (5): 251-265, 2012
ISSN 1557-4571 / DOI: 10.3923/ajft.2012.251.265

Effects of Probiotics on Lipid Profile: A Review

[1]Aziz Homayouni, [2]Laleh Payahoo and [3]Aslan Azizi
[1]Department of Food Science and Technology, Faculty of Health and Nutrition, Tabriz University of Medical Sciences, Tabriz, Islamic Republic of Iran
[2]Department of Nutrition, Faculty of Health and Nutrition, Tabriz University of Medical Science, Islamic Republic Iran
[3]Department of Food Engineering, Iranian Agricultural Engineering Research Institute, Ministry of Jihad Agriculture, Karaj, Islamic Republic of Iran

Corresponding Author: Aslan Azizi, Department of Food Engineering, Iranian Agricultural Engineering Research Institute, Ministry of Jihad Agriculture, Karaj, Islamic Republic of Iran Tel: +98-261-3202265 Fax: +98-261-2706277

ABSTRACT
Probiotics are live microorganisms which when consumed in enough amounts exert health effects on the host. Several animal and human studies showed that probiotics have beneficial effects in prevention and treatment of some diseases. In addition to improving gut health, immunity and protection against harmful microorganisms, antihypertensive and antioxidative effects, anticarcinogenic properties and prevention of cancer, improving of arthritis, reduction of dermatitis and allergic symptoms, prevention against gastrointestinal disease, dental carries, osteoporosis and obesity, probiotics have also been studied for their cholesterol-lowering effects. The purpose of this study was to review recent researches into the lipid profile improving effect of probiotics in animal and human studies and brief explanation about functional probiotic foods. Probiotics can be found in dairy and non-dairy products. It has been shown that, probiotics exert lowering lipid profile through several mechanisms such as deconjugate bile acids through bile salt hydrolase catalysis, take up and assimilate cholesterol for stabilization of their cell membrane and binding cholesterol to cell walls of probiotics in intestine, conversion of cholesterol into coprostanol, inhibit hepatic cholesterol synthesis by short chain fatty acids such as propionate produced by probiotic bacteria and/or redistribution of cholesterol from plasma to the liver. Certain strains of probiotics have demonstrated cholesterol lowering properties while others did not. However, not all trials have yielded conclusive results. Thus, more properly designed *in vivo* trials may appear additional understanding to eliminate the controversies, to better understand the underlying mechanisms and for safety assessment prior to consumption.

Key words: Cholesterol lowering, lipid profile, probiotics

INTRODUCTION
Probiotics: It is becoming increasingly difficult to ignore the influence of live microorganisms in foods and understanding of their effect especially lactic acid bacteria, on human health that has a very long history. In a Persian version of the Old Testament, it is said that ‘Abraham owed his longevity to the consumption of sour milk (Schrezenmeir and de Vrese, 2001). Metchnikoff (1908) stated that the longevity of the Bulgarians was in part related to their consumption of large quantities of fermented milk containing lactobacilli. The name probiotic comes from the Greek

'pro bios' which means 'for life' (Gismondo *et al.*, 1999). Probiotics was first used by Lilly and Stillwell (1965) to describe the 'substances secreted by one microorganism that stimulate the growth of another'.

It is clear that, a number of definitions of the term 'probiotic' have been used over the years but the one derived by the Food and Agriculture Organization of the United Nations/World Health Organization (FAO/WHO, 2001; Homayouni, 2009) and approved by the International Scientific Association for Probiotics and Prebiotics (Reid *et al.*, 2003) best exemplifies the breadth and scope of probiotics as they are known today: 'live microorganisms which, when administered in adequate amounts, exert health benefit on the host'. Use of probiotic term for microorganisms need criteria such as these microorganism must be capable of being prepared in a viable manner and on a large scale, during use and under storage, the probiotics should remain viable and stable, they are should be able to survive in the intestinal ecosystem and also the host animal should gain beneficially from harboring the probiotic (Ogueke *et al.*, 2010). The first recorded probiotic was fermented milk for human consumption. After that, probiotics became popular with animal nutrition. Across the globe, about 20 probiotic strains, alone or in combination, mainly Lactobacilli such as *L. acidophilus*, *L. casei*, *L. reuterii* and others; Bifidobacteria, safe spore forming lactic acid producing bacteria (such as Lactospore; *Bacillus coagulans* also known as *Lactobacillus sporogenes*) and a probiotic yeast culture *Saccharomyces boulardii*, are used in dietary supplements and functional foods or in mainstream food products (Maity and Misra, 2009).

A considerable amount of literature has been published on the application of probiotic bacterium in animal and human studies. In addition to improving gut health (FAO/WHO, 2001; Homayouni, 2009) and immunity (Galdeano *et al.*, 2007), protection against harmful microorganisms (Soccol *et al.*, 2010), probiotics have been documented to exert other health promoting effects by several mechanisms. Some of other health benefits of probiotics are reduce the severity of infection (Shu *et al.*, 2000), antihypertensive effects (Yeo and Liong, 2010), anticarcinogenic properties (Bengmark *et al.*, 1998; Mack *et al.*, 1999) and prevention of cancer especially colon and bladder (Sanders, 2006), antioxidative effects (Songisepp *et al.*, 2004), improving of arthritis (Baharav *et al.*, 2004), reduction of dermatitis and allergic symptoms especially in infants and pregnant womens (Weston *et al.*, 2005; Ouwehand, 2007), prevention against gastrointestinal disorders (Homayouni and Ejtahed, 2009) such as ulcerative colitis (Pronio *et al.*, 2008) and Crohn's disease (Vilela *et al.*, 2008), prevention of dental carries (Haukioja, 2010) improving of performance (Sultan *et al.*, 2006) and prevention of osteoporosis (Lourens-Hattingh and Viljoen, 2001) and obesity (DiBaise *et al.*, 2008). Probiotics have also been studied for their cholesterol-lowering effects (Ejtahed *et al.*, 2011; Pereira and Gibson, 2002a). The purpose of this study was to review recent researches into the lipid profile improving effects of probiotics in animal and human studies. This study first gives a brief overview of the functional probiotic foods and then focuses on cholesterol-lowering effect of probiotic in animal and human studies.

Probiotics in foods: Probiotics can be found in dairy and non dairy products (Soccol *et al.*, 2010). Functional foods, designer foods or medicinal foods are defined as: 'foods that contain some health-promoting component(s) beyond traditional nutrients'. Addition of probiotics is a way in which foods can be changed to become functional (FAO/WHO, 2001). Different types of food matrices have been used such as various types of cheese, ice cream, milk-based desserts, butter, mayonnaise, powder products or capsules and fermented foods of vegetable origin (Tamime *et al.*, 2005). In the production of probiotics an important factor is the food substrate.

Besides buffering the bacteria through the stomach, it may contain functional ingredients that interact with the probiotics, altering their activities. Fat content, type of protein, carbohydrates and pH can affect probiotic growth and survival (Soccol *et al.*, 2010).

Probiotics in dairy foods: Dairy products are mentioned as ideal vehicle for delivering probiotic bacteria to the human gastrointestinal tract. The matrices used most frequently are cheese, yoghurt, ice cream and other dairy products, The most common means to incorporate probiotics to fermented milk include: (1) addition of probiotics together with the starter cultures, (2) the production of two batches separately, one containing the probiotic microorganism in milk to achieve a high concentration of viable cells and another with starter cultures. When the fermentation stages are completed, the batches are mixed and (3) the use of a probiotic microorganism as a starter culture. In this situation, the time of fermentation is generally higher than traditional processes using non-probiotic starter cultures (Tamime *et al.*, 2005). In this respect, it is necessary to consider the supplementation of the culture medium and the production conditions (e.g., incubation temperatures), since metabolites produced by probiotics can lead to off-flavours (Saarela *et al.*, 2000; Ostlie *et al.*, 2003). In addition, the probiotic strains must be compatible with starter cultures, since the latter could produce inhibitory substances that damage the probiotics (Vinderola *et al.*, 2000). Yoghurts with high fat content showed inhibitory effects against probiotic cultures, particularly *B. bifidum* BBI. The supplementation with vitamins (e.g., ascorbic acid) has been reported to improve the viability of *L. acidophilus* in yoghurts (Dave and Shah, 1997). The addition of substances such as whey protein may also enhance the viabiliity of some probiotics, probably due to their buffering property. In addition, the employment of prebiotics in yoghurt formulations could stimulate the growth and activity of probiotics. In this regard, fructooligossacharides showed to be most effective in maintaining the probiotic viability (Capela *et al.*, 2006).

The utilization of probiotics in the cheese elaboration presents some challenges: low moisture content; presence of salt; starter cultures competing for nutrients and developing acid and flavour during the maturation stage; extended storage (over 3 months) which can influence biochemical activities, redox potential and alter the cheese structure. Moreover, probiotics should survive the entire shelf life of the cheese, not produce metabolites that affect the cheese quality and the starter culture activities and also, they should be able to grow in starter culture media (e.g., whey-based and phage inhibitory media). Tamime *et al.* (2005) reported that, Turkish white brined, Feta-type, Cheddar, Philippine white soft, Edam, Emmental, Domiati, Ras, Herrgard cheese, Quarg and cheese-based dips can be compared with yoghurts in delivering probiotics.

On the other hand ice cream and frozen dairy desserts are ideal vehicle to delivery of probiotics into human intestinal tract (Mountzouris and Gibson, 2003; Homayouni, 2008) that it refer to be stored at low temperatures which makes them less exposed to abusive temperatures having higher viability at the time of consumption (Cruz *et al.*, 2009). Besides, they are consumed by people of all ages and are composed of milk proteins, fat and lactose as well as other compounds that are required for bacterial growth. However, some probiotic species showed a decrease in the viability during the manufacture and freezing of ice cream (Alamprese *et al.*, 2002). So, selection of resistant probiotic strains and adjust the condition of production and storage for more survival rates (encapsulation) can be useful methods for increasing viability of them (Shah and Ravula, 2000; Homayouni *et al.*, 2008). Selection of suitable probiotic strains depend on to probiotic ability to survive simulated conditions of ice cream (high sucrose concentrations, high oxygen, freezing and storage tempreatures), gastric (acidic) and intestinal conditions (alkaline) (Homayouni *et al.*, 2012). As well as some prebiotics could be used to improve the characteristics of the probiotic ice creams. Inulin demonstrated to be beneficial to the firmness, melting properties and dripping time of the ice creams (Akalin and Erisir, 2008). Besides, the inulin level in ice cream enhanced the viability of *L. acidophilus* and *B. lactis* (Akin *et al.*, 2007). The addition of oligofructose in low-fat ice cream also improved the survival of *L. acidophilus* La-5 and *B. animalis* ssp. lactis Bb-12 during storage (Akalin and Erisir, 2008). However, to efficiently produce probiotic ice cream, it is important to select oxygen-resistant strains since the incorporation of air (overrun) in the mixture occurs in the production process which is harmful to microaerophilic and anaerobic strains such as *Lactobacillus* sp. and *Bifidobacterium* sp. This type of challenge can be resolved by the use of microencapsulation technique.

As an alternative, dairy dessert (e.g., chocolate mousse) has also been used as a potential agent to deliver probiotics (Aragon-Alegro *et al.*, 2007).

Probiotics in non dairy foods: Some limitations of the use of dairy products to deliver probiotics are the presence of allergens and requirement of cold environments. This fact has led to the launch of new products based on non-dairy matrices. Some claims related to probiotic products are lactose intolerance and fat content. Some matrices have been used in the development of non-dairy probiotic products such as fruits, vegetables, legumes and cereals.

Fruits and vegetables can be considered good matrices since they contain nutrients such as minerals, vitamins, dietary fibres and antioxidants. The development of different probiotic fruit juices has been studied (Yoon *et al.*, 2004; Soccol *et al.*, 2007). However, the incorporation of probiotics in fruit juices requires the protection against acid conditions. This can be achieved by microencapsulation technologies which allow the entrapment of cells into matrices with a protective coating (Soccol *et al.*, 2010).

Probiotic strains usually found in vegetable materials are species belonging to *Lactobacillus* and *Leuconostoc genera. L. plantarum*, *L. casei* and *L. delbrueckii*, for example, were able to grow in cabbage juice. In addition, it was found that these same bacteria grew in beet juice (Yoon *et al.*, 2005). Gelatin and vegetable gum have been demonstrated to provide a good protection for acid-sensitive *Bifidobacterium* and *Lactobacillus* (Sultana *et al.*, 2000; O'Riordan *et al.*, 2001).

In the case of cereals such as oat and barley, fermentation with probiotic microorganisms could be beneficial due to the decrease of nondigestible carbohydrates (poly-and oligosaccharides), the improvement of the quality and level of lysine, the availability of the vitamin B group, as well as the degradation of phytates and release of minerals (e.g., manganese, iron, zinc and calcium) (Blandino *et al.*, 2003). Oat-based substrates have proved promissory for the growth of *L. reuteri*, *L. acidophilus* and *B. bifidum* (Martensson *et al.*, 2002). Boza, an acid and low-alcohol beverage produced in the Balkan Peninsula, is a fermented product based on maize, wheat and other cereals.

Malt, wheat and barley extracts as non dairy foods demonstrated to have a good influence in increasing bile tolerance and viability of *L. acidophilus*, *L. reuteri* and *L. plantarum* (55, 56). Fermented foods with probiotic strains had an increment in the content of the vitamin B complex (Soccol *et al.*, 2010).

Soymilk is another non dairy product for delivery of probiotics. The survival of probiotics has been assayed in soymilk and this substrate has shown to be efficient for the growth of species such as *L. casei* (Garro *et al.*, 1999), *L. acidophilus* (Wang *et al.*, 2006), *B. infantis* and *B. longum*

(Chou and Hou, 2000, 2002). The antioxidative activities of soymilk can be increased after fermentation by lactic acid bacteria and bifidobacteria (Dave and Shah, 1997). This has led to the designing of the probiotic soybean yoghurt (Wang *et al.*, 2006).

HYPRELIPIDEMIA

Relationship between hyperlipidemia and CHD: Coronary Heart Disease (CHD) is one of the major causes of death and disability in industrialized countries (El-Shafie *et al.*, 2009). In Iran, as many countries, CHD associated with hyperlipidemia (hypertriglyceridemia and hypercholesterolemia) are considered as the main cause of death (Fazeli *et al.*, 2010). The world Health Organization (WHO) predicts that by the year 2020, up to 40% of all deaths will be related to cardiovascular diseases or disease of the heart. Although, cholesterol is an important basic block for body tissues, elevated blood cholesterol is a well-known major risk factor for CHD (Aloglu and Oner, 2006). The results from several epidemiological and clinical studies indicate a positive correlation between elevated total serum cholesterol levels, mainly reflecting the LDL-cholesterol fraction and risk of emergence of CHD (Lipid Research Clinics Program, 1984). It was reported that, hypercholesterolemia contributed to 45% of heart attacks in Western Europe and 35% of heart attacks in Central and Eastern Europe from 1999-2003 (Yusuf *et al.*, 2004). The risk of heart attack is three times higher in those with hypercholesterolemia, compared to those who have normal blood lipid profile. Also each increase in the serum cholesterol concentration by 1% results in 2-3% increase in the risk of CHD (Davis *et al.*, 1990; Manson *et al.*, 1992).

EFFECTS OF PROBIOTICS ON LIPID PROFILE

Recent modalities for lowering blood cholesterol levels involve dietary management, behavior modification regular exercise and drug therapy (Dunn-Emke *et al.*, 2001). Pharmacological agents are available for the treatment of high cholesterol, although they effectively reduce cholesterol levels, they are expensive and are known to have severe side effects (Bliznakov, 2002). Thereby use of probiotics for natural and safe properties and a low ability of triggering adverse effects can be useful strategy (Roberfroid, 2007).

Among the beneficial effects attributed to probiotics and probiotic-containing food products, the reduction of blood cholesterol is of particular interest (Cavalhini *et al.*, 2009). The first record of the influence of certain dairy products on blood lipids dates back more than 40 years. Shaper *et al.* (1963) and later Mann and Spoerry (1974) observed that men from the tribes of Samburu and Maasai warriors in Africa showed reduced serum cholesterol after consumption of large amounts of milk fermented with a wild Lactobacillus strain. The primary probiotic bacteria associated with cholesterol lowering have been lactobacilli and bifidobacteria, although, other lactic acid bacteria, such as enterococci, are able to produce this effect (Cavallini *et al.*, 2009).

Probiotics in animal studies: Hyopolipidemic effects of several strains of probiotics have been demonstrated in many animal studies (Table 1). El-Shafie *et al.* (2009) showed the effect of lactic acid bacteria *Lactobacillus plantarum* NRRL B-4524 used as single or mixed with *Lactobacillus paracasei* and/or other strains of bacteria in rat diets (high fat and high cholesterol-enriched) in lowering blood serum cholesterol (El-Shafie *et al.*, 2009).

Rossi *et al.* (1999) developed a soy yogurt, fermented by *Enterococcus faecium* CRL 183 (probiotic microorganism) and *Lactobacillus helveticus* ssp. *jugurti* 416 (Rossi *et al.*, 1999).

Table 1: Animal and human studies of probiotics in lipid profile levels

Probiotic strain	Animals/subjects	Dose; duration of the study	Effects	Reference
In animal studies				
Lactobacillus plantarum NRRL B-4524 and *Lactobacillus paracasei*	Rat		Lowerd blood serum cholesterol	El-Shafie *et al.* (2009)
L. plantarum A7	Rat	108 CFU mL^{-1} 14 day	Lowering serum lipid levels	Fazeli *et al.* (2010.)
L. plantarum PH04	Mice		Reduced cholesterol ($p<0.05$)	Nguyen *et al.* (2007)
L. plantarum	Twelve male hypercholesterolemic mice	4×10^{9} CFU mL^{-1} 14 days	Significant reduction of total serum cholesterol and triglycerides	Abd El-Gawada *et al.* (2005)
Bifidobacterium longum Bb-46	Forty-eight male albino hypercholesterolemic rats	0.07% (w/v) 35 days	Reduced total cholesterol (50.3%) ($p<0.05$) LDL cholesterol (56.3%) ($p<0.05$) Triglycerides (51.2%) ($p<0.05$)	Abd El-Gawada *et al.* (2005)
L. acidophilus-fermented rice bran	Male Fischer 344/Jcl rats	30 g kg^{-1} 4 week	Significant reduction in total cholesterol (21.3%) ($p<0.05$) reduction in liver cholesterol (22.9%) ($p<0.05$)	Fukushima *et al.* (1999)
Lactobacillus sporogenes	Broiler chickens	6×10^{9} spore g^{-1} at 100 mg kg^{-1} diet	Significantly lowered total cholesterol, VLDL cholesterol and TG	Arun *et al.* (2006)
In human studies				
Lactobacillus bulgaricus and *S. thermophilus*	Fifty four volunteers	Several weeks	Reductions of between 5-10% in serum cholesterol levels	Roo *et al.* (1998)
L. acidophilus	30 healthy men	Several weeks	Decreased total-C 4.4% and LDL cholesterol 5.4%	Roo *et al.* (1998)
B. longum BL1	Thirty-two subjects	10^{9} CFU g^{-1} 4 weeks	Decline in serum total cholesterol LDL-cholesterol and TG ($p<0.05$) increase HDL-C ($p>0.05$)	Xiao *et al.* (2003)
E. fæcium M-74	43 volunteer	56 weeks	Reduction cholesterol levels	Hivak *et al.* (2005)
Streptococcusthermophilus and *Lactobacillus bulgaricus*	33 female volunteers		Improve total/HDL and LDL/HDL cholesterol ratios	Fabian and Elmadfa (2006)
L. rhamnosus LC705	Thirty-eight men	10^{10} CFU g^{-1} 4 week	Did not influeuce blood lipid profile	Hatakka *et al.* (2008)
Lactobacillus fermentum	Forty-six volunteers	2×10^{9} CFU 10 weeks	Did not contribute to any lipid profile changes	Simons *et al.* (2006)
Lactobacillus acidophilus	Eighty volunteers	3×10^{10} CFU/2 six weeks	Not significantly changes in TC, LDL-C, HDL-C and TG	Lewis and Burmeister (2005)
Lactobacillus acidophilus La5 and *Bifidobacterium lactis* Bb12	60 people with type 2 diabetes	6 week	7.45 % reduction in LDL-C and 4.54% reduction in TC, no significant changes in TG and HDL-C	Ejtahed *et al.* (2011)

Fazeli *et al.* (2010) showed that the consumption of *L. plantarum* A7 (10^{8} CFU mL^{-1}) for 14 day is effective in lowering serum lipid levels in rats (Fazeli *et al.*, 2010).

In placebo-controlled studies (Park *et al.*, 2007; Liong and Shah, 2006) have been evaluate the effects of probiotic strains on cholesterol metabolism in hypercholesterolemia-induced mice and rats. It was found in all these investigation that the serum cholesterol levels decreased in the rats fed with a diet supplemented with probiotics.

In a study evaluating the effect of *L. plantarum* PH04 (isolated from infant feces) on cholesterol, Nguyen *et al.* (2007) administered *L. plantarum* (4×10^{8} CFU mL^{-1} dose per day in mouse) to twelve male hypercholesterolemic mice for 14 days. The authors found a significant ($p<0.05$) reduction of total serum cholesterol (reduced by 7%) and triglyceride (reduced by 10%) compared to the control group. In another study, Abd El-Gawada *et al.* (2005) conducted a randomized, placebo-controlled and parallel designed study to assess the efficiency of buffalo milk-yogurts (fortified with *Bifidobacterium longum* Bb-46 in exerting a cholesterol-lowering effect. In the study, the authors fed forty-eight male albino hypercholesterolemic rats (average weight 80-100 g) with 50 g of yogurt [contained 0.07% (w/v) *Bifidobacterium longum* Bb-46] daily for 35 days. The administration of *B. longum* Bb-46-fermented buffalo milk-yogurt significantly reduced concentration of total cholesterol by 50.3%, LDL cholesterol by 56.3% and triglycerides by 51.2% compared to the control ($p<0.05$). In another study, Fukushima *et al.* (1999) found that, 73 hypercholesterolemic male Fischer 344/Jcl rats (8 week old) fed with 30 g kg^{-1} of *L. acidophilus*-fermented rice bran significantly showed an improved lipid profile compared to the control (without *L. acidophilus*). In this 4 week study, the authors reported a significant ($p<0.05$) reduction in serum total cholesterol and liver cholesterol of 21.3 and 22.9%, respectively compared to the control.

Taranto *et al.* (2000) reported that, administration of *Lactobacilllus reuteri* was effective in preventing hypercholesterolemia in mice. In addition, he observed a decrease in total cholesterol (22%) and triglycerides (33%), as well as a 17% increase in the ratio of HDL to LDL.

Gilliland *et al.* (1985) fed a strain of *Lactobacillus* (strain RP32) to pigs with a high-fat diet which inhibited any rise in serum cholesterol. Daniela CU Cavallini showed that probiotic microorganism *E. faecium* CRL 183 in rabbits could be used to improve lipid profile as an alternative or an adjuvant for drug therapy (Cavallini *et al.*, 2009). In Hung *et al.* (2008) study, it has been shown that use of probiotic combination in fermented soybean meal resulted in reduction in TG, TC and LDL-C in forty eight pigs (Hung *et al.*, 2008).

Probiotics supplementation reduces cholesterol concentration in serum of chickens (Mohan *et al.*, 1995). Arun *et al.* (2006) showed that dietary supplementation of *Lactobacillus sporogenes* (6×10^{8} spore per gr) at 100 mg kg^{-1} diet significantly lowered total cholesterol, VLDL cholesterol and triglycerides concentrations in the serum of broiler chickens. Supplementation of probiotics (*Lactobacillus acidphilus*, *Bifidobacterium bifidum* and *Aspergillus oryzae*) at 100 mg kg^{-1} in the diet of broiler chickens significantly reduced the serum cholesterol concentration. Kalavathy *et al.* (2003) reported that, dietary supplementation of a mix culture of 12 strains of *Lactobacillus* at 1% in the basal diet of broilers resulted in higher body weight gain and lowered serum cholesterol concentration.

Probiotics in human studies: The hypocholesterolemic potential of probiotics has also been evaluated in human subjects (Table 1). In 1979, the first trial to evaluate the effects of lactic acid bacteria on serum cholesterol levels in humans was conducted. Fifty four volunteers participated in a randomized cross over trial; the results revealed reductions of 5-10% in serum cholesterol levels after several weeks of moderate consumption of yoghurt fermented with *Lactobacillus bulgaricus* and *S. thermophilus* (Schaafsma *et al.*, 1998).

A Dutch trial involving 30 healthy men also found that consuming yoghurt fermented with *L. acidophilus* cultures for several weeks decreased both total and LDL cholesterol levels by 4.4 and 5.4%, respectively compared with controls (Xiao *et al.*, 2003). Xiao *et al.* (2003) evaluated the effects of a low-fat yogurt containing 10^{8} CFU g^{-1} of *B. longum* BL1 on lipid profile of thirty-two subjects (baseline serum total cholesterol 220-280 mg dL^{-1}, body weight 55.4-81.8 kg, aged 28-60 years old). Results from this randomized, single-blind, placebo-controlled and parallel study showed a significant ($p<0.05$) decline in serum total cholesterol, LDL-cholesterol and triglycerides after 4 weeks. The authors also observed a 14.5% increase in HDL-cholesterol when comparing to the control (yoghurt without *B. longum* BL1; $p<0.05$) (Xiao *et al*., 2003).

Hivak *et al*. (2005) showed that, administration of the *E. faecium* M-74 as probiotic strain was associated with the reduction of serum cholesterol concentration by 12% after 56 weeks in 43 volunteers. Pawan and Bhatia (2007) showed that, probiotics given in the form of fermented milk product 'Dahi' and 'Lassi' in 60 male healthy volunteers had no significant reduction in cholesterol level and HDL-C in the human subjects. Ashar and Prajapati (2001) reported hypocholesterolemic effect of probiotic diet in humans and showed total cholesterol reduction to an extent of 12-21% by feeding on acidophilus milk. The lactic acid fermenters of yogurt can reduce the levels of total cholesterol, HDL-C and LDL-C, in a well-balanced way by assimilation of cholesterol by bacteria in yoghurt (*in vitro*). The effect of probiotic intake on cholesterol level on human subjects carried by Fabian and Elmadfa (2006) showed that, the consumption of fermented milk leads to decrease in cholesterolemia. Lewis and Burmeister (2005) showed that *L. acidophilus* in volunteers can not affect in serum lipids. Fabian and Elmadfa (2006) showed that, mean concentrations of total, HDL and LDL cholesterol in 33 female volunteers changed among the probiotic ($n = 17$) (enriched with *Streptococcus thermophilus* and *Lactobacillus bulgaricus*), as well as, the control ($n = 16$) group (*S. thermophilus* and *L. bulgaricus*). No relevant differences were observed between the two groups. The total/HDL and LDL/HDL cholesterol ratios improved in both groups. The authors found that *L. acidophilus* capsules did not significantly change plasma total cholesterol, LDL-cholesterol, HDL-cholesterol and triglycerides of the subjects. In a controlled trial lasting 6 weeks involving 78 healthy subjects which found that consumption of yoghurt fermented with *L. acidophilus* had no significant effect on serum cholesterol levels at all (De Roo *et al*., 1998). Human and animal studies of probiotics were summarized in Table 1.

Although, many studies have demonstrated convincing cholesterol-lowering effects of probiotics in both animals and humans, controversial results have been surfaced. A study by Hatakka *et al*. (2008) refuted the purported hypocholesterolemic effect of probiotics and reported that the administration of *L. rhamnosus* LC705 (10^{10} CFU g^{-1} per capsule; two capsules daily) did not influence blood lipid profile in thirty-eight men with mean cholesterol levels of 6.2 mmol L^{-1} after a 4 week treatment period. In another study, involving forty-six volunteers (aged 30-75 years old), Simons *et al*. (2006) found that the consumption of *Lactobacillus fermentum*, (2×10^9 CFU per capsule; four capsules daily) did not contribute to any lipid profile changes after 10 weeks. Lewis and Burmeister (2005) conducted a randomized, placebo-controlled double blind and crossover designed study to determine the effect of Lactobacillus acidophilus on human lipid profile. In this study, eighty volunteers (aged 20-65 years old; baseline total cholesterol of >5.0 mmol L^{-1}; mean Body Mass Index of 27.8 kg m^{-2}) consumed two capsules containing freeze-dried *L. acidophilus* (3×10^{10} CFU/2 capsules) three times daily for six weeks and crossed over for another six weeks after a 6 week washout period. These results may refer to semi-active properties of probiotic cells in capsules. Therefore, it can be concluded that probiotics may improve lipid profile in active form as are in functional foods.

MECHANISMS OF ACTION

Several mechanisms are suggested for cholesterol reducing activity of probiotics. These mechanisms including deconjugate bile acids through bile salt hydrolase catalysis. Since, cholesterol is the precursor for the synthesis of new bile acids, the use of cholesterol to synthesize new bile would lead to a decreased concentration of cholesterol in blood (Lye *et al*., 2009), to take up and

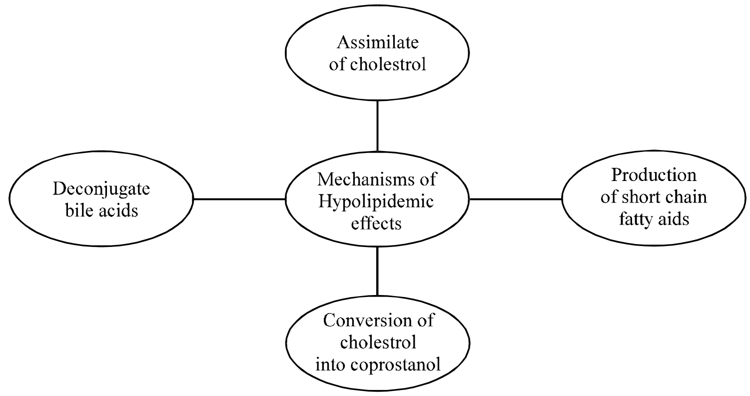

Fig. 1: Mechanisms of hypolipidemic effects of probiotics

assimilate cholesterol for stabilization of their cell membrane and binding cholesterol to cell walls of probiotics in intestine (Tanaka *et al.*, 1999; Lepercq *et al.*, 2004; Razin, 1975; Noh *et al.*, 1997), conversion of cholesterol into coprostanol (Lye *et al.*, 2010) and short chain fatty acids such as propionate produced by probiotic bacteria may also inhibit hepatic cholesterol synthesis and/or redistribution of cholesterol from plasma to the liver (Wolever *et al.*, 1996; Delzenne and Williams, 2002; Pereira and Gibson, 2002b) hypocholesterolemic effect via altering the pathways of cholesteryl esters and lipoprotein transporters (Ooi and Liong, 2010). Figure 1 shows mechanisms of hypolipidemic effects of probiotics.

CONCLUSION

This study has given an account of and the reasons for widespread use of probiotics for improving the lipid profile (total cholesterol, LDL-cholesterol, HDL-cholesterol and triglyceride) in animal and human studies. However, not all trials have yielded conclusive results. Certain strains of probiotics have demonstrated cholesterol lowering properties while others did not. Also, the matrix-as a probiotic carrier-may influence the cholesterol-lowering effect of probiotics. In order to justify the varying cholesterol-lowering effect exhibited by various strains of probiotics, researchers have endeavored to reveal the mechanisms of probiotics on hypocholesterolemic effect through *in vitro* and *in vivo* studies. Many of the proposed mechanisms and experimental evidence specifically targeting cholesterol-lowering effects remain controversial. Thus, more properly-designed *in vivo* trials may disclose additional understanding and knowledge to eliminate the controversies, to better understand the underlying mechanisms and for better safety assessment prior to consumption.

REFERENCES

Abd El-Gawada, I.A., E.M. El-Sayeda, S.A. Hafez, H.M. El-Zeinia and F.A. Saleh, 2005. The hypocholesterolaemic effect of milk yoghurt and soy-yoghurt containing bifidobacteria in rats fed on a cholesterol-enriched diet. Int. Dairy J., 15: 37-44.

Akalin, A.S. and D. Erisir, 2008. Effects of inulin and oligofructose on the rheological characteristics and probiotic culture survival in low-fat probiotic ice-cream. J. Food Sci., 73: 184-188.

Akin, M.B., M.S. Akin and Z. Kirmaci, 2007. Effects of inulin and sugar levels on the viability of yogurt and probiotic bacteria and the physical and sensory characteristics in probiotic ice cream. Food Chem., 104: 93-99.

Alamprese, C., R. Foschino, M. Rossi, C. Pompei and L. Savani, 2002. Survival of Lactobacillus johnsonii La1 and influence of its addition in retail-manufactured ice cream produced with different sugar and fat concentrations. Int. Dairy J., 12: 201-208.

Aloglu, Z.H and Oner, 2006. Assimilation of cholesterol in broth, cream and butter by probiotic bacteria. Eur. J. Lipid Sci. Technol., 108: 709-713.

Aragon-Alegro, L.C., J.H. Alarcon-Alegro, H.R. Cardarelli, M.C. Chiu and S.M.I. Sadd, 2007. Potentially probiotic and symbiotic chocolate mousse. LWT-Food Sci. Technol., 40: 669-675.

Arun, A., R. Murrugappan, A.D.D. Ravindran, V. Veeramanikandan and S. Balaji, 2006. Utilization of various industrial wastes for theproduction of poly-β. Murrugappan, A.D.D. Ravindran, V. Veeramanikandan and S. Balaji, 2006. Utilization of various industrial wastes for theproduction of poly-β-hydroxy butyrate (PHB) by *Alcaligenes eutrophus*. Afr. J. Biotechnol., 5: 1524-1527.

Ashar, M.N. and J.B. Prajapati, 2001. Serum choleserol levels in humans fed with acidophilus milk. Ind. J. Micro., 41: 257-263.

Baharav, E., F. Mor, M. Halpern and A. Weinberger, 2004. *Lactobacillus* GG bacteria ameliorate arthritis in lewis rats. J. Nutr., 134: 1964-1969.

Bengmark. S., S. Aherne, G. Molin and B. Jeppsson, 1998. Intestina; Colonizing lactobacilii. J. Nutr., 14: 585-594.

Blandino, A., M.E. Al-Aseeri, S.S. Pandiella, D. Cantero and C. Webb, 2003. Cereal-based fermented foods and beverages. Food Res. Int., 36: 527-543.

Bliznakov, E.G., 2002. Lipid-lowering drugs (statins), cholesterol, coenzyme Q10. The baycol case-a modern Pandoras box. Biomed. Pharm., 56: 56-59.

Capela, P., T.K.C. Hay and N.P. Shah, 2006. Effect of cryoprotectants, prebiotics and microencapsulation on survival of probiotic organisms in yoghurt and freezedried yoghurt. Food Res. Int., 39: 203-211.

Cavallini, D.C.U., R. Bedani, L.Q. Bomdespacho, R.C. Vendramini and E.A. Rossi, 2009. Effects of probiotic bacteria, isoflavones and simvastatin on lipid profile and atherosclerosis in cholesterol-fed rabbits: A randomized double-blind study. Lipids Health Dis., Vol. 8, 10.1186/1476-511X-8-1

Chou, C.C. and J.W. Hou, 2000. Growth of bifidobacteria in soymilk and their survival in the fermented soymilk drink during storage. Int. J. Food Microbiol., 56: 113-121.

Chou, C.C. and J.W. Hou, 2002. Growth and survival of bifidobacteria and lactic acid bacteria during the fermentation and storage of cultured soymilk drinks. Food Microbial., 19: 501-508.

Cruz, A.G., A.E.C. Antunes, A.L.O.P. Sousa, J.A.F. Faria and S.M.I. Saad, 2009. Ice-cream as a probiotic food carrier. Food Res. Int., 42: 1233-1239.

Dave, R.I. and N.P. Shah, 1997. Effectiveness of ascorbic acid as an oxygen scavenger in improving viability of probiotic bacteria in yoghurts made with commercial starter cultures. Int. Dairy J., 7: 435-443.

Davis, C.E, B.M. Rifkind, H. Brenner and D.J. Gordon, 1990. A single cholestrerol measurement underestimates the risk of coronary heart disease: An empirical example from the Lipid Research Clinics mortality follow-up study. J. Am. Med. Assur., 64: 3044-3046.

De Roo, N.M., G. Schouten and M.B. Katan, 1998. Yoghurt enriched with Lactobacillus acidophilus does not lower blood lipids in healthy men and women with normal to borderline high serum cholesterol levels. Eur. J. Clin. Nutr., 53: 277-280.

Delzenne, N.M. and C.M. Williams, 2002. Prebiotics and lipid metabolism. Curr. Opin. Lipidol., 13: 61-67.

DiBaise, J.K., H. Zhang, M.D. Crowell, R. Krajmalnik-Brown, G.A. Decker and B.E. Rittmann, 2008. Gut microbiota and its possible relationship with obesity. Mayo Clin. Proc., 83: 460-469.

Dunn-Emke. S., G. Weider and D. Ornish, 2001. Benefits of a low-fat-based diet. Obes Res., 9: 731-731.

Ejtahed, H.S., J. Mohtadi-Nia, A. Homayouni-Rad, M. Niafar, M. Asghari-Jafarabadi, V. Mofid and A. Akbarian-Moghari, 2011. Effect of probiotic yogurt containing Lactobacillus acidophilus and Bifidobacterium lactis on lipid profile in individuals with type 2 diabetes mellitus. J. Dairy Sci., 94: 3288-3294.

El-Shafie, H.A., N.I. Yahia, H.A. Ali, F.A. Khalil, E.M. El-Kady and Y.A. Moustafa, 2009. Hypocholesterolemic action of Lactobacillus plantarum NRRL-B-4524 and Lactobacillus paracasei in mice with hypercholesterolemia induced by diet. Aust. J. Basic Applied Sci., 3: 218-228.

FAO/WHO, 2001. Health and nutritional properties of probiotics in food including powder milk with live lactic acid bacteria. Report of a Joint FAO/WHO Expert Consultation on Evaluation of Health and Nutritional Properties of Probiotics in Food Including Powder Milk with Live Lactic Acid Bacteria. Cordoba, Argentina.

Fabian, E. and I. Elmadfa, 2006. Influence of daily consumption of probiotic and conventional yoghurt on plasma lipid profile in young healthy women. Annu. Nutr. Metabol., 50: 387-393.

Fazeli, H., J. Moshtaghian, M. Mirlohi and M. Shirzadi, 2010. Reduction in serum lipid parameters by incorporation of a nativestrain of lactobacillus plantarum A7 in mice. Iran. J. Diabetes Lipid Disorders, 9: 1-7.

Fukushima, M., A. Yamada, T. Endo and M. Nakano, 1999. Effects of a mixture of organisms, Lactobacillus acidophilus or streptococcus faecalis on D6-desaturase activity in the livers of rats fed a fat-and cholesterol-enriched diet. Nutrrients, 15: 373-378.

Galdeano, C.M., A.M. Leblanc, G. Vinderola, M.E. Bonet and G. Perdigon, 2007. Proposed model: mechanisms of immunomodulation induced by probiotic bacteria. Clin. Vaccine Immunol., 14: 485-492.

Garro, M.S., G.F. de Valdez, G. Oliver and G.S. de Giori, 1999. Starter culture activity in refrigerated fermented soymilk. J. Food Prot., 62: 808-810.

Gilliland. S.E., C.R. Nelson and C. Maxwell, 1985. Assimilation of cholesterol by Lactobacillus acidophilus. Applied Environ. Microbiol., 49: 377-381.

Gismondo, M.R., L. Drago and A. Lombardi, 1999. Review of probiotics available to modify gastrointestinal flora. Int. J. Antimicrob. Agents, 12: 287-292.

Hatakka, K., M. Mutanen, R. Holma, M. Saxelin and R. Korpela, 2008. *Lactobacillus rhamnosus* LC705 together with *Propionibacterium freudenreichii* ssp. *Shermanii* JS administered in capsules is ineffective in lowering serum lipids. J. Am. Coll. Nutr., 27: 441-447.

Haukioja, A., 2010. Probiotics and oral health. Eur. J. Dentistry, 4: 348-355.

Hivak, P., J. Odraska, M. Ferencik, L. Ebringer, E. Jahnova and Z. Mikes, 2005. One-year application of probiotic strain *Enterococcus faecium* M-74 decreases serum cholrstrol levels. Brastil Lek Listy, 106: 67-72.

Homayouni, A. and H.S. Ejtahed, 2009. The effects of Probiotics in prevention and treatment of gastrointestinal disorders: A review. J. Microb. Biotechnol., 2: 53-60.

Homayouni, A., 2008. Therapeutical Effects of Functional Probiotic, Prebiotic and Synbiotic Foods. 1st Edn., Tabriz University of Medical Sciences, Tabriz, Iran, Pages: 1-156.

Homayouni, A., 2009. Letter to the editor. Food Chem., 114: 1073-1073.

Homayouni, A., A. Azizi, M. Javadi, S. Mahdipour and H. Ejtahed, 2012. Factors influencing probiotic survival in ice cream: A review. International J. Dairy Sci., DOI: 10.3923/ijds.2012

Homayouni, A., M.R. Ehsani, A. Azizi, S.H. Razavi and M.S. Yarmand, 2008. Growth and survival of some probiotic strains in simulated ice cream conditions. J. Applied Sci., 8: 379-382.

Hung, A.T.Y., T.M. Su, C.W. Liao and J.J. Lu, 2008. Effect of probiotic combination fermented soybean meal on growth performance, lipid metabolism and immunological response of growing-finishing pigs. Asian J. Anim. Vet. Adv., 3: 431-436.

Kalavathy, R., N. Abdullah, S. Jalaludin and Y.W. Ho, 2003. Effects of Lactobacillus cultures on growth performance, abdominal fat deposition, serum lipids and weight of organs of broiler chickens. Br. Poult. Sci., 44: 139-144.

Lepercq, P., P. Relano and C. Cayuela *et al.*, 2004. Bifidobacterium animalis strain DN173 010 hydrolyses bile salts in the gastrointestinal tract of pigs. Scand J. Gastroenterol, 39: 1266-1271.

Lewis, S.J. and S. Burmeister, 2005. A double-blind placebo-controlled study of the effects of *Lactobacillus acidophilus* on plasma lipids. Eur. J. Clin. Nutr., 59: 776-780.

Lilly, D.M. and R.H. Stillwell, 1965. Probiotics: Growth-promoting factors produced by microorganisms. Science, 147: 747-748.

Liong, M.T. and N.P. Shah, 2006. Effects of a Lactobacillus casei symbiotic on serum lipoprotein, intestinal microflora and organic acids in rats. J. Dairy Sci., 89: 1390-1399.

Lipid Research Clinics Program, 1984. The lipid research clinics coronary primary prevention trial results. I. Reduction in the incidence of coronary heart disease. JAMA, 251: 351-364.

Lourens-Hattingh, A. and B.C. Viljoen, 2001. Yogurt as probiotic carrier food. Int. Dairy J., 11: 1-17.

Lye, H.S., C.Y. Kuan, J.A. Ewe, W.Y. Fung and M.T. Liong, 2009. The improvement of hypertension by probiotics: Effects on cholesterol, diabetes, Renin and phytoestrogens. Int. J. Mol. Sci., 10: 3755-3775.

Lye, H.S., G. Rusul and M.T. Liong, 2010. Removal of cholesterol by lactobacilli via incorporation and conversion to coprostanol. J. Dairy Sci., 93: 1383-1392.

Mack, D.R., S. Michail, S. Wei, L. McDougall and M.A. Hollingsworth, 1999. Probiotics inhibit enteropathogenic *E. coli* adherence *in vitro* by inducing intestinal mucin gene expression. Am. J. Physiol. Gastrointest Liver Physiol., 276: 941-950.

Maity, T.K. and A.K. Misra, 2009. Probiotics and human health. Synoptic Rev., 9: 1778-1796.

Mann, G.V. and A. Spoerry, 1974. Studies of a Surfactant and cholesterolemia in the Masai. Am. J. Clin. Nutr., 27: 464-469.

Manson, J.E., H. Tosteson, P.M. Ridker, S. Satterfield, P. Hebert and G.T. Oconnor, 1992. The primary prevention of myocardial infarction. N. Engl. J. Med., 326: 1406-1416.

Martensson, O., R. Oste and O. Holst, 2002. The effect of yoghurt culture on the survival of probiotic bacteria in oat-based, non-dairy products. Food Res. Int., 35: 775-784.

Metchnikoff, E., 1908. The Prolongation of Life. Putnam and Sons, New York.

Mohan, B., R. Kadirvel, M. Bhaskaran and A. Notarajan, 1995. Effect of probiotic supplementation on serum/yolk cholesterol and on egg shell thickness in layers. Br. Poult. Sci., 36: 799-803.

Mountzouris, K.C. and G.R. Gibson, 2003. Colonization of the gastrointestinal tract. Ann. Nestle, 61: 43-54.

Nguyen, T.D.T., J.H. Kang and M.S. Lee, 2007. Characterization of *Lactobacillus plantarum* PH04, a potential probiotic bacterium with cholesterol-lowering effects. Int. J. Food Microbiol., 113: 358-361.

Noh, O.D., S.H. Kim and S.E. Gilliland, 1997. Incorporation of cholesterol into the cellular membrane of *Lactobacillus acidophilus* ATCC 43121. J. Dairy. Sci., 80: 3107-3113.

Ogueke, C.C., C.I. Owuamanam, N.C. Ihediohanma and J.O. Iwouno, 2010. Probiotics and prebiotics: Unfolding prospects for better human health. Pak. J. Nutr., 9: 833-843.

Ooi, L.G. and M.T. Liong, 2010. Cholesterol-lowering effects of probiotics and prebiotics: A review of *in vivo* and *in vitro* findings. Int. J. Mol. Sci., 11: 2499-2522.

Ostlie, H., M.H. Helland and J. Narvhus, 2003. Growth and metabolism of probiotics in fermented milk. Int. J. Food Microbiol., 87: 17-27.

Ouwehand, A.C., 2007. Antiallergic effects of probiotics. J. Nutr., 137: 794-797.

O'Riordan, K., D. Andrews, K. Buckle and P. Conway, 2001. Evaluation of microencapsulation of a *Bifidobacterium* strain with starch as an approach to prolonging viability during storage. J. Applied Microbiol., 91: 1059-1066.

Park, Y.H., J.G. Kim, Y.W. Shin, S.H. Kim and K.Y. Whang, 2007. Effect of dietary inclusion of *Lactobacillus*, acidophilus ATCC 43121 on cholesterol metabolism in rats. J. Microbiol. Biotechnol., 17: 655-662.

Pawan, R. and A. Bhatia, 2007. Systemic immunomodulation and hypocholesteraemia by dietary probiotics. A Clin. Study J. Clin. Dia. Res., 1: 467-475.

Pereira, D.I. and G.R. Gibson, 2002a. Effects of consumption of probiotics and prebiotics on serum lipid levels in humans. Crit. Rev. Biochem. Mol. Biol., 37: 259-281.

Pereira, D.I.A. and G.R. Gibson, 2002b. Cholesterol assimilation by lactic acid bacteria and bifidobacteria isolated from the human gut. Applied Environ. Microbiol., 68: 4689-4693.

Pronio, A., C. Montesani, C. Butteroni, S. Vecchione and G. Mumolo *et al*., 2008. Probiotic administration in patients with ileal pouch-anal anastomosis for ulcerative colitis is associated with expansion of mucosal regulatory cells. Inflamm. Bowel Dis., 14: 662-668.

Razin, S., 1975. Cholesterol incorporation into bacterial membranes. J. Bacteriol., 124: 570-572.

Reid, G., M.E. Sanders, H.R. Gaskins, G.R. Gibson and A. Mercenier *et al*., 2003. New scientific paradigms for probiotics and prebiotics. J. Clin. Gastroenterol, 37: 105-118.

Roberfroid. M., 2007. Prebiotics: The concept revisited. J. Nutr., 137: 830S-837S.

Rossi, E.A., R.C. Vendramini, I.Z. Carlos, I.C. Pey and G.F. de Valdez, 1999. Development of a novel fermented soymilk product with potential probiotic properties. Eur. Food Res. Technol., 209: 305-307.

Saarela, M., G. Mogensen, R. Fonden, J. Matto and T. Mattila-Sandholm, 2000. Probiotic bacteria: Safety, functional and technological properties. J. Biotechnol., 84: 197-215.

Sanders, M.E., 2006. Summary of probiotic activities of Bifidobacterium lactis HN019. J. Clin. Gastroenterol, 40: 776-783.

Schaafsma, G., W.J.A. Meuling, W. Van Dokkum and C. Bouley, 1998. Effects of a milk product, fermented by *Lactobacillus acidophilus* and with fructooligosaccharides added, on blood lipids in male volunteers. Eur. J. Clin. Nutr., 521: 436-440.

Schrezenmeir, J. and M. de Vrese, 2001. Probiotics, prebiotics and synbiotics approaching a definition. Am. J. Clin. Nutr., 73: 361S-364S.

Shah, N.P. and R.R. Ravula, 2000. Microencapsulation of probiotics bacteria and their survival in frozen fermented dairy desserts. Aust. J. Dairy Technol., 55: 139-144.

Shaper, A.G., K.W. Jones, M. Jones and J. Kyobe, 1963. Serum lipids in three nomadic tribes of northern Kenya. Am. J. Clin. Nutr., 13: 135-146.

Shu, Q., H. Lin, K.J. Rutherfurd, S.G. Fenwick, J. Prasad, P.K. Gopal and H.S. Gill, 2000. Dietary Bifidobacterium lactis (HN019) enhances resistance to oral Salmonella typhimurium infection in mice. Microbiol. Immunol., 44: 213-222.

Simons, L.A., S.G. Amansec and P. Conway, 2006. Effect of *Lactobacillus fermentum* on serum lipids in subjects with elevated serum cholesterol. Nutr. Metabolism Cardiovas. Dis., 16: 531-535.

Soccol, C.R., F.C. Prado and J.L. Parada, 2007. Technological process to produce a coconut fermented beverage with probiotic properties. BR Patent PI0703244-7.

Soccol, C.R., L.P. de Souza Vandenberghe, M.R. Spier, A.B.P. Medeiros and C.T. Yamaguishi *et al*., 2010. The potential of probiotics: A review. Food Technol. Biotechnol., 48: 413-434.

Songisepp, E., T. Kullisaar, P. H?tt, P. Elias, T. Brilene, M. Zilmer and M. Mikelsaar, 2004. A new probiotic cheese with antioxidative and antimicrobial activity. J. Dairy Sci., 87: 2017-2023.

Sultan, A., F.R. Durrani, S.M. Suhail, M. Ismail, Z. Durrani and N. Chand, 2006. Comparative effect of yogurt as probiotic on the performance of broiler chicks. Pak. J. Biol. Sci., 9: 88-92.

Sultana, K., G. Godward, N. Reynolds, R. Arumugaswamy, P. Peiris and K. Kailasapathy, 2000. Encapsulation of probiotic bacteria with alginate-starch and the evaluation of survival in simulated gastrointestinal conditions and in yoghurt. Int. J. Food Microbiol, 62: 47-55.

Tamime, A.Y., M. Saarela, A.K. Sondergaard, V.V. Mistry and N.P. Shah, 2005. Production and Maintenance of Viability of Probiotic Micr Organisms in Dairy Products. In: Probiotic Dairy Products, Tamime, A.Y. (Ed.). Blackwell Publishing, Oxford, UK, pp: 44-51.

Tanaka, H., K. Doesburg, T. Iwasaki and I. Mireau, 1999. Screening of lactic acid bacteria for bile salt hydrolase activity. J. Dairy Sci., 82: 2530-2535.

Taranto, M.P., M. Medici, G. Perdigon, A.P. Ruiz-Holgado and G.F. Valdez, 2000. Effect of lactobacillus reuteri on the prevention of hypercholesterolemia in mice. J. Dairy Sci., 83: 401-403.

Vilela, E.G., M.D.L.D.A. Ferrari, H.O.D.G. Torres, A.G. Pinto and A.C.C. Aguirre *et al*., 2008. luence of *Saccharomyces boulardii* on the intestinal permeability of patients with Crohn's disease in remission. Scand. J. Gastroenterol., 43: 842-848.

Vinderola, C.G., N. Bailo and J.A. Reinheimer, 2000. Survival of probiotic microflora in Argentinian yogurths during refrigerated storage. Food Res. Int., 33: 97-102.

Wang, Y.C., R.C. Yu and C.C. Chou, 2006. Antioxidative activities of soymilk fermented with lactic acid bacteria and bifidobacteria. Food Microbiol., 23: 128-135.

Weston, S., A. Halbert, P. Richmond and S.L. Prescott, 2005. Effects of probiotics on topic dermatitis: A randomised controlled trial. Arch. Dis. Child, 90: 892-897.

Wolever, T.M., J. Fernandes and A.V. Rao, 1996. Serum acetate: Propionate ratio is related to serum cholesterol in men. J. Nutr, 126: 2790-2797.

Xiao, J.Z., S. Kondo, N. Takahashi, K. Miyaji and K. Oshida *et al*., 2003. Effects of milk products fermented by *Bifidobacterium longum* on blood lipids in rats and healthy adult male volunteers. J. Dairy Sci., 86: 2452-2461.

Yeo, S.K. and M.T. Liong, 2010. Angiotensin I-converting enzyme inhibitory activity and bioconversion of isoflavones by probiotics in soymilk supplemented with prebiotics. Int. J. Food Sci. Nutr., 61: 161-181.

Yoon, K.Y., E.E. Woodams and Y.D. Hang, 2004. Probiotication of tomato juice by lactic acid bacteria. J. Microbiol., 42: 315-318.

Yoon, K.Y., E.E. Woodams and Y.D. Hang, 2005. Fermentation of beet juice by beneficial lactic acid bacteria. Wiss. Technol., 38: 73-75.

Yusuf, S., S. Hawken, S. Ounpuu, T. Dans and A. Avezum *et al.*, 2004. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): Case-control study. Lancet, 364: 937-952.