Probiotic Bacteria: A Promising Approach for Managing CVD Risk Factors

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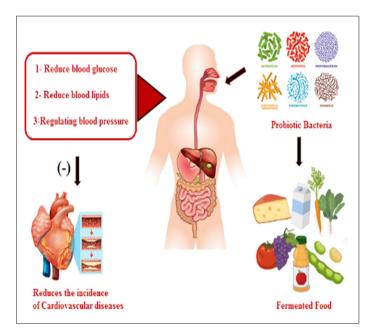
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ABSTRACT

The presence of the microbiota in the human gut is reported to have a significant impact on the health of the individual. Recent studies have shown that the microbial imbalance in the gut may play a role in the development of cardiovascular disease. Therefore, as an approach to preventing and treating cardiovascular disease, several studies have examined the role of gut microbiota alteration with probiotics. The World Health Organization's definition of probiotics is that they are a type of living microorganism whose effects on the person's health can be observed in sufficient quantities. Strategies for human dietary intervention with probiotic strains and their impact on cardiovascular risk factors such as hypercholesterolemia, hypertension, obesity and type 2 diabetes are the subject of this review. The accumulation of evidence suggests that probiotics can reduce LDL/HDL cholesterol and enhance blood pressure, inflammatory mediators, blood glucose levels, and body mass index. Therefore, it is possible to develop probiotics as dietary supplements with potential benefits for health of the heart. However, there is not only ambiguity regarding the exact strains and dosages of the probiotics that will bring about positive health effects, but also factors like immunity and genetics of the individual that might influence the efficacy of probiotics. For that reason, further studies should be carried out to determine the mechanisms by which probiotics might have beneficial effects on cardiovascular system and also exclude any possible negative impact on health. The aim of this review is to assess the effects of probiotics on cardiovascular disease.

Keywords : Probiotic bacteria, Cardiovascular diseases (CVD), gut microbiota

Graphical Abstract



INTRODUCTION

The human body has trillions of microorganisms, and together they shape an intuitively biological system within and without the exterior world. Changes and interactions in this ecosystem affect health and disease in the human body. The associated microflora in the host is called the microbiome. The digestive tract, specifically the large intestine, contains most of the microflora that exist in the human body. The gut microbiota plays a major role in maintaining nutrition and the immune system, which, in turn, affects the host's susceptibility and response to pathologic conditions. Several illnesses, such as GI disorders, asthma, allergies, Central Nervous System

Disorders, Metabolic Syndromes, Cancer, and Cardiovascular Diseases, are linked to an imbalance in the intestinal microbiome, called gut dysbiosis (2,3). CVD has become the leading cause of death worldwide due to the significant increase in incidence over the last few decades. This is particularly evident in high and middle-income countries. Due to the intricate nature of cardiovascular diseases and the lack of understanding of their underlying mechanisms, preventive measures cannot be developed (4). An unhealthy diet has long been regarded as an important cause of cardiovascular disease. The impact of genetic variation on body mass index and body fat distribution is significant, but it is believed to have an unexplained influence on the extent of variation in obesity among individuals (5,6). The role of dietary components in the microbiota and the metabolites involved in them is only recently discovered as important for cardiovascular health. Researchers are increasingly interested in the potential role of probiotics in preventing cardiovascular diseases and atherosclerosis, as they understand the significance of the gut microbiome in this area(6,7). While the impact of changes in microbiome composition related to CHD or atherosclerosis is still poorly understood, there is mounting evidence to back up this connection (7). Several cardiovascular risk factors may be influenced by functional dietary choices. However, little is known about the role of probiotics as important dietary components in the prevention and treatment of cardiovascular disease (8). Therefore, the purpose of this review is to discuss the role of probiotics in the management of CVD risk factors.

IMPORTANCE OF MANAGING CVD RISK FACTORS

Coronaryartery disease, stroke, hypertension, cardiomy opathy (infection), heart disease, or blood vessel blockage are among the most common cardiovascular diseases. CVD is a growing global health problem(9–11). In 2015, cardiovascular disease accounted for 18 million deaths, accounting for about a third of all deaths, up 12.5% from 2005. The American Heart Association reports that 92.1 million adults in the United States currently have cardiovascular disease. Approximately 43.9% of the total US population is projected to have CVD by 2030 (12). Atherosclerosis is a chronic inflammation caused by the accumulation and development of atherosclerotic plaques in arterial walls. It is controlled by these factors. Atherosclerosis is a major risk factor for stroke and heart attack. Several immune-mediated mechanisms are involved in the onset and progression of the disease (13). Risk factors for cardiovascular disease include genetics and unhealthy lifestyle choices such as poor exercise, bad diet, smoking habits, and drinking. Hypertension is the most common modifiable risk factor for cardiovascular disease (14,15). The presence of high blood cholesterol levels is often linked to a

metabolic disorder that damages blood vessels and causes atherosclerosis, similar to type 2 diabetes. Atherosclerosis can be caused by the dysfunction of endothelial dysfunction in the renin–angiotensin–aldosterone system and at high levels due to hypertension and hypercholesterolemia (16,17).

Determination of Cardiovascular Diseases

In humans, maintaining a healthy gut balance between pathogenic and non-pathogen microorganisms is essential for survival. diet is an external factor that affects the composition of the gut microbiome. Various studies have analyzed diets and their effects on gut microbiota and the prevention of cardiovascular diseases (18). Other vital diets for the avoidance of CVD are plant-based diets, which are characterized by tall utilization of seeds, cereals, natural product, berries, nuts and vegetables. Both dietary sources contain important filaments, fiber optic cables (fiberglass), synthetic substances, and bioactive compounds that are metabolized by organisms to produce different specialized metabolic compounds such as acetate, propionate, or butyrate. These compounds serve as an essential component in suppressing incendiary processes. Although the mechanisms by which these diets produce beneficial effects are still unknown, their bioactive nourishment components, including unsaturated greasy acids (19), complex carbohydrates and filaments (20), and polyphenols (21), are highly prized. Unsaturated fatty acids, in particular n-3 polyunsaturated fatty acids, are generally considered cardiovascular-protective. Fish oil is the main source of animal oil whereas flaxseed oil is obtained from plants(19). Finally, the best strategy for preventing and treating diseases caused by gut microbiota is to consume a healthy diet with an intake of saturated fatty acids, fruits, and vegetables (22).

current approaches for managing CVD risk factors

here are various rules for the treatment and administration of person chance variables such as hypertension (23,24) and dyslipidemia (25), as well as joint rules for the avoidance of atherosclerosis and CVD. The basic principles of these guidelines are as follows::

- CV risk assessment.
- For the management of those who may be susceptible to disease.
- Management adjusted to patient's total risk of CHD or CVD; the higher the risk, the greater the intensity of management.
- Business of an extend of mediations to address chance components for CVD, counting treatment of hypertension, treatment of dyslipidemia, smoking cessation, expanded physical action, cardioprotective eat less, treatment of hyperglycemia, weight administration, antiplatelet/ anticoagulant treatment, and psychosocial support

Preventing cardiovascular disease is crucial, given the rapid and significant rise in worldwide mortality rates (26). Medical authorities have published local guidelines recommending appropriate treatment, healthy lifestyles, and screening for high-risk cardiovascular diseases such as diabetes, hypertension, and hyperlipidemia. Common medications such as aspirin and statins may be considered in high-risk individuals, according to published guidelines. Secondary prevention is necessary for individuals with a history of cardiovascular disease, and in addition to lifestyle changes, effective medications are prescribed to prevent future events (27).

DEFINITION AND TYPES OF PROBIOTIC BACTERIA

The presence of probiotics is attributed to various beneficial microorganisms. Most of them belong to lactic acid bacteria as Lactobacillus, Bifidobacterium, Lactococcus, such Streptococcus and Enterococcus. The yeast genus Saccharomyces is also one of the known probiotics (28). Currently, the main sources of probiotic strains are humans and fermented foods like yogurt, kefir, sauerkraut, and kimchi. These foods are all consumed in their natural state. In clinical trials, there are several criteria based on which it is evaluated whether probiotics can be used in food. These criteria are (1) proper identification, characterization, and preservation of probiotic strains; (2) to sustain the studied probiotics; and (3) to ensure that they are alive at the study site. In addition, according to the WHO, the number of living microorganisms in foods containing probiotics for human consumption should be more than 106 cells/ml or cells/g, and the therapeutic dose in a clinical trial is 108-109 cells/ml or cells/g (29). Strong evidence shows that probiotics benefit human health and play an important role in the prevention of various diseases (30). Probiotic consumption can cross directly into the GIT and has been reported to be effective in the treatment of various types of diarrhea, especially traveler's diarrhea, antibiotic-induced diarrhea, rotavirus diarrhea in infants, and inflammatory bowel disease (IBD) suppressing the activity of pathogenic intestinal microbes and promoting the correct balance between pathogens and commensal bacteria necessary for the normal functioning of the intestine (31). Probiotics' ability to prevent disease or promote human health is primarily attributed to their interactions with pathogenic microorganisms, antagonizing pathogens and altering the intestinal microbiome, as well as modulating the host immune response (30). Although the therapeutic benefits of traditional probiotics have been extensively researched, recent research has suggested that they could be next-generation proniotes produced by the gut microbiota for example, Bacteroides fragilis exerts anticancer effects and suppresses inflammation, Faecalibacterium

prausnitzii protects mice against intestinal diseases, and Prevotella copri and Christensenella minuta play a role in controlling insulin resistance (32).

ROLE OF PROBIOTIC BACTERIA IN CVD MANAGEMENT

Sánchez et al. Proposed four distinct processes that aid in the advantageous properties of probiotics for human well-being include enhanced epithelial barrier function, competition with pathogen toxins for nutrients and attachment sites, immune system effects and neurotransmitter production on other tissues, and immunomodulation (33). The mechanisms underlying probiotics in cardiovascular disease are relatively complex and have not yet been elucidated. The mechanisms by which probiotics prevent cardiovascular disease, restore gut microbiota dysbiosis, and reduce anti-inflammatory responses are likely to be beneficial, but reducing oxidative stress, hypercholesterolemia, or high blood pressure also may be helpful (34).

Beneficial Effects of Probiotics on CVD

Probiotics have pulled in a parcel of intrigue in terms of their well-being benefits. Although research is still ongoing, it appears that probiotics can help with various ailments such as treating loose bowels caused by anti-microbial, treating urinary tract diseases, improving the treatment of IBS, expediting intestinal contamination treatment, and potentially decreasing the severity of colds and flu. Their testimony typically is based on natural but actually factual synonyms, which can be achieved through a variety of food items or more refined through supplements, as necessary. Prove proposes that probiotics may improve metabolic disarranges, such as corpulence, diabetes, and CVD (35). oxidative stress, adjusting microbiota changes in the utilitarian and auxiliary intestines, and improving resistant reactions (36). Probiotics may be beneficial for heart patients as they act as colony agents of friendly bacteria in the gut, according to researchers. After all, heart disease is on a list of inflammatory problems such as rheumatoid arthritis, psoriasis, inflammatory bowel disease, and multiple sclerosis that also originate in the gut, all of which are linked to gut microbiota imbalances (37,38). Probiotics, which have beneficial effects on the microbial and metabolic composition of the intestinal microbiota, can be considered as a potential treatment for cardiovascular disease.

CONCLUSION

Many studies have investigated the health benefits of probiotics for host populations. A range of conditions, including irritable colon syndrome, urinary tract infections, and symptoms of cold and flu, can be treated with probiotics. The matter is still being investigated. Probiotics may help

treat metabolic disorders such as obesity, diabetes, and cardiovascular disease, according to growing evidence. Probiotic bacteria have been shown to protect against cardiovascular disease by reducing cholesterol levels, reducing oxidative stress, balancing functional and structural changes in gut microbiota, and increasing the immune response. Scientific literature shows that regular intake of probiotics, which improve the balance of gut microbiota and are beneficial for cardiovascular health due to their ability to decrease oxidation stress, has been shown to be beneficial in this area. Although there are still many unanswered questions and conflicting results, it is clear that consumption of probiotics can be a promising complement to more conventional cardiovascular therapy as well as other pharmacological measures commonly used to prevent the development or progression of CVD. Moreover, in order to maximise the potential beneficial effects of probiotics in any given situation, it will be necessary to increase knowledge of the different strains of bacteria present in them and how they should be consumed. Research on the gut microbiota, which generates enzymes, peptides, and biochemical pathways that differ from the host's resources, can offer innovative avenues for developing drugs to treat cardiovascular diseases.

REFERENCES

- Wang Z, Wu J, Tian Z, Si Y, Chen H, Gan J. The mechanisms of the potential probiotic Lactiplantibacillus plantarum against cardiovascular disease and the recent developments in its fermented foods. Foods. 2022;11(17):2549.
- Nicholson JK, Holmes E, Wilson ID. Gut microorganisms, mammalian metabolism and personalized health care. Nat Rev Microbiol. 2005;3(5):431–8.
- Carding S, Verbeke K, Vipond DT, Corfe BM, Owen LJ. Dysbiosis of the gut microbiota in disease. Microb Ecol Health Dis. 2015;26(1):26191.
- Katsimichas T, Antonopoulos AS, Katsimichas A, Ohtani T, Sakata Y, Tousoulis D. The intestinal microbiota and cardiovascular disease. Cardiovasc Res. 2019;115(10):1471–86.
- Attaye I, Pinto-Sietsma S-J, Herrema H, Nieuwdorp M. A crucial role for diet in the relationship between gut microbiota and cardiometabolic disease. Annu Rev Med. 2020;71:149–61.
- 6. Jonsson AL, Bäckhed F. Role of gut microbiota in atherosclerosis. Nat Rev Cardiol. 2017;14(2):79–87.

- Tang WHW, Kitai T, Hazen SL. Gut microbiota in cardiovascular health and disease. Circ Res. 2017;120(7):1183–96.
- Gerdes V, Gueimonde M, Pajunen L, Nieuwdorp M, Laitinen K. How strong is the evidence that gut microbiota composition can be influenced by lifestyle interventions in a cardio-protective way? Atherosclerosis. 2020;311:124– 42.
- 9. Guarner F, Malagelada J-R. Gut flora in health and disease. Lancet. 2003;361(9356):512–9.
- Mendis S, Puska P, Norrving B editors, Organization WH. Global atlas on cardiovascular disease prevention and control. World Health Organization; 2011.
- Olas B. Probiotics, prebiotics and synbiotics—a promising strategy in prevention and treatment of cardiovascular diseases? Int J Mol Sci. 2020;21(24):9737.
- Xu C, Weng Z, Zhang L, Xu J, Dahal M, Basnet TB, et al. HDL cholesterol: A potential mediator of the association between urinary cadmium concentration and cardiovascular disease risk. Ecotoxicol Environ Saf. 2021;208:111433.
- Kurilenko N, Fatkhullina AR, Mazitova A, Koltsova EK. Act locally, act globally—microbiota, barriers, and cytokines in atherosclerosis. Cells. 2021;10(2):348.
- Krasi G, Precone V, Paolacci S, Stuppia L, Nodari S, Romeo F, et al. Genetics and pharmacogenetics in the diagnosis and therapy of cardiovascular diseases. Acta Bio Medica Atenei Parm. 2019;90(Suppl 10):7.
- Doughty KN, Del Pilar NX, Audette A, Katz DL. Lifestyle medicine and the management of cardiovascular disease. Curr Cardiol Rep. 2017;19:1–10.
- Paganelli F, Mottola G, Fromonot J, Marlinge M, Deharo P, Guieu R, et al. Hyperhomocysteinemia and cardiovascular disease: is the adenosinergic system the missing link? Int J Mol Sci. 2021;22(4):1690.
- Ma W, Zhang B, Yang Y, Qi L, Meng L, Zhang Y, et al. Correlating the relationship between interarm systolic blood pressure and cardiovascular disease risk factors. J Clin Hypertens. 2017;19(5):466–71.
- Lăcătuşu C-M, Grigorescu E-D, Floria M, Onofriescu A, Mihai B-M. The Mediterranean diet: from an environment-

driven food culture to an emerging medical prescription. Int J Environ Res Public Health. 2019;16(6):942.

- He Z, Hao W, Kwek E, Lei L, Liu J, Zhu H, et al. Fish oil is more potent than flaxseed oil in modulating gut microbiota and reducing trimethylamine-N-oxide-exacerbated atherogenesis. J Agric Food Chem. 2019;67(49):13635–47.
- 20. Ciecierska A, Drywien M, Hamulka J, Sadkowski T. Nutraceutical functions of beta-glucans in human nutrition. Rocz Państwowego Zakładu Hig. 2019;70(4).
- Liu JianHui LJ, He ZouYan HZ, Ma Ning MN, Chen ZhenYu CZ. Beneficial effects of dietary polyphenols on highfat diet-induced obesity linking with modulation of gut microbiota. 2020;
- 22. Sanchez-Rodriguez E, Egea-Zorrilla A, Plaza-Díaz J, Aragón-Vela J, Muñoz-Quezada S, Tercedor-Sánchez L, et al. The gut microbiota and its implication in the development of atherosclerosis and related cardiovascular diseases. Nutrients. 2020;12(3):605.
- Chobanian A V, Bakris GL, Black HR, Cushman WC, Green LA, Izzo Jr JL, et al. The seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure: the JNC 7 report. Jama. 2003;289(19):2560–71.
- 24. Mancia G, De Backer G, Dominiczak A, Cifkova R, Fagard R, Germano G, et al. 2007 Guidelines for the management of arterial hypertension: The Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). Eur Heart J. 2007;28(12):1462–536.
- 25. Expert Panel on Detection E. Executive summary of the third report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (adult treatment panel III). Jama. 2001;285(19):2486–97.
- Franco M, Cooper RS, Bilal U, Fuster V. Challenges and opportunities for cardiovascular disease prevention. Am J Med. 2011;124(2):95–102.
- 27. Arnett DK, Blumenthal RS, Albert MA, Buroker AB, Goldberger ZD, Hahn EJ, et al. 2019 ACC/AHA guideline on the primary prevention of cardiovascular disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation. 2019;140(11):e596–646.

- 28. Kothari D, Patel S, Kim S-K. Probiotic supplements might not be universally-effective and safe: A review. Biomed Pharmacother. 2019;111:537–47.
- 29. Pandey KR, Naik SR, Vakil B V. Probiotics, prebiotics and synbiotics-a review. J Food Sci Technol. 2015;52:7577–87.
- Alam Z, Shang X, Effat K, Kanwal F, He X, Li Y, et al. The potential role of prebiotics, probiotics, and synbiotics in adjuvant cancer therapy especially colorectal cancer. J Food Biochem. 2022;46(10):e14302.
- 31. Shapiro D, Kapourchali FR, Santilli A, Han Y, Cresci GAM. Targeting the gut microbiota and host immunity with a bacilli-species probiotic during antibiotic exposure in mice. Microorganisms. 2022;10(6):1178.
- 32. Chang C-J, Lin T-L, Tsai Y-L, Wu T-R, Lai W-F, Lu C-C, et al. Next generation probiotics in disease amelioration. J food drug Anal. 2019;27(3):615–22.
- Sánchez B, Delgado S, Blanco-Míguez A, Lourenço A, Gueimonde M, Margolles A. Probiotics, gut microbiota, and their influence on host health and disease. Mol Nutr Food Res. 2017;61(1):1600240.
- 34. Oniszczuk A, Oniszczuk T, Gancarz M, Szymańska J. Role of gut microbiota, probiotics and prebiotics in the cardiovascular diseases. Molecules. 2021;26(4):1172.
- Mishra S, Wang S, Nagpal R, Miller B, Singh R, Taraphder S, et al. Probiotics and prebiotics for the amelioration of type 1 diabetes: present and future perspectives. Microorganisms. 2019;7(3):67.
- Al Bander Z, Nitert MD, Mousa A, Naderpoor N. The gut microbiota and inflammation: an overview. Int J Environ Res Public Health. 2020;17(20):7618.
- 37. Kitai T, Tang WHW. Gut microbiota in cardiovascular disease and heart failure. Clin Sci. 2018;132(1):85–91.
- 38. Li DY, Tang WHW. Gut microbiota and atherosclerosis. Curr Atheroscler Rep. 2017;19:1–12.