

Probiotics as complementary therapy for hypercholesterolemia

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Abstract

The role of probiotic organisms as alternative or complementary therapy in combating large number of gastro intestinal disorders and their ability to enhance immune response attracts global attention. In addition, their therapeutic use towards cholesterol-lowering activities has further increased their applications as effective probiotics for humans as supplements in milk and yoghurt, since there are no other supplements for hypercholesterolemia, which is the crucial risk factor for cardiovascular diseases. Changes in dietary habits, stressful life and lack of physical activities are the precursors for increasing incidences of hypercholesterolemia and subsequently cardiovascular diseases. The present review focuses on some of the animal studies and clinical trials conducted with probiotic lactobacilli and bifidobacteria. This review may throw some light to prove the ability of these probiotics as a novel alternative or adjuvants to chemical drugs to help fight hypercholesterolemia.

Keywords: Probiotics, lactobacilli, bifidobacteria, hypercholesterolemia, adjuvants.

Introduction

Probiotics and their Health Benefits

Probiotics are defined as “living microorganisms, which upon ingestion in certain numbers exert health benefits on the host beyond inherent basic nutrition” (Guarner and Schaafsma, 1998). Various studies have indicated that probiotics may alleviate lactose intolerance; have a positive influence on the intestinal flora of the host; stimulate/modulate mucosal immunity; reduce inflammatory or allergic reactions; reduce blood cholesterol; possess anti-colon cancer effects; reduce the clinical manifestations of atopic dermatitis, Crohn’s disease, diarrhea, constipation, candidiasis, and urinary tract infections; and competitively exclude pathogens (Mercenier et al., 2003; Reid et al, 2003; Gill and Guarner, 2004)

Considering this impressive list of potential health-promoting benefits, it is not surprising that there continues to be considerable interest in the use of probiotics as biotherapeutic agents (Mercenier et al., 2003; Shanahan, 2003). Furthermore, given a heightened awareness among consumers of the link between diet and health and the fact that probiotic-containing foods are generally perceived as “safe” and “natural,” the global market for such foods is on

the increase, particularly dairy-based products marketed for the prophylaxis or alleviation of gastrointestinal disorders (Stanton et al., 2001). The selection of potential probiotic strains that would be capable of performing effectively in the gastrointestinal tract is a significant challenge (Figure-1). Strain selection is generally based on *in vitro* tolerance of physiologically relevant stresses: e.g., low pH, elevated osmolarity, and bile (Saarela et al., 2000; Dunne et al., 2001; Tuomola et al., 2001).

Probiotics may play a beneficial role in several medical conditions, including diarrhea, gastroenteritis, irritable bowel syndrome, inflammatory bowel disease, cancer, depressed immune function, infant allergies, failure-to-thrive, hyperlipidemia, hepatic diseases, *Helicobacter pylori* infections and others mentioned earlier, all of which were suggested by certain research studies to improve with the use of probiotics. Probiotics should be further investigated for their possible benefits to patients affected by these and possibly other medical conditions. At the same time, the potential for negative side effects from probiotics should also be researched. The correct combination and concentration of gastrointestinal microflora is determined by nature and numerous interdependent variables. Changing one factor such as concentration and trying to “optimize” nature’s delicately balanced

gastrointestinal environment may very well be altering a condition that nature never intended to alter. The short- and long-term effects of this change may be difficult to evaluate given the multifactorial nature of the gastrointestinal environment (Brown and Valiere, 2004).

Risk Factors: Obesity and Hypercholesterolemia

Weight gain beyond normal limits and obesity is a significant problem in both developing and developed countries. It is estimated that there are roughly 40 to 50 million overweight subjects in India as on today and the obesity has reached epidemic proportions in India affecting 5% of the country's population. Obesity is not only a physiological disorder but also is the root cause of several diseases and pose increased risk of health problems such as cardiovascular disease, hypertension, diabetes, arthritis and certain type of cancers (American Academy of Pediatrics). In spite of the fact that cholesterol is the main lipid found in blood, bile and brain tissues it is required for the formation of sterols and cellular membranes. It is well known that higher levels of serum cholesterol are generally considered to be a risk factor for coronary heart disease.

Hypercholesterolemia occurs when there is an elevated level of total cholesterol in the bloodstream. It is the result of high levels of low-density lipoprotein (LDL) as compared to high-density lipoprotein (HDL) cholesterol. LDL, the 'bad' cholesterol, leaves behind fatty deposits or *plaques* in the blood vessels. Accumulation of these plaques congests blood vessels and blocks blood supply to the organs. HDL, the 'good' cholesterol, cleans up excess cholesterol from the body, thus minimizing the amount of congestion and blockage. Hypercholesterolemia hardens and narrows blood vessels in various parts of the body, leading to fatal diseases such as chest pains, heart attack and stroke. Blocked blood vessels in the limbs can cause pain, ulcers, infections and gangrene.

During the last few decades, numerous epidemiological, laboratory, and clinical studies have demonstrated a connection between high serum cholesterol and increased risk for atherosclerosis and coronary heart disease, the latter being a major cause of death in Western countries (Barr et al., 1951). Potential hypocholesterolemic pharmaceuticals and food products are continuously being developed to control hypercholesterolemia in humans

(McNamara and Sabb, 1989; Suckling et al., 1991). With the emergence of a more health-conscious society, the role of probiotic food products has gained attention from consumers and producers (Perdigon et al., 1991). In this respect, the ingestion of probiotic lactic acid bacteria might be a more natural way to decrease serum cholesterol in humans (Taranto et al., 1999).

Cholesterol Biosynthesis and Uptake

Although humans synthesize cholesterol to maintain minimum levels for biological functioning, diet also is known to play a role in serum cholesterol levels. The extent of influence varies significantly from person to person. HDL cholesterol, known as good cholesterol, is an important scavenger of surplus cholesterol by transporting it from cell membrane to the liver, where it is degraded or converted into bile acids. The increase in HDL cholesterol level is known to have protective effect on the risk of coronary heart disease. A number of mechanisms involving cholesterol itself and a number of hormones regulate the synthesis, uptake and metabolism of cholesterol. HMG-CoA Reductase is a key reaction in the biosynthesis of cholesterol.

Bile and Cholesterol

Bile is a yellow-green aqueous solution whose major constituents include bile acids, cholesterol, phospholipids, and the pigment biliverdin (De Smet et al., 1994; Hofmann, 1994). It is synthesized in the pericentral hepatocytes of the liver, stored and concentrated in the gallbladder inter-digestively, and released into the duodenum after food intake. Bile functions as a biological detergent that emulsifies and solubilizes lipids, thereby playing an essential role in fat digestion. This detergent property of bile also confers potent antimicrobial activity, primarily through the dissolution of bacterial membranes (Begley et al., 2005). The primary bile acids, cholic and chenodeoxycholic acid are synthesized *de novo* in the liver from cholesterol. The solubility of the hydrophobic steroid nucleus increases by conjugation of an *N*-acyl amidate with either glycine (glycoconjugated) or taurine (tauroconjugated) prior to secretion. The resulting molecules are therefore amphipathic and can solubilize lipids to form mixed micelles. Bile acids are efficiently conserved under normal conditions by a process termed enterohepatic

recirculation. Conjugated and unconjugated bile acids are absorbed by passive diffusion along the entire gut and by active transport in the terminal ileum (Carey and Duane, 1994). Reabsorbed bile acids enter the portal bloodstream and are taken up by hepatocytes, reconstituted, and resecreted into bile. Approximately 5% of the total bile acid pool (0.3 to 0.6 g) per day eludes epithelial absorption and may be extensively modified by the indigenous intestinal bacteria (Bortolini et al., 1997). One important transformation is deconjugation, a reaction that must occur before further modifications are possible (Batta et al., 1990). Deconjugation is catalyzed by bile salt hydrolase (BSH) enzymes (EC 3.5.1.24), which hydrolyzes the amide bond and liberates the glycine/taurine moiety from the steroid core. The resulting acids are termed unconjugated or deconjugated bile acids (Begley et al., 2006).

Treatment for Hypercholesterolemia

3-Hydroxy 3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors, also known as statins, are considered the most effective drugs in the management of hypercholesterolemia and prevention of atherosclerosis-related disorders (Vaughan et al., 2000; Cortese and Liberatoscioli, 2003). Statins are selective inhibitors of HMG CoA reductase, the rate-limiting enzyme of cholesterol biosynthesis, reducing low-density lipoprotein (LDL), very low density lipoprotein (VLDL) and triglyceride levels (Lutgens et al., 2004). Besides lipid lowering, statins have additional effects on atherosclerosis vascular disease, that includes anti-inflammatory (Sparow et al., 2001), anti-thrombotic properties (Halcox and Deanfield, 2004) and improve the endothelial function (Wassmann et al., 2003).

Statins competitively inhibit HMG-CoA reductase, the rate-limiting enzyme of the mevalonate pathway, thereby decreasing intracellular cholesterol synthesis. The resulting decrease in hepatic intracellular cholesterol concentration results in compensatory increase in the expression of hepatic LDL receptors, which clear LDL from the circulation (Lutgens et al., 2004).

Currently, the high cost of medicines is a limitation for pharmacological therapy adherence. Therefore, alternative strategies for CVD prevention, such as dietary therapy, have

received considerable attention of scientific community (Cavallini et al., 2009).

Significance of Some Probiotic Strains

Some of the products available in the USA market are listed in Table-1. Some commercially available strains are listed below:

Lactobacillus acidophilus

Lactobacillus acidophilus, being the natural inhabitant of intestine and possessing bile-salt hydrolase activity, can be exploited for the manufacture of acidophilus milk and its application as a means for reducing cholesterol level is recommended. Anderson and Gilliland et al (1985) reported that *Lactobacillus acidophilus* reduces the blood cholesterol by direct breakdown of cholesterol and deconjugation of bile salt. Anderson and Gilliland (1999) also examined effects of consumption of one daily serving of yogurt on serum lipids and found a significant reduction in serum cholesterol by performing two controlled clinical studies. Therefore, it can be concluded that since every 1% reduction in serum cholesterol concentration is associated with an estimated 2% to 3% reduction in risk for coronary heart disease, regular intake of fermented milks containing an appropriate strain of *L. acidophilus* has the potential of reducing risk for coronary heart disease by 6 to 10%.

The cholesterol-reducing abilities of six strains of *L. acidophilus* were investigated and it was reported that *in vivo* cholesterol lowering ability was due to the assimilation of cholesterol by *L. acidophilus* cells or/and attachment of cholesterol to the surface of *L. acidophilus* cells. Sarkar (2003) in his study reported the factors influencing the efficacy of acidophilus milk to lower serum cholesterol and the type of milk employed for product manufacture, in addition data on age, sex, food habits and initial concentration of cholesterol of test subjects was noted before after treatment. Liang and Shah (2005) screened eleven strains of lactobacilli and analyzed bile salt deconjugation ability, bile salt hydrolase activity (BSH) and co-precipitation of cholesterol with deconjugated bile. *Lactobacillus acidophilus* strains had higher deconjugation ability than *L. casei* strains. Cholesterol co-precipitation with deconjugated bile increased with decreasing pH. *L. acidophilus* showed highest deconjugation ability

and BSH activity towards bile mixtures that resembled the human bile, and may be a promising candidate to exert beneficial bile deconjugation activity *in vivo*.

The study performed by Kim and coworkers (2008) characterized the factors responsible for the cholesterol reduction by *Lactobacillus acidophilus* ATCC 43121. The results showed that the cell-free supernatant (CFS) produced by ATCC 43121 in the presence of bile salts could also reduce the cholesterol in the broth, unlike previous reports which suggested a mechanism by live cells only.

Lactobacillus plantarum

In a study conducted by Nguyen *et al.*, (2007), a strain of *Lactobacillus plantarum*, *L. plantarum* PH04 was fed to hypercholesterolemic mice with 10^7 CFU per mouse per day for 14 days. Compared with a control group, the serum cholesterol and triglycerides were respectively 7% and 10% lower in the group fed *L. plantarum* PH04 and fecal lactic acid bacteria increased while no other significant differences ($P < 0.05$) in body weight, visceral weight index or bacteria translocation between two groups were observed. The results indicated that *L. plantarum* PH04 could be effectively used as a probiotic with cholesterol-lowering activities. In another study made by Ha *et al.*, (2006) *Lactobacillus plantarum* strains were isolated from human faeces and evaluated for bile salt hydrolase (BSH) production and its effects on serum cholesterol level. The cholesterol lowering effect by *L. plantarum* CK 102 could be utilized as an additive for health-assistance foods. In conclusion, these results suggest that the *L. plantarum* strains could be used commercially as a Probiotic with sound cholesterol lowering activity.

Lactobacillus casei

Initial studies in poultry have demonstrated the ability of food fermented or inoculated with *Lactobacillus casei* and other lactic acid bacteria to significantly lower serum levels of total cholesterol and/ or LDL (Mohan *et al.*, 1996). Takeshi (2003) reviewed the biological activities of *L. casei* that favorably influenced human health. Liong and Shah, (2004) evaluated the combination of *Lactobacillus casei* ASCC 292 and six prebiotics, namely, sorbitol, mannitol, maltodextrin, high-amylose maize,

fructooligosaccharide (FOS) and inulin, in order to determine probiotic activity that would remove the highest level of cholesterol. The concentration of *L. casei* ASCC 292 had the most significant quadratic effect on all responses studied. In another study by same workers in 2006, the effectiveness of 3 synbiotic diets [(a) containing *Lactobacillus casei* ASCC 292 and fructooligosaccharides (LF diet), (b) containing *L. casei* ASCC 292 and maltodextrin (LM diet), and (c) containing *L. casei* ASCC 292, fructooligosaccharide, and maltodextrin (LFM diet)] were evaluated to reduce serum cholesterol in male Wistar rats. Results from this study showed that the synbiotic diet that contained *L. casei* ASCC 292, fructooligosaccharide, and maltodextrin beneficially altered cholesterol levels and produced a healthier bowel microbial population without translocation of lactobacilli to other organs (Liong and Shah, 2006).

Similarly, four selected *Lactobacillus casei* strains were examined by Minelli *et al.* (2004) for their potential use as novel probiotics in rats by evaluating their technological performances, i.e. *in vitro* adhesion capacity and intestinal transit tolerance after oral administration in fermented milks. Serum, tissue and faecal samples were analyzed before and during treatments. In treated rats it was reported that the levels of serum triglycerides, cholesterol, transaminase and total bilirubin decreased. In addition, microbiological and haematological parameters indicated that all four *L. casei* strains presented favourable strain-specific properties for their utilization in functional, health-favouring foods (Minelli *et al.*, 2004). Kawase *et al.* (2000) reported a decrease of triglyceride levels in humans by with combined supplementation of *L. casei* and *S. thermophilus*.

Lactobacillus bulgaricus

Lactobacillus bulgaricus is known to everyone as dairy starter bacteria that make yoghurt (a type of fermented milk) in symbiosis with *Streptococcus thermophilus*. *Lactobacillus bulgaricus* is an acid-producing bacterium and in general, it occurs in dairy products and some plant products. In 1979, the first trial to evaluate the effects of lactic acid bacteria on serum cholesterol levels in human subjects was conducted. Fifty four volunteers participated in a randomised cross over trial; the results of which revealed reductions of between 5-10% in serum cholesterol levels after several weeks of

moderate consumption of yoghurt fermented with *Lactobacillus bulgaricus* and *S. thermophilus* (Fried *et al.*, 1979]. Studies in rats have demonstrated the ability of fermented food inoculated with *Lactobacillus bulgaricus* to significantly lower serum levels of total cholesterol (Beena and Prasad, 1997).

Lactobacillus fermentum

Lactobacillus fermentum is a normal resident of the human gut microflora and is reported to be able to adhere to the epithelial cells, with a preference for the small intestine (Henriksson *et al.*, 1991; Rojas *et al.*, 2002). It has also been shown to colonize the intestine after oral administration (Reid *et al.*, 2001). Moreover, it produces surface-active components, which can inhibit the adhesion of uropathogenic bacteria (Gusils and Oliver, 1999; Heinemann *et al.*, 2000). The effect of *L. fermentum* on representative microbial populations and overall metabolic activity of the human intestinal microbiota was investigated using a three-stage continuous culture system. In addition, the use of galacto-oligosaccharides as a prebiotic to enhance growth and/or activity of the *Lactobacillus* strain was also evaluated. Administration of *L. fermentum* resulted in a decrease in the overall bifidobacterial population (ca. 1 log unit). In the *in vitro* system, no significant changes were observed in the total bacterial (*Lactobacillus*, *Bacteroides*, and clostridial) populations through *L. fermentum* supplementation. Acetate production decreased by 9 to 27%, while the propionate and butyrate concentrations increased considerably (50 to 90% and 52 to 157%, respectively). A general, although lesser, increase in the production of lactate was observed with the administration of the *L. fermentum* strain. Supplementation of the prebiotic to the culture medium did not cause statistically significant changes in either the numbers or the activity of the microbiota, although an increase in the butyrate production was seen (29 to 39%). Results from this *in vitro* study suggest that *L. fermentum* KC5b is a probiotic candidate, which may affect cholesterol metabolism. The short-chain fatty acid concentrations, specifically the molar proportion of propionate and/or bile salt deconjugation are probably the major mechanism involved in the purported cholesterol-lowering properties of this strain.

Other lactobacilli

Taranto *et al.* (2000) reported that administration of *Lactobacillus 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. In a study conducted by Usman (2000) *Lactobacillus gasseri* was shown to lower serum lipids in hypercholesterolemic rats, receiving nonfermented milk produced from *L. gasseri*. The total reduction in cholesterol and LDL levels was found to be 42 and 64%, respectively.

Bacillus coagulans

Bacillus coagulans, formerly known as *Lactobacillus Sporogenes*, is a shelf stable, non-pathogenic Gram positive spore-forming bacteria that produces L(+) lactic acid (dextrorotatory) in homofermentation conditions. In particular, *B. coagulans* strains were used to reduce serum cholesterol in certain formulations (Mohan, 1990). Seok, (1987) concluded that *L. sporogenes* lowers LDL cholesterol by eliminating it directly from inside the intestines before it can be absorbed into the blood stream. In another clinical study, *L. sporogenes* not only lowered total serum cholesterol and LDL cholesterol in humans, it also improved the ratio of "good" HDL cholesterol to total cholesterol. The American Heart Association says that HDL cholesterol is beneficial because, they quote that- "high levels of HDL seem to protect against heart attack".

US patent was given to a therapeutic composition including *Bacillus coagulans*, in combination with bifidogenic oligosaccharides or other cholesterol-reducing agents for use in reducing LDL cholesterol and serum triglycerides (US patent 7232571). This unique microorganism proved effective in lowering cholesterol by 104 points in a three-month study performed at the G.B. Pant hospital in New Delhi, India. There was a highly significant reduction in the LDL cholesterol levels, and a small but significant increase in HDL cholesterol levels. Use of this microorganism is an attractive alternative to drug therapy since there are no side effects. It also provides an excellent preventative effect against various diseases of the intestine according to one researcher. [Information:www.needs.com/insights.probiotics.asp]

Bifidobacterium longum

Kim et al., (2004) purified Bile salt hydrolases from *Bifidobacterium bifidum* ATCC 11863, *Bifidobacterium infantis* KL412, *Bifidobacterium longum* ATCC 15708, *Bifidobacterium longum* KL507, and *Bifidobacterium longum* KL515 to a maximum extent. All BSH enzymes from five strains hydrolyzed six major human bile salts, and showed a better deconjugation rate on glycine-conjugated bile salts than on taurine-conjugated forms. Tahri *et al.* (1966) studied the removal of cholesterol by *B. longum*, *B. infantis*, *B. breve*, *B. animalis* and *B. thermophyllum* in the presence of bile salts and observed that the removal of cholesterol from the growth medium by *Bifidobacteria* strains is due to both bacterial assimilation and precipitation of cholesterol. In one study, the hypocholesterolaemic effect of yoghurt supplemented with *Lactobacillus acidophilus* and *Bifidobacterium longum* have been assessed on twenty-nine healthy women, aged 19-56 years. Fifteen of these were normocholesterolaemic and 14 women were hypercholesterolaemic. They found that long-term daily consumption of 300 g yoghurt over a period of 21 weeks (control and synbiotic) increased the serum concentration of HDL cholesterol and lead to the desired improvement of the LDL/HDL cholesterol ratio [60] (Kiessling *et al.*, 2005).

Mechanistic Approach of Probiotic Action

There are number of reports regarding health benefits of probiotics and their promising role as safe and natural therapeutics (Ötles *et al.*, 2003). Probiotics could be helpful in controlling excess weight by reducing glucose absorption from the intestine and increase the metabolic use of glucose, though the expected results could only be achieved with adoption of balanced and healthy lifestyle. Moreover, probiotic lactobacilli strains are also known to produce conjugated linoleic acid (CLA), which has anti-obesity effect. There are various reports in animal subjects inferring the role of lactobacilli in alleviating the symptoms of hypercholesterolemia by lowering the levels of serum cholesterol to a significant level (Gilliland *et al.*, 1985; Suzuki *et al.*, 1992; Derodas *et al.*, 1996). Ashar and Prajapathi (1998) confirmed the hypocholesterolemic activity of *Lactobacillus acidophilus* in human beings.

Probiotic strains assimilate cholesterol for their own metabolism. The organisms bind to the

cholesterol molecule, degrading it to its catabolic products. Thus, the cholesterol level gets reduced indirectly by deconjugating the cholesterol to bile acids, thereby reducing the total body pool. The bile acids commonly occur in the form of bile salts with glycine and taurine. The cholesterol lowering effect of *L. acidophilus* is due to inhibition of 3-hydroxy 3-methyl glutamyl CoA reductase, which is a rate limiting enzyme and responsible for the endogenous cholesterol biosynthesis in the body. The enzyme is also responsible for deconjugation of bile acids in the intestine, which is an important mechanism in reducing the cholesterol concentrations. Increase in deconjugation of bile acids also results in the greater excretion of bile salts from the intestinal tract that again stimulates synthesis and replacement of bile acids from cholesterol levels in the body (Naidu *et al.*, 1999). The lowering of triglycerides may be due to production of lipase by probiotic organisms, which breaks larger molecules of fats in to simple and easily digestible substrates.

One beneficial effect that has been suggested to result from human consumption of LAB is a reduction in serum cholesterol levels, as demonstrated in several human and animal studies (Pereira and Gibson, 2002). This can partly be ascribed to the enzymatic deconjugation activity of bile acids (Klaver *et al.*, 1993; Tahri and Schneider, 1996; Usman, 2000). Deconjugated bile salts are less soluble and less efficiently reabsorbed from the intestinal lumen than their conjugated counterparts, which results in excretion of larger amounts of free bile acids in feces (De Smet *et al.*, 1994; De Rodas *et al.*, 1996). Also, free bile salts are less efficient in the solubilization and absorption of lipids in the gut (Reynier *et al.*, 1981). Therefore, the deconjugation of bile acids by LAB bacteria could lead towards a reduction in serum cholesterol either by increasing the demand of cholesterol for de novo synthesis of bile acids to replace that lost in feces or by reducing cholesterol solubility and, thereby, absorption of cholesterol throughout the intestinal lumen. Moreover, Gilliland *et al.*, (1985) have observed a significant relationship between cholesterol assimilation by lactobacilli and their degree of bile deconjugation.

Bile salt hydrolase (BSH), the enzyme responsible for bile salt deconjugation during enterohepatic circulation, has been detected in several LAB species indigenous to the

gastrointestinal tract (Chikai et al., 1987; Walker and Gilliland, 1993; De Smet et al., 1994). It has also been suggested that BSH activity should be a requirement in the selection of probiotic organisms with cholesterol-lowering properties, as non deconjugating organisms do not appear to be able to remove cholesterol from the culture medium to any significant extent (Tahri et al., 1996, 1997).

Effect of Fermented Dairy Products in Lowering Of Blood Cholesterol

Mann and Spoerry (1974) were the first to report that consumption of fermented milk was associated with reduced serum cholesterol levels in the Maasai people. This stimulated much interest in the cholesterol lowering effects of fermented milks and lactic acid bacteria. Several animal studies have shown that administration of fermented milks or specific strains of lactic acid bacteria are effective in lowering blood cholesterol levels. Studies in human subjects, however, have yielded conflicting results. The most frequently used probiotics found in dairy-based food products are Lactobacilli and Bifidobacteria. Since these belong to the indigenous human microflora, they have a long history of safe use and there are evidences to support their positive roles, some of these have been designated as GRAS (generally regarded as safe) by the FDA (Food and Drug Administration) due to their long history of use in food fermentations (Teitelbaum and Walker, 2002).

Human and animal studies have suggested that the use of dairy products fermented with probiotics (lactic acid bacteria and bifidobacteria) may reduce serum lipid levels (Meydani and Ha, 2000; de Vrese et al., 2001; Heyman, 2001) Two studies with normal-lipidemic subjects reported that probiotic administration resulted in a reduction in serum triglycerides (19% and 27%, respectively), along with slight changes in serum total and LDL cholesterol.⁹⁴ The proposed mechanism by which probiotics may decrease serum cholesterol is suggested to be related to the fermentation of indigestible dietary carbohydrates. Products of bacterial fermentation, specifically short-chain fatty acids, may inhibit cholesterol synthesis in the liver and/or mobilize plasma cholesterol to the liver (Rafter, 2002) Some gastrointestinal bacteria may also prevent cholesterol absorption by

deconjugating bile salts that then affect cholesterol metabolism.

Future Perspectives

Gill and Guarner (2004) reported that there is unequivocal evidence that administration of probiotics could be effective in the treatment of acute infectious diarrhoea in children and the prevention of antibiotic associated diarrhoea and nosocomial/community acquired diarrhoea.

The future will see the development of new, well-characterized, scientifically proven probiotic strains with specific health benefits. There are enough evidences to support the beneficial effects of probiotics on hosts over a wide range of clinical conditions. However, some issues like dosage and viability of probiotic strains, industrial standardization and safety aspects need to be dealt with. At present, cholesterol, cancer and immunology are the three major areas of research on probiotics. Genetic engineering and other approaches are being used to enhance the beneficial effects of probiotic microbes. Supplementation of promising strains of probiotic organisms may offer exciting solution to minimize the problem of high cholesterol levels in human beings. However, extensive research is required to screen the potent probiotic strains and their evaluation for the effective management of good and bad cholesterol in the body and the sustainability of the desired results. In addition to the clinically proven benefits (grade A recommendations) described above, the use of probiotics for the prevention and management of over expressed immune function such as atopy and inflammatory bowel diseases, and for enhancing immune function and improving efficacy of vaccines in population groups with less than optimum immune functions (for example, infants, elderly, immunocompromised) hold great promise.

Treatment with microencapsulated LF11976 formulation produces significant reductions in serum total cholesterol, LDL cholesterol, and serum triglyceride levels in diet-induced hypercholesterolemic hamsters. Findings suggest the potential of the oral microencapsulated probiotic cell formulation as a functional nutritional alternative for managing excessive serum cholesterol and triglyceride levels (Bhathena J, Martoni C, Kulamarva A et al

2009). With the increased evidence of multidrug resistance among pathogens and a continued failure to manage gastrointestinal virus infections, plus a desire by consumers to use natural methods for health maintenance rather than long-term chemotherapeutic agents, the time is right for probiotics to be taken seriously. It is also time for scientists to provide the data, which give a basis and mechanism of action for the human utilization of well-studied organisms.

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Table-1 and Figure-1 follow.....

Biology and Medicine

Table-1

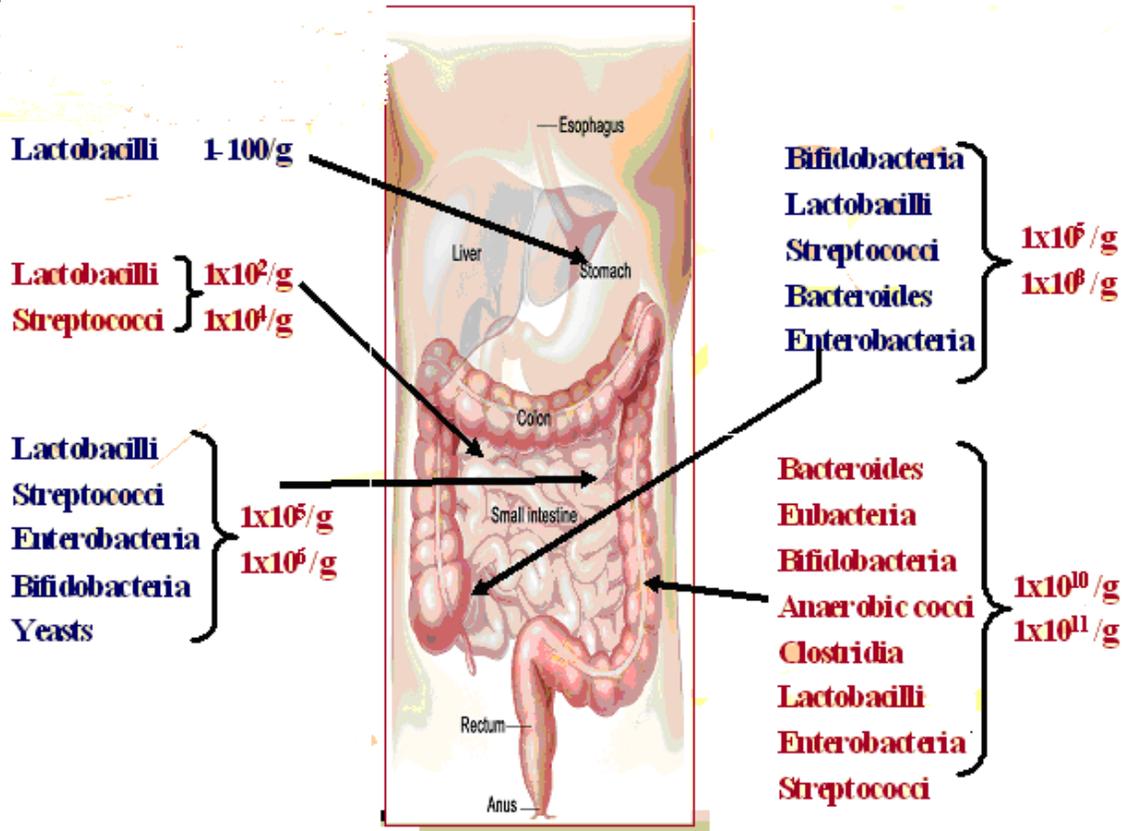
Some products available in the USA which have been evaluated in controlled human studies as indicated

Indication	Strain (Commercial Strain Designation)	Products (Format)
Infant diarrhea	<i>L. rhamnosus</i> GG (LGG)	Culturelle (capsule) www.culturelle.com
	<i>L. casei</i> DN-114 001 (Immunitas)	DanActive (fermented milk) www.danactive.com
Inflammatory bowel conditions (primary evidence in pouchitis)	8-strain combination of 3 <i>Bifidobacterium</i> strains, 4 <i>Lactobacillus</i> strains and <i>S. thermophilus</i>	VSL#3 (powder) www.vsl3.com
Antibiotic associated diarrhea; <i>C. difficile</i>	<i>S. cerevisiae</i> (<i>S. boulardii</i>)	Florastor (powder) www.florastor.com Lalflor (capsule) www.institut-rosell.com
	<i>L. rhamnosus</i> GG (LGG)	Culturelle (capsule) www.culturelle.com
	<i>L. casei</i> DN-114 001	DanActive (fermented milk) www.danactive.com
	<i>L. acidophilus</i> CL1285 plus <i>L. casei</i> Lbc80r	BioK+CL1285 (fermented milk, soy milk, capsule) www.biokplus.com
Gut transit time/bowel function	<i>B. animalis</i> DN-173 010 (<i>Bifidus regularis</i>)	Activia (yogurt) www.activia.com
	<i>L. casei</i> Shirota	Yakult (daily dose drink) www.yakultusa.com
Keeping healthy	<i>L. reuteri</i> ATCC 55730 (Protectis)	BioGaia Chewable Gut Health Tablets BioGaia Gut Health Probiotic Straws www.everidis.com
	<i>L. casei</i> DN-114 001	DanActive (fermented milk) www.danactive.com
Lactose intolerance	Most strains <i>L. bulgaricus</i> and/or <i>S. thermophilus</i>	All yogurts with live, active cultures
Colic in infants	<i>L. reuteri</i> ATCC 55730 (Protectis)	Reuteri drops www.biogaia.com
Immune support	<i>B. lactis</i> HN019 (HOWARU or DR10)	Strain sold as an ingredient for dairy and supplement products – contact Danisco www.danisco.com
	<i>L. rhamnosus</i> GG (LGG)	Culturelle (capsule) www.culturelle.com Danimals (drinkable yogurt) www.danimals.com
	<i>L. casei</i> Shirota	Yakult (daily dose drink) www.yakultusa.com
	<i>B. lactis</i> Bb-12	Good Start Natural Cultures (infant formula) www.verybestbaby.com/GoodStart/Overview.aspx LiveActive cheese www.kraft.com/Brands/featured-brands/live_active.htm Yo-Plus yogurt www.yo-plus.com
	<i>L. casei</i> DN-114 001	DanActive (fermented milk) www.danactive.com
Vaginal applications	<i>L. rhamnosus</i> GR-1 plus <i>L. reuteri</i> RC-14	Fem-Dophilus (capsules) www.urexbiotech.com ; www.jarrow.com
Irritable bowel syndrome symptoms	<i>B. infantis</i> 35264 (Bifantis™)	Align (capsules) www.allanqi.com
	<i>L. plantarum</i> 299v (Lp299v)	Verb Good Belly (juice)

Source - Internet

Figure-1

TYPICAL MICROFLORA OF THE GASTRO-INTESTINAL TRACT OF MAN



Source - Internet

Biologs