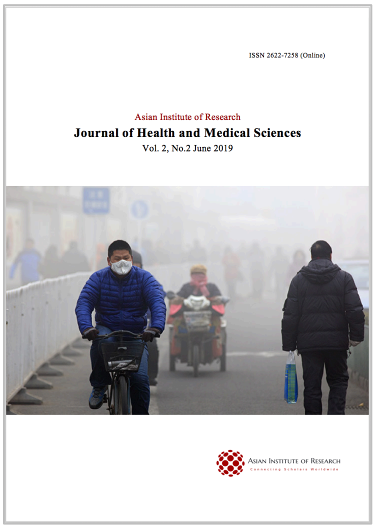

Journal of Health and Medical Sciences

Habib, Mohammad Asadul, Mamun, Md. Abdullah Al, Kabir, Md. Ruhul, Chowdhury, Mohammad Hasan, Tumpa, Farzana Afroz, and Nayeem, Jannatul. (2019), Probiotics for Cardiovascular Diseases, Hypertension, Hypercholesterolemia, and Cancer Condition: A Summary of the Evidence. In: *Journal of Health and Medical Sciences*, Vol.2, No.2, 131-141.

ISSN 2622-7258

DOI: 10.31014/aior.1994.02.02.30

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The Asian Institute of Research
Journal of Health and Medical Sciences
Vol.2, No.2, 2019: 131-141
ISSN 2622-7258

DOI: 10.31014/aior.1994.02.02.30

Probiotics for Cardiovascular Diseases, Hypertension, Hypercholesterolemia, and Cancer Condition: A Summary of the Evidence

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Abstract
For a few decades, bacteria called probiotics have been added to some foods because of their salutary effects for human health. Although only various clinical studies have been conducted, that probiotic could be feasible in obstructing and treating some leading diseases such as cardiovascular disease, hypertension, hypercholesterolemia, cancer & other potential diseases. Probiotics have been suggested to reduce cholesterol via various mechanisms without any deleterious effect on human health. Among their various effects, anti-cancer properties have been highlighted in recent years. Such effect includes suppression of the growth of microbiota implicated in the production of mutagens and carcinogens, alteration in carcinogen metabolism and protection of DNA from oxidative damage as well as regulation of the immune system. Outcomes from animals and human studies suggest a tolerable cholesterol-lowering action of dairy products fermented with adequate strain(s) of LAB (lactic acid bacteria) and bifidobacteria. Mechanistically, probiotic bacteria ferment food-derived indigestible carbohydrates to produce short-chain fatty acids in the gastrointestinal tract, which can then cause a reduction in the systemic levels of blood lipids by suppressing hepatic cholesterol synthesis and/or redistributing cholesterol from plasma to the liver. Besides, some bacteria may intervene with cholesterol absorption from the gut by deconjugating bile salts and therefore affecting the metabolism of cholesterol, or by directly embodying cholesterol which is then helpful for reducing coronary heart disease, including hypertension and hypercholesterolemia. In this review, we will focus mainly on reviewing existing studies concerning the effects of probiotic food in ameliorating health and treating diseases particularly cardiovascular diseases, hypertension, hypercholesterolemia & cancer.

Keywords: Cholesterol, Functional Foods, Bifidobacteria, Cancer, Hypertention

Introduction

Probiotics (i.e., subsisting microbial food supplements) considered as a functional food, have obtained much attention and they target the gastrointestinal microbiota (Ziemer and Gibson, 1998; Saarela et Al., 2002). It is exactly documented that the large intestine is one of the most deeply populated ecosystems in nature comprising of over 500-1,000 different species of bacteria (Xu and Gordon, 2003; Meyer and Stasse-Wolthuis, 2009) of which bifidobacteria are usually predicted to be health improving and favorable (Kimura et al., 1997). Impacts of probiotics can be affected by the hereditary attributes of intestinal microbiota in every person, natural factors, diet, and use of antibiotics. Additionally, different impacts of probiotics in various ages of consumers are expected (Salminen and Isolauri, 2006; Eckburg et al., 2005).

A. Probiotics

The name probiotic comes from the Greek 'pro bios' which implies 'for life' (Gismondo et al., 1999). The term "probiotics" was 1st introduced in 1953 by Werner Kollath. In 1989, Roy Fuller recommended a definition of probiotics that has been wide used: "A live microorganism feed supplement that beneficially affects the host animal by raising its intestinal microbial balance". Parker in 1974, proposed that "probiotics are organisms and substances that contribute to intestinal microorganism balance" (Parker, 1974). Salminen et al. (1998) outlined probiotics as the 'food that contains live microorganisms useful to health', whereas Marteau et al. (2001) outlined them as 'microbial cell preparations or parts of microorganism cells that have a useful impact on the health and well-being. Some fashionable definitions embrace a lot of exactly a preventive or therapeutic action of probiotics. Charteris et al. (1997) For instance, outlined probiotics as 'microorganisms that, when ingested, could have a positive impact within the interference and treatment of a particular pathologic condition. The presently used accord definition of probiotics was advised by the Planet Health Organization and by the Food and Agriculture Organization of the U.S. in 2001. They outlined probiotics as "live microorganisms that when administered in adequate amounts confer a health benefit on the host" (Shah, 2007).

Probiotics are microorganisms, molds, yeast. Among them, the carboxylic acid manufacturing microorganism is more common. A number of the species are (Srionnual et al., 2007) -

1. Lactic acid manufacturing microorganism (LAB): *Lactobacillus*, *Bifidobacterium*, *Streptococci*.
2. Non lactic acid manufacturing microorganism species: *Bacilli*, *Propionibacterium*.
3. Non-pathogenic yeasts: *Saccharomyces*.
4. Non reproductive structure forming and non-flagellated rod or coccobacilli.

The *lactobacillus* species facilitate in production of enzymes to digest and metabolize proteins and carbohydrates. Necessary probiotic microorganism species helpful in the oral cavity are *L. Acidophilus*, *L. Case*, *L. Rhamnosus Gc*, *L. Sporogens*, *L. Bulgaricus*, *L. Johnson*, *L. Termophilus*, *L. Bifidum*, *L. Reuteri*, *L. Salivaricus*, *L. Paracasei*, *S. Thermophilus*, *S. Salivarius*, *W. Siberia* and *Bifidobacterium*. They aid in the synthesis of vitamin B, fat-soluble vitamin and facilitates breakdown of digestive juice salts. They're sometimes distributed in gel, paste, powder and liquid forms. Commonest vehicles for probiotics in oral health embrace lozenges, tablets, yoghurt, cheese, milk and mouth rinse (Kamal et al., 2013).

Fuller in 1989 listed the subsequent as the options of a good probiotic (Narang et al., 2011) -

1. It ought to be a strain, that is capable of exerting a useful impact on the host animal, e.g. magnified growth or resistance to sickness.
2. It ought to be non-pathogenic and non-toxic.
3. It ought to be present as viable cells, ideally in massive numbers.
4. It ought to be capable of living and metabolizing within the gut surroundings.
5. It ought to be stable and capable of remaining viable for periods under storage and field conditions.

Methods

We searched for articles in the PubMed (1974–2013), from which we also found some additional relevant references. The keywords were 'beneficial bacteria', 'probiotics', '*lactobacilli*', 'lactic acid bacteria' and 'bifidobacteria'. We focused on microbiological studies and clinical trials. Specifically, we found relevant information from original articles and reviews regarding the role of probiotics in human health and nutrition, probiotics and health effect, probiotic and cancer, etc. These have been overviewed to find out the overall function of probiotic on the human body and also find out how probiotic food preventing and treating some major diseases such as cardiovascular disease, hypertension, hypercholesterolemia, cancer & other potential diseases.

Result:

Kim et al. (2011) reported that consumption of Kimchi (Korean Fermented Vegetables) as a probiotic food leads to a reduction in body weight, BMI, and percent body fat in overweight and obese subjects, which might reduce the risk for CVD and metabolic syndrome related to the metabolic parameters. Probiotic bacteria, which take part in the bile salt metabolism, can be useful in patients with CVD (Jones et al., 2013).

Yamamoto et al. (1994) suggested that the peptides liberated from casein by the proteinase in the culture medium showed antihypertensive effect in Spontaneously Hypertensive (*SHR*) *rat.* Therefore, this soymilk could potentially be used as a dietary therapy to reduce the risks of hypertension.

The use of bioactive foods has been recommended for the cure and prevention of human diseases like hypercholesterolemia (Rao, 2003). Bile acids are essential for absorption of cholesterol molecules from the intestinal lumen since cholesterol is hardly soluble in water. The so-called cholesterol micelle formation and thus cholesterol absorption is also impaired via deconjugation of bile salts. This information is used for production of probiotic strains to treat hypercholesterolemia. The activity of BSH (a non-allosteric, oxygen non-sensitive enzyme that is found inside the cell and its activity is dependent on an optimum pH (5 ~ 6) and an adequate biomass density (Begley et al., 2006 and Li, 2012) and other bile salt modifiers may lower cholesterol level (Martin et al., 2007 and Jones et al., 2008).

Bacterial fermentation has been reported to produce some specific end products, such as Short-chain fatty acids, that allegedly reduce the risk of cancer (Cho et al., 2010).

A placebo-controlled trial showed that oral administration of *Lb. salivarius* UCC118 in IL-10 KO mice decreased the prevalence of colon cancer (O'mahony et al., 2001). Regular consumption of beverages containing *Lb. casei* Shirota and soy isoflavones was inversely associated with the incidence of breast cancer in Japanese women (Toi et al., 2013).

Table 1: Impact of probiotics on the treatment of cardiovascular diseases

Reference	Study name	Findings
Gilliland et al., 1985 & Rašić et al., 1992	Assimilation of cholesterol by *Lactobacillus acidophilus*. Assimilation of cholesterol by some cultures of lactic acid bacteria and bifidobacteria.	There is also some in vitro evidence to support the hypothesis that certain bacteria can assimilate (take up) cholesterol. It was reported that *Lactobacillus acidophilus* and *Bifidobacterium bifidum* had the ability to assimilate cholesterol in vitro studies, but only in the presence of bile and under anaerobic condition.
Hylemon, 1985	Metabolism of bile acids in intestinal microflora.	Probiotics' mechanism of action on cholesterol reduction include physiological actions of the end products of fermentation short chain fatty acids (SCFAs), cholesterol assimilation, cholesterol binding to bacterial cell walls, and deconjugation of bile acids which is catalyzed by conjugated bile acid hydrolase enzyme produced exclusively by bacteria. It has been well documented that microbial bile acid metabolism is an irregular probiotic effect involved in the therapeutic role of some bacteria. Deconjugation ability is widely found in many intestinal bacteria including genera *Enterococcus, Peptostreptococcus, Bifidobacterium, Fusobacterium*, *Clostridium, Bacteroides,* and *Lactobacillus*.
Klaver and Van Der Meer, 1993	The assumed assimilation of cholesterol by *Lactobacilli* and *Bifidobacterium bifidum* is due to their bile salt-deconjugating activity.	They concluded that the removal of cholesterol from the growth medium in which *L. acidophilus* and *Bifidobacterium spp*. were growing was not due to assimilation but due to bacterial bile salt deconjugase activity.
Mann and Spoerry, 1974	Studies of a surfactant and cholesteremia.	As a result of low consumer compliance of low-fat diets, attempts have been made to identify other dietary components that can reduce blood cholesterol levels. These have included investigations into the possible hypocholesterolaemic properties of milk products, especially in a fermented form. An 18% fall in plasma cholesterol occurred after feeding 4-5 L of fermented milk per day for three weeks.
Usman and Hosono, 1999	Binding of cholesterol with lactic acid bacterial cells.	Cholesterol binding to cell surfaces is the mechanism by which *L. gasseri* could remove cholesterol from the medium. Since there was a significant variation in the cholesterol binding ability in 28 different strains of *L. gasseri*, it has been suggested that cholesterol-binding property is growth- and strain-specific, a difference that originates from differing chemical and structural characteristics of bacterial cell wall peptidoglycans.

Table 2: Impact of probiotics on the treatment of hypertension

Reference	Study name	Findings
Aihara et al., 2005	Effect of powdered fermented milk with *Lactobacillus helveticus* on subjects with high-normal blood pressure of mild hypertension.	In this study were able to reduce blood pressure in patients with high-normal blood pressure or mild hypertension by daily feeding of tablets containing powdered milk fermented with *L. helveticus* CM4 for four weeks.
Appel et al., 1997	A clinical trial of the effects of dietary patterns on blood pressure.	In this clinical trial, dietary approaches to stop hypertension with almost 459 normotensive or mildly hypertensive subjects, which showed that a diet rich in fruits, vegetables, and low-fat dairy products (the so-called combination diet) was found to reduce blood pressure significantly.
Nakamura et al., 1995	Antihypertensive effect of sour milk and peptides isolated from it that are inhibitors of angiotensin I-converting enzyme.	In animal studies, the authors demonstrated that oral administration of Calpis sour milk or the peptides to spontaneously hypertensive rats was able to lower systolic blood pressure in these animals.
Seppo et al., 2003	A fermented milk high in bioactive peptides has a blood pressure-lowering effect in hypertensive subjects.	Studies in humans also have shown promise for the use of probiotic bacteria in the reduction of hypertension. In this study hypertensive subjects were fed milk fermented with *L. helveticus* LBK-16H containing bioactive peptides. At the end of 21 weeks, test subjects showed a significant lowering of their blood pressure.

Table 3: Impact of probiotics on the treatment of hypercholesterolemia

Reference	Study name	Findings
Ataie-Jafari et al., 2009	Cholesterol-lowering effect of probiotic yogurt in comparison with ordinary yogurt in mildly to moderately hypercholesterolemic subjects.	In humans, a study demonstrated that hypercholesterolemic patients fed probiotic yogurt containing *Lactobacillus acidophilus* and *Bifidobacterium lactis* were able to reduce their cholesterol levels compared to cohorts who consumed ordinary yogurt.
Bhathena et al., 2009	Orally delivered microencapsulated live probiotic formulation lowers serum lipids in hypercholesterolemic hamsters.	Several studies have reported lowering of cholesterol levels by probiotic bacteria. For example, hypercholesterolemic hamsters consuming microencapsulated live *L. fermentum* 11976 led to significant reductions in their serum total cholesterol and triglyceride levels as well as low density lipoprotein cholesterol levels.
Danielson et al., 1989 & Gilliland et al., 1985	Assimilation of cholesterol by *Lactobacillus acidophilus.* Anticholesterolemic property of *Lactobacillus acidophilus* yoghurt fed to mature boars.	Probiotic bacteria have demonstrated abilities to reduce blood cholesterol and are thought to work by several mechanisms including assimilation of cholesterol, binding cholesterol and bile acids to the cell surface thus inhibiting absorption from the small intestine.
Wang et al., 2009	Effects of *Lactobacillus plantarum* MA2 isolated from Tibet kefir on lipid metabolism and intestinal microflora of rats fed on high-cholesterol diet.	Similar results were seen in rats fed a high cholesterol diet supplemented with lyophilized *L. plantarum* MA2 to significant reductions in their serum total cholesterol and triglyceride levels as well as low density lipoprotein cholesterol levels.

Table 4: Impact of probiotics on different types of cancer

Reference	Probiotic strain	Subjects	Dose and duration of study	Efects (P<0.05)
El-Nezami et al., 2006	*Lactobacillus rhamnosus* LC705 and *Propionibacterium freudenreichii subsp. shermanii strains*	(i) Afatoxin-induced liver cancer (ii) 90 male students with high afatoxin level in urine	5 weeks , (1:1, wt: wt) at a dose of 2–5×10^{10} colony-forming units/day	61.5% reduction of a liver cancer biomarker which leads to reduced urinary excretion of afatoxin B1-N7guanine (AFB-N7-guanine)
Liu et al., 2013	*Lactobacillus plantarum* CGMCC, *Lactobacillus acidophilus*-11 and *Bifdobacterium longum*-88	(i) Colorectal cancer patients (ii) 150 patients (1;1 ratio of probiotic and placebo group)	(i) *Lactobacillus plantarum* CGMCC no.1258;10^{11}(CFU)/g (ii) *Lactobacillus acidophilus*;10^{11}CFU/g, (iii) *Bifidobacterium longum*-88$10^{10}$ (CFU/g) (iv) The patients administrated with probiotic 6 days preoperatively and 10 days postoperative.	Probiotics decreased the serum zonulin concentration, duration of postoperative pyrexia, duration of antibiotic therapy, and rate of postoperative infectious complications as well as inhibited the p38 mitogen-activated protein kinase signalling pathway.
Ma et al., 2010	*Lactobacillus casei Shirota* (LcS)	(i) Cervical cancer (ii) 54 women with an HPV-positive intra epithelial lesion	Daily administration of (Yakult) containing LcS for 6 months.	60 % reduction in human papilloma virus (HPV) associated infection and cervical cancer precursors.
Ohashi et al., 2002	*Lactobacillus acidophilus* L1	(i) Bladder cancer (ii) A total of 180 cases (mean age: 67 years, SD 10) and 445 population-based controls	200 g of yoghurt containing *L. acidophilus* L1 for 10 weeks	Habitual intake of lactic acid bacteria reduces the risk of bladder cancer.
Toi et al., 2013	*Lactobacillus casei* Shirota (LcS)	(i) Breast cancer (ii) 968 breast cancer patients (306 probiotic group; 662 control) aged 40 to 55.	Frequent consumption of Yakult containing *Lactobacillus casei Shirota* and isofavones from soy product for 2 years	Regular consumption of LcS and isofavones since adolescence was inversely associated with the incidence of breast cancer in Japanese women.

Discussion

An expanding number of clinical trials supporting the probiotic-dependent weakening of hypertension and hypercholesterolemia could give colossal help for the application of such cultures to improve cardiovascular health. Subsequently, dietary mediation to correct gut microbiota could be an imaginative nutritional therapeutic technique for hypertension. The knowledge gained on probiotic potential against cardiovascular diseases is still at the earliest stage and current discoveries propose that hypotensive impacts of probiotics are exceptionally encouraging and worth investigating to promote cardiovascular health. Probiotics have obtained expanding medicinal significance in view of their helpful impacts upon the host wellbeing. Oral administration of probiotics has various impacts, such as standardization of the intestinal microflora, improvement of the gastrointestinal obstruction, and hindrance of potential pathogens or carcinogenesis in the gut. Together with the enhancement of systemic immune or/and anti-inflammatory activities, probiotics may have an impact on the concealment of tumor development and development. While research center based investigations have exhibited encouraging outcomes that probiotics have antitumor impacts, the advantages ought not to be overstated before we get more outcomes from human subjects. In any case, more examinations are required for a superior comprehension of gut microbiota-host cross talk and biochemical networks underlying the control of hypertension. Randomized double-blind, placebo-controlled clinical trials ought to be done to pick up the acceptance of the broader medical community and to investigate the capability of probiotics as an alternative therapy for cancer control.

Future Challenges

Owing to their perceived health advantages, probiotics are currently widely added to yogurts and fermented milks (Özer et al., 2005; Menrad, 2003 and Stanton et al., 2001). However, the production of probiotics at industrial scale faces many challenges, as well as (i) the affordable production of probiotics; (ii) the advance of probiotic viability after storage, during the manufacturing method of the functional food and during transit through the abdomen.

A. Affordable production of probiotics

Low-cost production of concentrated cultures of probiotics are a key challenge to satisfy the increasing demand for probiotics in the market (Mattila-Sandholm et al., 2002). Probiotic micro-organisms are normally difficult to grow as they lack the biosynthetic capacity of most vitamins and amino acids, so culture media for probiotic production must be supplemented with both amino acids and vitamins (Altermann et al., 2005 & Remacle et al., 2004). The reduction of production costs at an industrial scale might start with the use of some agro-industrial residual effluents as cultivation media for probiotics. In this regard, effluents from fruit and vegetable processing usually contain high amounts of proteins, carbohydrates, lipids and vitamins.

B. Improving viability of probiotics

The quality of probiotic micro-organisms depend greatly on their viability that may be a basic fulfillment to reach and colonize the intestine (Lahtinen et al., 2005 & Tuomola et al., 2001). Probiotics must retain their viability during three important stages: (i) storage; (ii) manufacturing method of the functional food; (iii) transit through the stomach and small intestine. Therefore the viability of probiotics is an issue of vital importance from both associate economic and a technological viewpoint.

Conclusions

This review confirms the potential effectiveness of probiotics in disease interference and/or management by many mechanisms, for example, stimulating and decreasing the incidence of duration and complaints of rotavirus-induced or antibiotic-associated diarrhea as well as alleviation of complaints because of lactose intolerance, the concentration of cancer-promoting enzymes and/or putrefacient (bacterial) metabolites within the gut, general and irregular complaints of the gastrointestinal tracts in healthy people, allergies and atopic diseases in infants, Respiratory tract infections (common cold, influenza) and different infectious diseases as well as treatment of urogenital infections, etc. Probiotics food has beneficial effects on microbial aberrancies, inflammation and other complaints in connection with inflammatory diseases of the

GIT, *Helicobacter pylori* infection or bacterial overgrowth. It is also normalization of passing stool and stool consistency in subjects suffering from constipation or an irritable colon. The presence of bacteria in the gut is critical and barriers and containments in the gut are crucial for preventing bacterial infection in other areas of the body. Microorganisms in the gut interact with the host in many ways, including functions as diverse as the uptake of nutrients and preventing and/or modifying toxic substances from reaching critical organs in a toxic form. Due to its essential function, these are preventing & alleviating different types of diseases and improves human health. While the mechanisms of their effects on gut bacteria are slowly being unraveled, their effects on health are much more difficult to demonstrate.

Conflict of interests
The authors declare that they have no competing interests.

Sources of financial support
There is no funding to be disclosed.

Author's Contribution
Mohammad Asadul Habib carried out the studies, participated in the sequence alignment, performed in the analysis of the findings and drafted the manuscript. Mohammad Hasan Chowdhury participated in the design of the study, sequence alignment & drafted the manuscript. Farzana Afroz Tumpa, Jannatul Nayeem participated in the design of the study and drafted the manuscript. Md. Abdullah Al Mamun, Md. Ruhul Kabir; Assistant Professor, Noakhali Science & Technology University conceived of the study, and participated in its design and coordination and helped to draft the manuscript. All authors read and approved the final manuscript.

Abbreviations
DNA – Deoxyribonucleic Acid
LAB – Lactic Acid Bacteria
CVD – Cardiovascular Disease
BMI – Body Mass Index
BSH – Bile Salt Hydrolase
GIT – Gastrointestinal Tract

References

Aihara, K., Kajimoto, O., Hirata, H., Takahashi, R. and Nakamura, Y., 2005. Effect of powdered fermented milk with Lactobacillus helveticus on subjects with high-normal blood pressure or mild hypertension. Journal of the American College of Nutrition, 24(4), pp.257-265.

Altermann, E., Russell, W.M., Azcarate-Peril, M.A., Barrangou, R., Buck, B.L., McAuliffe, O., Souther, N., Dobson, A., Duong, T., Callanan, M. and Lick, S., 2005. Complete genome sequence of the probiotic lactic acid bacterium Lactobacillus acidophilus NCFM. Proceedings of the National Academy of Sciences, 102(11), pp.3906-3912.

Appel, L.J., Moore, T.J., Obarzanek, E., Vollmer, W.M., Svetkey, L.P., Sacks, F.M., Bray, G.A., Vogt, T.M., Cutler, J.A., Windhauser, M.M. and Lin, P.H., 1997. A clinical trial of the effects of dietary patterns on blood pressure. New England Journal of Medicine, 336(16), pp.1117-1124.

Ataie-Jafari, A., Larijani, B., Majd, H.A. and Tahbaz, F., 2009. Cholesterol-lowering effect of probiotic yogurt in comparison with ordinary yogurt in mildly to moderately hypercholesterolemic subjects. Annals of Nutrition and Metabolism, 54(1), pp.22-27.

Begley, M., Hill, C. and Gahan, C.G., 2006. Bile salt hydrolase activity in probiotics. Appl. Environ. Microbiol., 72(3), pp.1729-1738.

Bhathena, J., Martoni, C., Kulamarva, A., Urbanska, A.M., Malhotra, M. and Prakash, S., 2009. Orally delivered microencapsulated live probiotic formulation lowers serum lipids in hypercholesterolemic hamsters. Journal of Medicinal Food, 12(2), pp.310-319.

Charteris, W.P., Kelly, P.M., Morelli, L. and Collins, J.K., 1997. Selective detection, enumeration and identification of potentially probiotic Lactobacillus and Bifidobacterium species in mixed bacterial populations. International journal of food microbiology, 35(1), pp.1-27.

Cho, S.S., Finocchiaro, E.T. (Eds.), 2010. Handbook of Prebiotics and Probiotics Ingredients Health Benefits and Food Application. CRC Press Taylor & Francis Group, New York, pp. 435.

Danielson, A.D., Peo Jr, E.R., Shahani, K.M., Lewis, A.J., Whalen, P.J. and Amer, M.A., 1989. Anticholesteremic property of Lactobacillus acidophilus yogurt fed to mature boars. Journal of Animal Science, 67(4), pp.966-974.

El-Nezami, H. S., Polychronaki, N. N., Ma, J., Zhu, H., Ling, W., Salminen, E. K., ... & Mykkänen, H. M. (2006). Probiotic supplementation reduces a biomarker for increased risk of liver cancer in young men from Southern China. The American journal of clinical nutrition, 83(5), 1199-1203.

Eckburg, P.B., Bik, E.M., Bernstein, C.N., Purdom, E., Dethlefsen, L., Sargent, M., Gill, S.R., Nelson, K.E., Relman, D.A., 2005. Diversity of the human intestinal microbial flora. Science 308, 1635–1638.

Gilliland, S.E., Nelson, C.R. and Maxwell, C., 1985. Assimilation of cholesterol by Lactobacillus acidophilus. Appl. Environ. Microbiol., 49(2), pp.377-381.

Gismondo, M.R., Drago, L. and Lombardi, A., 1999. Review of probiotics available to modify gastrointestinal flora. International journal of antimicrobial agents, 12(4), pp.287-292.

Hylemon, P.B., 1985. Metabolism of bile acids in intestinal microflora. In New comprehensive biochemistry (Vol. 12, pp. 331-343).

Jones, R.M., Luo, L., Ardita, C.S., Richardson, A.N., Kwon, Y.M., Mercante, J.W., Alam, A., Gates, C.L., Wu, H., Swanson, P.A. and Lambeth, J.D., 2013. Symbiotic lactobacilli stimulate gut epithelial proliferation via Nox-mediated generation of reactive oxygen species. The EMBO journal, 32(23), pp.3017-3028.

Jones, B.V., Begley, M., Hill, C., Gahan, C.G. and Marchesi, J.R., 2008. Functional and comparative metagenomic analysis of bile salt hydrolase activity in the human gut microbiome. Proceedings of the national academy of sciences, 105(36), pp.13580-13585.

Kimura, K., McCartney, A. L., McConnell, M. A., & Tannock, G. W. (1997). Analysis of fecal populations of bifidobacteria and lactobacilli and investigation of the immunological responses of their human hosts to the predominant strains. Appl. Environ. Microbiol., 63(9), 3394-3398.

Kamal, R., Dahiya, P., Kumar, M. and Tomar, V., 2013. Probiotics in oral health–A new tool in pharmaceutical science. Indian J Pharm Biol Res, 1(4), pp.168-73.

Kim, E.K., An, S.Y., Lee, M.S., Kim, T.H., Lee, H.K., Hwang, W.S., Choe, S.J., Kim, T.Y., Han, S.J., Kim, H.J. and Kim, D.J., 2011. Fermented kimchi reduces body weight and improves metabolic parameters in overweight and obese patients. Nutrition Research, 31(6), pp.436-443.

Klaver, F.A. and Van Der Meer, R., 1993. The assumed assimilation of cholesterol by Lactobacilli and Bifidobacterium bifidum is due to their bile salt-deconjugating activity. Appl. Environ. Microbiol., 59(4), pp.1120-1124.

Li, G., 2012. Intestinal probiotics: interactions with bile salts and reduction of cholesterol. Procedia Environmental Sciences, 12, pp.1180-1186.

Lahtinen, S.J., Gueimonde, M., Ouwehand, A.C., Reinikainen, J.P. and Salminen, S.J., 2005. Probiotic bacteria may become dormant during storage. Appl. Environ. Microbiol., 71(3), pp.1662-1663.

Liu, Z. H., Huang, M. J., Zhang, X. W., Wang, L., Huang, N. Q., Peng, H., ... & Liu, W. J. (2012). The effects of perioperative probiotic treatment on serum zonulin concentration and subsequent postoperative infectious complications after colorectal cancer surgery: a double-center and double-blind randomized clinical trial. The American journal of clinical nutrition, 97(1), 117-126.

Meyer, D. and Stasse-Wolthuis, M., 2009. The bifidogenic effect of inulin and oligofructose and its consequences for gut health. European journal of clinical nutrition, 63(11), p.1277.

Marteau, P.R., Vrese, M.D., Cellier, C.J. and Schrezenmeir, J., 2001. Protection from gastrointestinal diseases with the use of probiotics. The American journal of clinical nutrition, 73(2), pp.430s-436s.

Martin, F.P.J., Dumas, M.E., Wang, Y., Legido-Quigley, C., Yap, I.K., Tang, H., Zirah, S., Murphy, G.M., Cloarec, O., Lindon, J.C. and Sprenger, N., 2007. A top-down systems biology view of microbiome-mammalian metabolic interactions in a mouse model. Molecular systems biology, 3(1), p.112.

Menrad, K., 2003. Market and marketing of functional food in Europe. Journal of food engineering, 56(2-3), pp.181-188.

Mann, G.V. and Spoerry, A., 1974. Studies of a surfactant and cholesteremia in the Maasai. The American journal of clinical nutrition, 27(5), pp.464-469.

Mattila-Sandholm, T., Myllärinen, P., Crittenden, R., Mogensen, G., Fondén, R. and Saarela, M., 2002. Technological challenges for future probiotic foods. International Dairy Journal, 12(2-3), pp.173-182.

Ma, E. L., Choi, Y. J., Choi, J., Pothoulakis, C., Rhee, S. H., & Im, E. (2010). The anticancer effect of probiotic Bacillus polyfermenticus on human colon cancer cells is mediated through ErbB2 and ErbB3 inhibition. International journal of cancer, 127(4), 780-790.

Narang, S., Gupta, R. and Narang, A., 2011. Probiotics in oral healthcare–A review. Int J Sci Eng Res, 2, pp.1-5.

Nakamura, Y., Yamamoto, N., Sakai, K. and Takano, T., 1995. Antihypertensive effect of sour milk and peptides isolated from it that are inhibitors to angiotensin I-converting enzyme. Journal of dairy science, 78(6), pp.1253-1257.

Özer, D., Akin, S. and Özer, B., 2005. Effect of inulin and lactulose on survival of Lactobacillus acidophilusla-5 and Bifidobacterium bifidum bb-02 in Acidophilus-bifidus yoghurt. Food Science and Technology International, 11(1), pp.19-24.

Ohashi, Y., Nakai, S., Tsukamoto, T., Masumori, N., Akaza, H., Miyanaga, N., ... & Naito, S. (2002). Habitual intake of lactic acid bacteria and risk reduction of bladder cancer. Urologia Internationalis, 68(4), 273-280.

O'mahony, L., Feeney, M., O'halloran, S., Murphy, L., Kiely, B., Fitzgibbon, J., Lee, G., O'sullivan, G., Shanahan, F. and Collins, J.K., 2001. Probiotic impact on microbial flora, inflammation and tumour development in IL-10 knockout mice. Alimentary pharmacology & therapeutics, 15(8), pp.1219-1225.

Parker, R.B., 1974. Probiotics, the other half of the antibiotic story. Anim Nutr Health, 29, pp.4-8.

Rao, B.N., 2003. Bioactive phytochemicals in Indian foods and their potential in health promotion and disease prevention. Asia Pacific Journal of clinical nutrition, 12(1).

Rašić, J.L., Vujičić, I.F., Škrinjar, M. and Vulić, M., 1992. Assimilation of cholesterol by some cultures of lactic acid bacteria and bifidobacteria. Biotechnology letters, 14(1), pp.39-44.

Remacle, C. and Reusens, B. eds., 2004. Functional foods, ageing and degenerative disease.

Saarela, M., Lahteenmaki, L., Crittenden, R., Salminen, S., Mattila-Sandholm, T., 2002. Gut bacteria and health foods—the European perspective. Int. J. Food Microbiol. 78, 99–117.

Salminen, S., von Wright, A., Morelli, L., Marteau, P., Brassart, D., de Vos, W.M., Fondén, R., Saxelin, M., Collins, K., Mogensen, G. and Birkeland, S.E., 1998. Demonstration of safety of probiotics—a review. International journal of food microbiology, 44(1-2), pp.93-106.

Srionnual, S., Yanagida, F., Lin, L.H., Hsiao, K.N. and Chen, Y.S., 2007. Weissellicin 110, a newly discovered bacteriocin from Weissella cibaria 110, isolated from plaa-som, a fermented fish product from Thailand. Appl. Environ. Microbiol., 73(7), pp.2247-2250.

Salminen, S., Isolauri, E., 2006. Intestinal colonization, microbiota, and probiotics. J. Pediatr. 149, 115–120.

Seppo, L., Jauhiainen, T., Poussa, T. and Korpela, R., 2003. A fermented milk high in bioactive peptides has a blood pressure–lowering effect in hypertensive subjects. The American journal of clinical nutrition, 77(2), pp.326-330.

Stanton, C., Gardiner, G., Meehan, H., Collins, K., Fitzgerald, G., Lynch, P.B. and Ross, R.P., 2001. Market potential for probiotics. The American journal of clinical nutrition, 73(2), pp.476s-483s.

Shah, N.P., 2007. Functional cultures and health benefits. International dairy journal, 17(11), pp.1262-1277.

Toi, M., Hirota, S., Tomotaki, A., Sato, N., Hozumi, Y., Anan, K., Nagashima, T., Tokuda, Y., Masuda, N., Ohsumi, S. and Ohno, S., 2013. Probiotic beverage with soy isoflavone consumption for breast cancer prevention: A case-control study. Current Nutrition & Food Science, 9(3), pp.194-200.

Tuomola, E., Crittenden, R., Playne, M., Isolauri, E. and Salminen, S., 2001. Quality assurance criteria for probiotic bacteria. The American Journal of Clinical Nutrition, 73(2), pp.393s-398s.

Usman, Hosono, A., 1999. Bile tolerance, taurocholate deconjugation, and binding of cholesterol by lactobacillus gasseri strains. J. Dairy Sci. 82, 243–248.

Wang, Y., Xu, N., Xi, A., Ahmed, Z., Zhang, B. and Bai, X., 2009. Effects of Lactobacillus plantarum MA2 isolated from Tibet kefir on lipid metabolism and intestinal microflora of rats fed on high-cholesterol diet. Applied Microbiology and Biotechnology, 84(2), pp.341-347.

Xu, J. and Gordon, J.I., 2003. Honor thy symbionts. Proceedings of the National Academy of Sciences, 100(18), pp.10452-10459.

Yamamoto, N., Akino, A. and Takano, T., 1994. Antihypertensive effect of the peptides derived from casein by an extracellular proteinase from Lactobacillus helveticus CP790. Journal of dairy science, 77(4), pp.917-922.

Ziemer, C.J. and Gibson, G.R., 1998. An overview of probiotics, prebiotics and synbiotics in the functional food concept: perspectives and future strategies. International Dairy Journal, 8(5-6), pp.473-479.