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Mapping the Landscape: Indonesian Fermented Foods, Probiotics, and Cardiovascular Disease Prevention - A Bibliometric and Scoping Review

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KEYWORDS:
blood pressure; cholesterol-lowering probiotic; cardiovascular disease; Indonesian fermented food; noncommunicable disease

ABSTRACT

Cardiovascular disease (CVD) constitutes a significant health burden in Indonesia, accounting for approximately one-third of all deaths. Hypercholesterolemia and dyslipidemia are established primary risk factors for CVD. This mini-review synthesizes current knowledge on CVD, the characteristics of probiotic bacteria, and the potential of Indonesian fermented foods to mitigate CVD risk. Indonesia boasts a rich and diverse array of traditional fermented foods, including tape, tempeh, dadih, sayur asin, tempoyak, and growol. Notably, many of these foods harbor diverse probiotic microorganisms, such as *Lactobacillus, Bifidobacterium, Lactococcus, Streptococcus, Enterococcus, Weissella, Pediococcus, Rhizopus, Penicillium,* and *Saccharomyces*. Various studies have explored the beneficial effects of probiotics, with hypocholesterolemic and hypolipidemic effects increasing in recent years. Consistent consumption of probiotics has demonstrated the potential to reduce total serum cholesterol, low-density lipoprotein cholesterol, liver cholesterol, and triglycerides, while concurrently elevating high-density lipoprotein cholesterol. The impact of probiotics on lipid profiles is influenced by many factors, such as the specific probiotic strain, dosage, and the individual's dietary habits and overall health status. This review highlighted the promising role of probiotics derived from Indonesian fermented foods as a complementary strategy in preventing cardiovascular disease.

1. INTRODUCTION

The ongoing process of urbanization and changes in people's lifestyles have significantly contributed to rising rates of various chronic diseases, especially cardiovascular disease. Globally, cardiovascular disease remains the leading cause of death. In 2019, it caused more than 17.9 million deaths worldwide, accounting for nearly one-third (32%) of all global deaths (World Health Organization, 2021). This disease is also the main cause of death and illness in Indonesia. Similarly, over 30% of all deaths in Indonesia are attributed to CVD, with coronary heart disease and stroke being the leading causes of death (Ministry of Health, 2017). The impact of CVD extends beyond suffering, resulting in substantial economic costs and increased healthcare spending for the country.

Hypercholesterolemia and dyslipidemia are major underlying factors in the development of CVD. Unhealthy lifestyle choices and dietary habits, such as smoking, lack of physical activity, and high-fat diets, can contribute to these conditions. Recognizing this public health challenge, the Indonesian government has launched programs to prevent non-communicable diseases, including

CVD. For example, the Healthy Community Movement (GERMAS) promotes policies that support healthy lifestyles and eating habits. In addition to public health initiatives, nutritional supplements, often classified as functional foods, have gained attention for their potential health effects on various disease risk factors. Although the relationship between probiotics and cardiovascular health is still being studied, existing research has identified several promising pathways and potential benefits, highlighting the need for further research into their therapeutic and preventive applications.

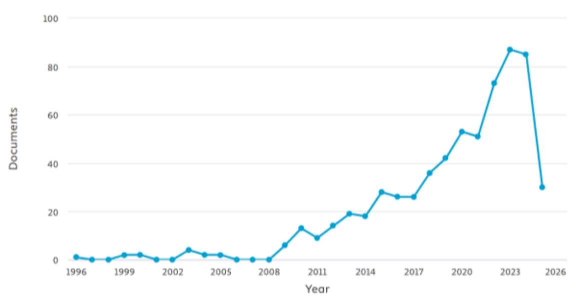
2. MATERIALS AND METHODS

A bibliometric analysis was performed on Scopus-indexed publications using the search terms "probiotic" AND ("cardiovascular" OR "cholesterol") to provide a quantitative overview of the research landscape supporting this review. This analysis aimed to identify key research trends, commonly investigated keywords, and the timeline of studies linking probiotics with cardiovascular health, contextualizing the qualitative synthesis of findings within broader scientific literature. Insights from the bibliometric analysis, such as dominant research themes and emerging investigation areas, directly relate to the review's goal of exploring the potential of Indonesian probiotics in tackling cardiovascular disease. This mini-review summarized findings from scientific publications focused on isolating probiotics from Indonesian fermented foods. We also included studies reporting on in vivo probiotic supplementation. The scope of this review covered discussions on cardiovascular disease, the characteristics and properties of probiotic bacteria, and the potential role of Indonesian fermented foods in reducing the risk of cardiovascular disease.

3. RESULTS AND DISCUSSION

3.1. Bibliometric Analysis

Publications concerning the potential of probiotics with hypocholesterolemic and hypolipidemic effects have increased in recent years (**Figure 1A**). The most common publications fall within the area of Agriculture and Biological Sciences (**Figure 1B**). China has become the leading country in this research, contributing over 130 documents to the database (**Figure 1C**). The researcher affiliated with the Ministry of Education of the People's Republic of China has been the most productive, publishing the largest number of documents in this field (**Figure 1D**). An overview of the top 10 most-cited papers is shown in **Table 3.1**, highlighting their significant influence. Notably, the research group led by Prakash has been the most prolific, with more than seven publications (**Figure 1E**). Meanwhile, the paper published by Ejtahed et al. in 2011 in the Journal of Dairy Science has received the highest number of citations, totaling 356 (**Table 3.2**).



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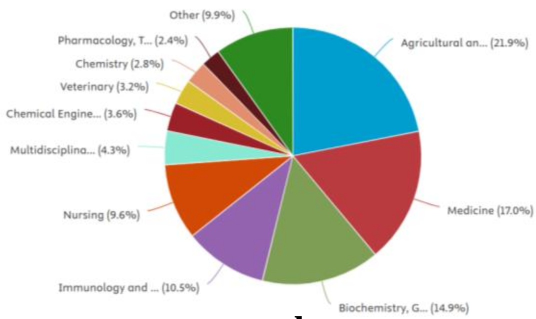

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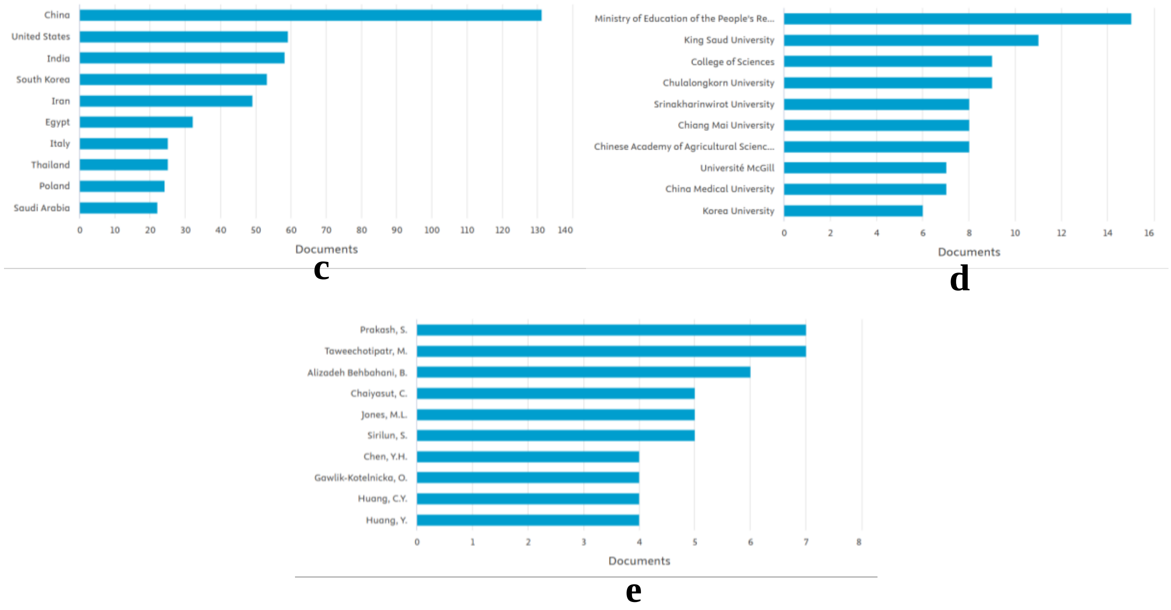

Figure 1. Scopus database analysis on published papers related to the "probiotic and cardiovascular or cholesterol" topic

Table 3.1. The top 10 most cited papers related to the "probiotic and cardiovascular or cholesterol" topic from the Scopus database

Title	Probiotic	Author	Source	Citation
Effect of probiotic yogurt containing *Lactobacillus acidophilus* and *Bifidobacterium lactis* on lipid profile in individuals with type 2 diabetes mellitus.	*Lactobacillus Bifidobacterium*	(Ejtahed et al., 2011)	Journal of Dairy Science, 94(7), pp. 3288–3294	356
Effects of milk products fermented by *Bifidobacterium longum* on blood lipids in rats and healthy adult male volunteers.	*Bifidobacterium*	(Xiao et al., 2003)	Journal of Dairy Science, 86(7), pp. 2452–2461	311
Supplementation *of Lactobacillus curvatus* KY1032 in diet-induced obese mice is associated with gut microbial changes and reduction in obesity.	*Lactobacillus*	(Park et al., 2013)	PLoS ONE, 8(3), e59470	284
Effect of 8-week intake of probiotic milk products on risk factors for cardiovascular diseases.	*Lactobacillus Streptococcus Enterococcus*	(Agerholm-Larsen et al., 2000)	European Journal of Clinical Nutrition, 54(4), pp. 288–297	282
Removal of cholesterol by lactobacilli via incorporation and conversion to coprostanol.	*Lactobacillus*	(Lye et al., 2010)	Journal of Dairy Science, 93(4), pp. 1383–1392	277
Cholesterol-lowering efficacy of a microencapsulated bile salt hydrolase-active *Lactobacillus reuteri* NCIMB 30242 yoghurt formulation in hypercholesterolaemic adults.	*Lactobacillus*	(Jones et al., 2012)	The British Journal of Nutrition, 107(10), pp. 1505–1513	271

Title	Probiotic	Author	Source	Citation
Probiotic *Lactobacillus rhamnosus* GG prevents liver fibrosis through inhibiting hepatic bile acid synthesis and enhancing bile acid excretion in mice.	*Lactobacillus*	(Liu et al., 2020)	Hepatology, 71(6), pp. 2050–2066	259
Functional and probiotic attributes of an indigenous isolate of *Lactobacillus plantarum*.	*Lactobacillus*	(Kaushik et al., 2009)	PLoS ONE, 4(12), e8099	259
Alleviation of cyclic heat stress in broilers by dietary supplementation of mannan-oligosaccharide and *Lactobacillus*-based probiotic: dynamics of cortisol, thyroid hormones, cholesterol, C-reactive protein, and humoral immunity.	*Lactobacillus*	(Sohail et al., 2010)	Poultry Science, 89(9), pp. 1934–1938	237
Effect of probiotic (VSL#3) and omega-3 on lipid profile, insulin sensitivity, inflammatory markers, and gut colonization in overweight adults: a randomized, controlled trial.	*Bifidobacterium* *Lactobacillus* *Streptococcus*	(Rajkumar et al., 2014)	Mediators of Inflammation, 2014, 348959	227

The analysis included 629 articles that met specific criteria: published in English, available as open access, classified as research articles, and containing the keyword "probiotics." The network visualization showcases interconnected keywords from Scopus publications on "probiotic," "cardiovascular," and "cholesterol" (**Figure 2A**). A prominent red cluster highlights the impact of probiotics on "cholesterol" and "gut microbiota." A green cluster emphasizes "human" studies examining effects on "blood," "glucose," often using "randomized controlled trials," supported by frequently used keywords (**Table 3.2**). Other clusters explore related areas like "animal models," "dietary interventions," "obesity," and "hypertension," illustrating the diverse research on probiotics and cardiovascular health. The overlay analysis reveals evolving research trends (**Figure 2B**). Ongoing interest in "probiotics" and "cholesterol" is clear. At the same time, newer terms in the green cluster, such as "randomized controlled trial," "glucose blood level," and "insulin resistance," indicate a growing focus on human trials and specific metabolic outcomes related to cardiovascular risk. The density visualization reinforces key research areas with bright yellow highlighting the most common keywords: "probiotics," "cholesterol," "human," "blood," "controlled study," and "microbiota" (**Figure 2C**). This highlights an intense focus on probiotic effects on cholesterol and cardiovascular health in human studies, often employing controlled designs and analyzing gut microbiota.

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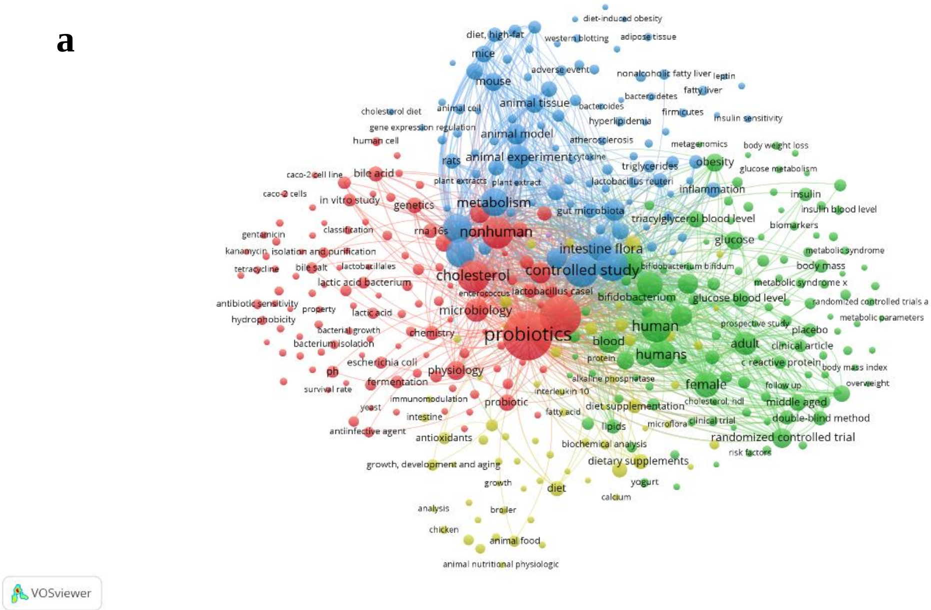
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diet, high-fat
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adverse event
nonalcoholic fatty liver
leptin
mouse
bacteroidetes
fatty liver
cholesterol diet
animal cell
animal tissue
bacteroides
firmicutes
insulin sensitivity
gene expression regulation
hyperlipidemia
human cell
animal model
atherosclerosis
metagenomics
body weight loss
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cytokine
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kanamycin
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microflora
clinical trial
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randomized controlled trial
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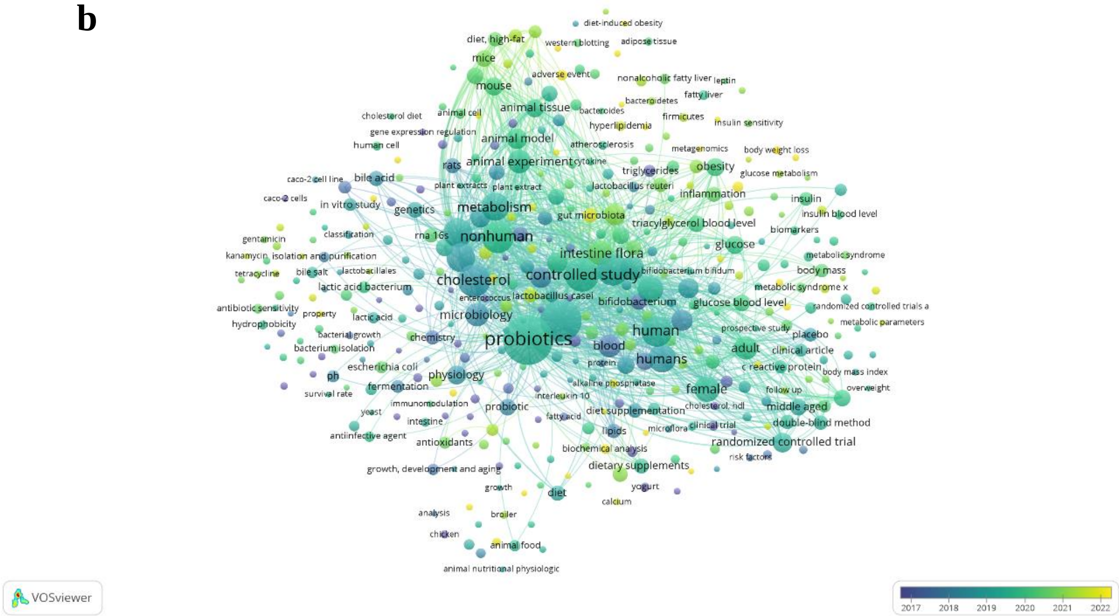
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insulin sensitivity
gene expression regulation
hyperlipidemia
human cell
animal model
atherosclerosis
metagenomics
body weight loss
rats
animal experiment
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triglycerides
obesity
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lactobacillus reuteri
inflammation
caco-2 cells
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genetics
metabolism
gut microbiota
insulin blood level
gentamicin
classification
rna 16s
nonhuman
triacylglycerol blood level
biomarkers
kanamycin
isolation and purification
intestine flora
glucose
metabolic syndrome
tetracycline
bile salt
lactobacillales
cholesterol
controlled study
bifidobacterium bifidum
body mass
lactic acid bacterium
metabolic syndrome x
enterococcus
lactobacillus casei
bifidobacterium
glucose blood level
randomized controlled trials a
antibiotic sensitivity
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microbiology
metabolic parameters
hydrophobicity
bacterial growth
human
prospective study
placebo
chemistry
probiotics
bacterium isolation
blood
adult
clinical article
escherichia coli
humans
protein
c reactive protein
body mass index
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physiology
alkaline phosphatase
fermentation
female
follow up
overweight
survival rate
interleukin 10
immunomodulation
probiotic
cholesterol, hdl
middle aged
diet supplementation
yeast
fatty acid
intestine
lipids
microflora
clinical trial
double-blind method
antiinfective agent
antioxidants
randomized controlled trial
biochemical analysis
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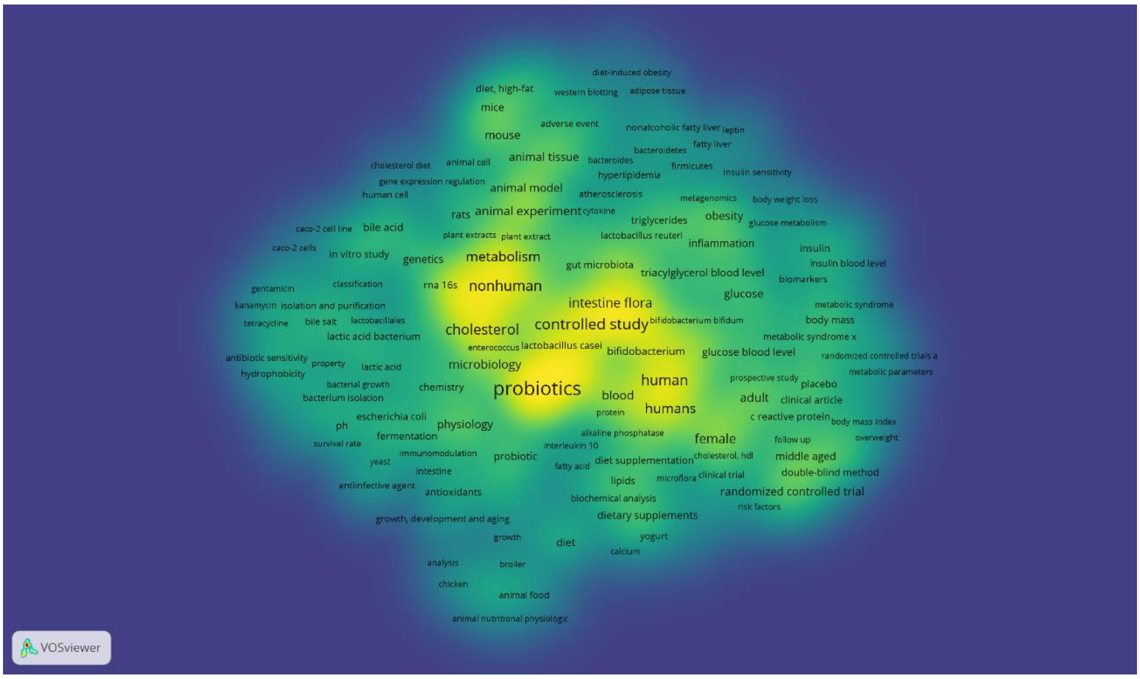

Figure 2. Bibliometric analysis related to the "probiotic and cardiovascular or cholesterol" topic from the Scopus database. a) visualization analysis, b) overlay analysis, and c) density analysis.

Table 3.2. The top 10 keywords related to the "probiotic and cardiovascular or cholesterol" topic from the Scopus database

Keyword	Occurrences	Total link strength
Probiotics	629	14727
Cholesterol	276	8406
Human	243	7592
Animals	219	7032
Metabolism	208	6747
Triacylglycerol	172	6480
Cholesterol blood level	153	5762
Intestine flora	163	5709
Low-density lipoprotein cholesterol	118	4706
High-density lipoprotein cholesterol	108	4358
Lactobacillus	115	3587

3.2. What are Probiotics?

Probiotics are defined as live microorganisms that, when taken in sufficient amounts, provide a health benefit to the host (World Health Organization, 2002). These helpful microorganisms work through various mechanisms, such as boosting the host's immune system by producing immunoglobulins and activating cell-mediated immune responses. Additionally, probiotics have successfully reduced multiple intestinal disorders, including irritable bowel syndrome, gastric ulcers, lactose intolerance, and antibiotic-associated diarrhea (Liu et al., 2016; World Health Organization, 2021; Yan et al., 2017). To deliver health benefits effectively, the World Health Organization (WHO) requires that probiotic strains be able to survive the tough conditions of human digestion, like gastric juices and bile, and still be able to grow within the digestive system.

Probiotic bacteria and yeasts have been extensively studied for their potential health benefits. These include species from the genus *Lactobacillus (L. acidophilus, L. bulgaricus, L. delbrueckii subsp. bulgaricus, L. casei, L. paracasei, L. fermentum, L. lactis, L. plantarum, L. rhamnosus, L. gallinarum, L. reuteri, L. amylovorus, L. brevis, L. helveticus, L. johnsonii, L. cellobiosus, L. crispatus, L. curvatus), Lactococcus (L. lactis), Leuconostoc (L. mesenteroides), Pediococcus (P. pentosaceus, P. acidilactici), Streptococcus (S. thermophilus, S. salivarius), Bifidobacterium (B. animalis, B. bifidum, B. longum, B. breve, B. infantis, B. laterosporus, B. thermophilum, B. essensis), Propionibacterium (P. acidipropionici, P. jensenii, P. thoenii, P. freudenreichii), Enterococcus (E. faecalis, E. faecium), Bacillus (B. cereus, B. cereus var. toyoi, B. clausii, B. coagulans, B. subtilis),* and the yeasts *Saccharomyces cerevisiae* and *S. boulardii* (Brunser & Gotteland, 2010; Hendrati et al., 2017; Kusharyati et al., 2020; Pavlović et al., 2012; Rahayu, 2003; Wang et al., 2021).

The genera Lactobacillus and Bifidobacterium are the most widely studied and commonly used probiotics in producing functional foods. Lactobacillus is a Gram-positive bacterium that can perform both obligate and facultative anaerobic respiration and is a major producer of lactic acid. These bacteria are often part of the natural microbiota of the digestive tract (Hardiningsih et al., 1970; Okamoto et al., 2008). Bifidobacterium, another Gram-positive bacterium, is non-spore-forming, strictly anaerobic, and appears as pleomorphic rods. Notably, Bifidobacterium species can produce lactic and acetic acids (Hadadji et al., 2005; Kusharyati et al., 2020; Venkatesan et al., 2012).

Probiotics provide many benefits to the host, including balancing the gut microbiota, modulating the immune system, and affecting metabolic processes (Fuentes et al., 2016; Hegazy, 2010; Song et al., 2015). Some probiotics can positively influence the symbiotic gut microbiota by encouraging the growth of helpful bacteria while decreasing harmful microorganisms (Blaabjerg et al., 2017; Zhou et al., 2015). This competitive edge is partly due to probiotics' ability to compete with pathogenic bacteria for key nutrients, limiting the growth of the latter. For example, the metabolism of monosaccharides by various probiotics can inhibit the growth of *Clostridium difficile*, an opportunistic pathogen that mainly depends on monosaccharide utilization (Blaabjerg et al., 2017). Additionally, probiotics use other methods to lower the number of harmful bacteria in the gastrointestinal tract. These methods include producing and releasing antimicrobial substances such as organic acids, amino acids, short-chain fatty acids, hydrogen peroxide, and bacteriocins (Kusharyati et al., 2020; 2025; Zhou et al., 2015). Organic acids, in particular, can interfere with the internal pH of pathogens, preventing their growth and survival.

Probiotics are also thought to be capable of adhering to the intestinal mucosa and colonizing the digestive system, which is crucial for their long-lasting beneficial effects. Research has shown the colonization of Bifidobacteria and Lactobacilli in the human digestive tract, though their abundance varies (O'Callaghan & van Sinderen, 2016; Sirilun et al., 2015; Vaughan et al., 2005). Several studies have reported that the concentration of Bifidobacterium cells in feces can reach 10^{10} cells per gram, with a notably higher presence in infant stool compared to adult samples (Arboleya et al., 2012; Kusharyati et al., 2020; Sirilun et al., 2015). In contrast, Lactobacillus populations generally range from 10^8 to 10^9 cells per gram of adult stool (Chul-gyu et al., 2006).

The effective colonization of probiotics can lower the number of harmful bacteria in the digestive system. For example, studies have shown that *Lactobacillus plantarum* 299 and *Lactobacillus rhamnosus* GG effectively prevent enteropathogenic *Escherichia coli* from attaching within the gastrointestinal tract (Kaźmierczak-Siedlecka et al., 2020; Kekkonen et al., 2008). Additionally, Lactobacillus species boost the intestinal barrier by regulating and increasing the expression of genes related to tight junctions, such as β-catenin and E-cadherin (Yu et al., 2012, 2015). The intestinal barrier, a single layer of epithelial cells, acts as the main interface, blocking potentially toxic substances in the intestinal lumen from reaching underlying tissues and the bloodstream (Vancamelbeke & Vermeire, 2017). Importantly, various Lactobacillus proteins have been shown to help bacteria stick to the mucosa by acting as surface adhesins and interacting with complex glycoprotein mixtures secreted by intestinal epithelial cells, which helps exclude pathogens from the mucus layer (Vancamelbeke & Vermeire, 2017; Yu et al., 2012, 2015).

Dysbiosis, an imbalance in the gut microbiota, can weaken the integrity of the intestinal barrier, leading to the translocation of lipopolysaccharide (LPS) and other bacterial components into the bloodstream (Salguero et al., 2019). This systemic leakage of microbial products triggers an inflammatory response, which is involved in the development of atherosclerosis. Specifically, LPS can increase monocyte recruitment to the activated endothelium and promote macrophage foam cell formation by enhancing the uptake of modified LDL and decreasing cholesterol efflux from these foam cells (Khera et al., 2011; Vancamelbeke & Vermeire, 2017).

3.3. Indonesian Traditional Fermented Foods

Indonesia features a wide range of traditional fermented foods that have been a vital part of its culinary heritage for generations. Fermentation is an important method of food preservation, effectively extending the shelf life of perishable items like vegetables, meat, fruits, and fish. This is especially important in tropical regions, where the high water content and nutritional value of these foods make them prone to spoilage. Food preservation through fermentation in Indonesia includes various techniques such as alcoholic fermentation, high-salt fermentation, lactic acid fermentation, mold fermentation, and combinations of these methods.

Indonesia has a rich tradition of fermented foods, many of which are known as natural sources of probiotics. Importantly, most traditional fermented foods in Indonesia are made through spontaneous fermentation, relying on the native microorganisms in the raw ingredients rather than adding a specific inoculum. Probiotic microorganisms are crucial in fermenting a variety of Indonesian food products, including staple foods, meat products, snacks, fruits, and juices. Besides their natural presence in the digestive tract and oral cavity, different probiotic bacteria and yeasts are found in many Indonesian fermented foods (**Table 3.2**).

Indonesia has a wide variety of traditional fermented foods, many of which are important sources of probiotics. The following examples highlight some of these culturally important and health-beneficial foods:

1. Tempe: A staple Indonesian food, tempeh is produced through the controlled fermentation of soybeans. The fermentation process, primarily driven by the beneficial mold *Rhizopus oligosporus,* produces enzymes that break down complex carbohydrates and proteins within the soybeans. This not only enhances digestibility but also contributes to the unique texture and nutritional profile of tempeh.
2. Tape: A popular sweet and slightly alcoholic fermented parboiled rice (or cassava) product enjoyed throughout Indonesia. The fermentation of rice or cassava involves the synergistic action of lactic acid bacteria (LAB) and yeasts. These microorganisms convert the starches present into simple sugars, yielding the characteristic sweetness, and produce lactic acid, which imparts a subtle sour tang to the tape.
3. Dadih: A traditional Indonesian yogurt-like product made from the fermentation of water buffalo milk. The fermentation process is carried out by LAB, resulting in the coagulation and acidification of the milk. Following fermentation, the dadih is traditionally hung in cloth bags to drain excess whey, producing a thick, tangy yogurt with a distinct regional flavor.

4. Pickle vegetable “sayur asin”: A traditional Indonesian pickle prepared through the fermentation of various vegetables in a brine solution. This fermentation process is dominated by LAB, which contributes to the preservation of the vegetables and imparts a sour and slightly salty flavor. Pickle vegetable “sayur asin” is a widely enjoyed side dish with a unique taste and potential probiotic benefits in many Indonesian meals.

Table 3.3. Lists isolated probiotics from various Indonesian fermented traditional foods

Fermented traditional foods	Identified probiotics (genus)	References
Mangos (*Mangifera* sp.) Kedondong (*Spondias cytherea*)	*Lactobacillus, Enterococcus*	(Rahayu, 2003)
Mandai Cempedak (*Artocarpus champeden*)	*Lactobacillus, Pediococcus*	(Emmawati et al., 2015; Rahayu, 2003; Siregar et al., 2014)
Mandai Nangka (*Artocarpus heterophyllus*)	*Lactobacillus, Streptococcus*	(Rahayu, 2003)
Tempoyak durian (*Durio zibethinus*)	*Lactobacillus, Streptococcus, Weisella, Pediococcus, Enterococcus, Rhizopus, Penicillium, Leuconostoc*	(Aisyah et al., 2014; Hasanuddin, 2010; Rahayu, 2003)
Asinan rebung (*Bambusa* sp.)	*Lactobacillus*	(Rahayu, 2003; Wasis et al., 2019)
Asinan kobis (*Brassica oleracea*)	*Lactobacillus, Pediococcus*	(Rahayu, 2003)
Bekasam, Gabus fish (*Ophiocephalus striatus*)	*Lactobacillus, Pediococcus, Streptococcus, Leuconostoc*	(Lestari et al., 1970; Rahayu, 2003)
Peda, Kembung fish (*Rastrelliger neglectus*)	*Lactobacillus, Streptococcus, Pediococcus*	(Hasanah, 2014; Rahayu, 2003)
Terasi, shrimp, or small fish	*Lactobacillus, Pediococcus, Streptococcus, Enterococcus*	(Rahayu, 2003; Sumardianto et al., 2019)
Gatot (dried, uncooked cassava)	*Lactobacillus, Pediococcus*	(Rahayu, 2003)
Growol (fresh, uncooked cassava)	*Lactobacillus*	(Puspaningtyas et al., 2019; Putri et al., 2012; Rahayu, 2003)
Tape Ketan (cooked, sticky rice)	*Lactobacillus, Pediococcus, Weissella*	(Rahayu, 2003; Ramona & Ariwathi, 2022; Zaenal Mustopa & Fatimah, 2014)
Tape ubi (cooked cassava)	*Lactobacillus, Pediococcus, Saccharomyces, Bacillus*	(Hasanah et al., 2019; Rahayu, 2003)
Moromi (fermented soybean)	*Lactobacillus, Pediococcus*	(Rahayu, 2003)
Tempe (fermented soybean)	*Lactobacillus, Pediococcus, Weisella, Rhizopus*	(Rahayu, 2003; Yudianti et al., 2020)
Pickle vegetable “sayur asin” (mustard cabbage leaf)	*Lactobacillus, Pediococcus*	(Rahayu, 2003; Sulistiani et al., 2014)
Kecap (soy sauce)	*Lactobacillus, Tetragenococcus, Pediococcus, Saccharomyces*	(Rahayu, 2003; Sulistyo & Nikkuni, 2005)
Dadih (buffalo milk)	*Leuconostoc, Lactococcus, Lactobacillus, Enterococcus*	(Collado et al., 2007; Nur et al., 2015; Rahayu, 2003)
Fermented mare's milk	*Lactobacillus, Streptococcus*	(Murti et al., 2021; Rahayu, 2003)

Fermented traditional foods	Identified probiotics (genus)	References
Dangke (cow/buffalo milk)	*Lactobacillus*	(Nur et al., 2015)
Oncom (soybean-based)	*Neurospora, Rhizopus, Bacillus*	(Hartanti et al., 2019)
Petis (fish/shrimp-based)	*Pediococcus*	(Pramono et al., 2013)
Peuyeum (cassava-based)	*Saccharomyces, Candida*	(Barus & Natalia Wijaya, 2011)
Lemea (young bamboo/ freshwater fish)	*Lactobacillus*	(Okfrianti et al., 2018; Zuidar et al., 2016)
Urutan (traditional Balinese sausage)	*Lactobacillus, Pediococcus*	(Antara et al., 2002)
Tauco (fermented yellow soybean)	*Rhizopus*	(Harmayani et al., 2017; Herlina et al., 2022)
Jambal roti, marine catfish (*Arius thalassinus*)	*Staphylococcus, Lactobacillus, Pediococcus*	(Hui & Evranuz, 2012; Karyantina et al., 2020)
Kecap ikan (fish sauce)	*Bacillus, Lactobacillus*	(Farida et al., 2019; Hui & Evranuz, 2012)
Naniura, carp (*Cyprinus carpio*) tilapia (*Oreochromis mossambica*)	*Lactobacillus*	(Hui & Evranuz, 2012; Manik et al., 2019)
Bakasang (fish's organs)	*Lactobacillus, Micrococcus, Streptococcus, Bacillus, Pediococcus*	(Hui & Evranuz, 2012; Ijong & Ohta, 1996)
Budu, Spanish mackerel (*Scomberomorus* sp.) and leather skin (*Chorinemus* sp.)	*Lactobacillus*	(Abbasiliasi et al., 2011; Liasi et al., 2009)
Cincalok (shrimp-based)	*Lactobacillus, Pediococcus*	(Hui & Evranuz, 2012)
Picungan (fish-based)	*Lactobacillus*	(Hui & Evranuz, 2012; Syafitri et al., 2022)
Rusip, anchovy (*Stolephorus* sp.)	*Leuconostoc, Streptococcus, Lactococcus, Lactobacillus, Staphylococcus, Pediococcus, Enterococcus*	(Hui & Evranuz, 2012; Kusmarwati et al., 2014)
Tukai, barracuda-based (*Sphyraena* sp.)	*Micrococcus, Staphylococcus, Pediococcus, Lactobacillus, Pseudomonas, Streptococcus, Bacillus*	(Hui & Evranuz, 2012)
Ronto (shrimp-based)	*Pediococcus*	(Khairina et al., 2016)
Semayi	*Bacillus*	(Harmayani et al., 2017)
Cabuk	*Bacillus*	(Harmayani et al., 2017)
Acar ketimun (cucumber pickle)	*Lactobacillus*	(Farida et al., 2019; Surbakti & Hasanah, 2021)
Pliek-U	*Lactobacillus, Enterococcus*	(Septi, 2019)
Chao, tembang fish-based (*Sardinella fimbriata*)	*Lactobacillus, Pediococcus*	(Matti et al., 2021)
Kempong (tofu-based)	*Rhizopus*	(Arfina et al., 2013)
Jruek drien	*Lactobacillus, Bacillus*	(Yulvizar et al., 2015)

3.4. Cardiovascular Diseases

The World Health Organization (WHO) projects that cardiovascular disease (CVD) will continue to be the leading cause of death worldwide by 2030. Notably, heart attacks and strokes cause more than 80% of all CVD-related deaths, with about one-third of these occurring in adults under 70 years old (World Health Organization, 2021). Alarmingly, nearly 80% of global CVD deaths happen in low- and middle-income countries, where the burden of CVD and its risk factors is growing due to the ongoing epidemiological transition.

Key behavioral risk factors for CVD include unhealthy dietary habits, physical inactivity, and tobacco and alcohol use (Sabzmakan et al., 2014; World Health Organization, 2021). These behaviors can cause physiological changes like higher blood glucose levels, increased blood pressure, dyslipidemia (abnormal blood lipid levels), and the development of overweight and obesity. Specifically, elevated low-density lipoprotein (LDL) cholesterol mainly contributes to hypertension, hyperlipidemia, and coronary heart disease (Ogita et al., 2014; Tsukinoki et al., 2014). Increased LDL cholesterol encourages the formation of atherosclerotic plaques in the arterial walls.

Atherosclerosis, a chronic inflammatory disease of the blood vessels, is the main cause of morbidity and mortality related to cardiovascular disease (Kobiyama & Ley, 2018). People with hypercholesterolemia have a threefold higher risk of experiencing a heart attack compared to those with normal blood lipid levels. Keeping LDL cholesterol levels below 100 mg/dL is linked to a lower risk of coronary heart disease (Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults, 2001; National Institutes of Health, 2002). Therefore, controlling serum LDL cholesterol is an essential step in reducing the risk of various cardiovascular diseases.

Elevated cholesterol levels are a key factor in the development of atherosclerosis-related diseases, including peripheral vascular disease and coronary artery disease (Lusis, 2000). Although cholesterol has essential and generally harmless roles in body functions—such as building cell membranes and producing steroid hormones and bile salts—keeping serum levels within a healthy range is crucial for heart health. Cholesterol levels from 100 to 129 mg/dL are considered near optimal, but the risk of coronary heart disease rises beyond this level. Interestingly, even a 1% increase in serum cholesterol has been linked to a higher risk of cardiovascular disease. Levels between 160 and 189 mg/dL are classified as high, and those over 190 mg/dL are considered very high, greatly increasing the likelihood and progression of coronary heart disease (Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults, 2001; National Institutes of Health, 2002). For people with cardiovascular disease, access to effective medications like statins, angiotensin-converting enzyme inhibitors, beta-blockers, and aspirin is essential for managing their health (World Health Organization, 2021).

3.5. Potential Mechanisms of Probiotics in Reducing Cardiovascular Disease Risk

Probiotics are believed to provide their heart-protecting effects through multiple interconnected mechanisms. One key proposed mechanism is the ability of probiotics to lower blood pressure (Tsukinoki et al., 2014). Since hypertension is a major risk factor for cardiovascular disease, the finding that specific probiotic strains can reduce blood pressure in both hypertensive and normotensive individuals is highly relevant clinically. Another important mechanism being studied is the capacity of probiotics to reduce systemic inflammation (Salguero et al., 2019).

Chronic inflammation is increasingly seen as a key factor in the development of cardiovascular disease, and research has shown that probiotic supplements can lower circulating markers of inflammation. Additionally, probiotics may positively influence lipid levels by reducing low-density lipoprotein cholesterol (LDL-C) and raising high-density lipoprotein cholesterol (HDL-C) (Jeun et al., 2010; Zheng et al., 2013). Certain probiotic strains have also been demonstrated to decrease total cholesterol and triglyceride levels in the blood, which are known risk factors for cardiovascular disease.

Several in vitro mechanisms have been suggested to explain how probiotics lower cholesterol. These include: (1) cholesterol assimilation, where probiotics incorporate cholesterol into their cell membranes during growth; (2) binding of cholesterol to probiotic cell walls (Kimoto et al., 2002; Li, 2012; Lin & Chen, 2020; Taranto et al., 2003), preventing its absorption in the gut; (3) fermentation processes that may lead to the destabilization or coprecipitation of cholesterol within cholesterol-containing micelles; (4) inhibition of endogenous cholesterol synthesis as a downstream effect of short-chain fatty acid (SCFA) metabolism (Conterno et al., 2011; Rai et al., 2017); (5) bile acid deconjugation through the activity of bile salt hydrolase (BSH) enzymes secreted by Lactobacillus species (Jeun et al., 2010; Liong & Shah, 2005; Schillinger et al., 2005; Sirilun et al., 2010; Vyas & Ranganathan, 2012; Yusuf et al., 2020), which can lead to reduced cholesterol absorption and increased cholesterol excretion; (6) coprecipitation of cholesterol with deconjugated bile acids (Al-Saleh et al., 2006; Grill et al., 2000; Li, 2012); (7) oxidation of cholesterol by cholesterol oxidase enzymes (Ahire et al., 2012); (8) binding of bile salts to exopolysaccharides produced by some probiotics (Pigeon et al., 2002); (9) production of various functional peptides that may influence lipid metabolism (Kim et al., 2008; Madani et al., 2013); and (10) conversion of cholesterol to the less absorbable sterol, coprostanol (Chiang et al., 2008; Lye et al., 2009; Ooi & Liong, 2010). Recent in vitro studies suggest that the cholesterol-reducing effects of probiotics are often mediated by a combination of these processes, primarily involving cholesterol binding to the cell membrane, cholesterol assimilation during bacterial growth, and bile salt deconjugation (Liong & Shah, 2005; Lye et al., 2009).

Table 3.4. Structured overview of in vivo studies on cholesterol reduction by probiotics

Probiotic strains	Dose (cell density)	Results	Subject	Diets	Intervention period	Reference
L. plantarum CAAS 18008	LAB suspension (10^9 CFU)	Reduced by 28.8% LDL, 21.7% TC serum, and 30.9% TC liver	Hamster	High cholesterol (0.4%)	4 weeks	(Ma et al., 2019)
Lactobacillus plantarum Dad-13	Tape ketan containing 1×108 CFU/g LAB	Significantly reduced cholesterol, triglyceride, and LDL levels. Significantly increased HDL level	Rats	Wet tape product at 1.8 g per head per day	7 weeks	(Yulianto et al., 2023)
B. longum CBG-C11, *B. lactis* CBG-C10, *B. breve* CBG-C2, *L. reuteri* CBG-C15 and *L. plantarum* CBG-C21	Dried biomass of LAB (10^9 and 10^{10} CFU)	Reduced 1.2-1.5-fold of total cholesterol, 1.32-1.4-fold of TG, 1.3-1.5-fold of LDL	Mice	High cholesterol (1.25%)	8 weeks	(Kim et al., 2017)
L. acidophilus LA15, *L. plantarum* B23 and *L. kefiri* D17	LAB cells (10^9 CFU)	Significantly reduced LDL, TC, and TG	Mice	High cholesterol (1%)	4 weeks	(Zheng et al., 2013)
L. plantarum 9-41	LAB suspension (10^9 CFU)	Reduced 25.5% of total cholesterol, 32.9% of LDL, and 16% of TG	Mice	High cholesterol (1%)	6 weeks	(Xie et al., 2011)
L. fermentum M1-16		Reduced 12.5% of TC, 17.3% of LDL, and 15.7% of TG				
L. acidophilus ATCC 4356	Dried biomass of LAB (10^9 CFU)	Reduced 92% of TC, 35% of LDL, and 51% of TG	Mice	High cholesterol (1%)	4 weeks	(Huang et al., 2010)

Probiotic strains	Dose (cell density)	Results	Subject	Diets	Intervention period	Reference
L. plantarum MA2	Dried biomass of LAB (10^{11} CFU)	Reduced 31% of total serum cholesterol, 20% of LDL, and 31.18% of TG	Mice	High cholesterol (1%)	5 weeks	(Wang et al., 2009)
L. plantarum KCTC3928	Double-coated LAB (10^{9} CFU)	Reduced 33% of TC by living cells, 40% of LCL by living cells, 20% of LDL by dead cells, and 32% of TG	Mice	High lipid	4 weeks	(Jeun et al., 2010)
L. kefiri DH5	LAB suspension (2×10^{8} CFU)	Reduced 7.2 mg/dL of TC and 3.7 mg/dL of LDL	Mice	High lipid (60% calories)	6 weeks	(Kim et al., 2017)
L. plantarum K21	LAB suspension (10^{9} CFU)	Reduced 24% of TC and 45% of TG in the liver	Mice	High lipid (40% calories)	8 weeks	(Wu et al., 2015)
L. acidophilus NSI	LAB suspension (10^{8} CFU)	Significantly reduced TC, TG and LDL, but not significantly to HDL	Mice	High lipid (45% calories)	10 weeks	(Song et al., 2015)
L. plantarum LS/07	Mixed suspension of skim milk and LAB (3×10^{9} CFU)	Reduced 20% of TC, 28% of TG, and 24% of LDL	Mice	High lipid (20% lard)	10 weeks	(Salaj et al., 2013)
L. plantarum Biocenol LP96		Reduced 8.9% of TC and 38.8% of TG				
Bifidobacterium pseudocatenulatum SPM 1204, *B. longum* SPM 1205, and *B. longum* SPM 1207	LAB suspension (10^{8}-10^{9} CFU)	Reduced 2.7% of TC, 5.9% of TG, and 9.1% of LDL	Mice	High lipid (40% calories)	5 weeks	(An et al., 2011)
L. acidophilus KBc, *L. brevis* KBa	LAB suspension (10^{11} CFU)	Reduced 51.70%-53.74% of TC	Rabbit	High cholesterol	4 weeks	(Antara et al., 2019)

Probiotic strains	Dose (cell density)	Results	Subject	Diets	Intervention period	Reference
L. casei NCDC-19	LAB cells (10^6 CFU)	Reduced 37% of LDL, but not significantly to HDL and TG	Mice	High cholesterol (1%)	6 weeks	(Sindhu & Khetarpaul, 2003)
L. reuteri CRL 1098	LAB suspension (10^4 CFU)	Reduced 38% of TC, 40% of TG, and increased 20% of HDL	Mice	High lipid	A week	(Taranto et al., 1998)
L. plantarum PH04	LAB suspension (10^7 CFU)	Reduced 7% of TC, 10% of TG	Mice	High cholesterol (10%)	2 weeks	(Nguyen et al., 2007)
B. longum Bb-46	LAB cells (10^8 CFU)	Reduced 50.3% of TC, 56.3% of LDL, 51.2% of TG	Rat	High cholesterol (0.5%)	5 weeks	(Abd El-Gawad et al., 2005)
L. acidophilus	*L. acidophilus* supplementation on rice bran	Reduced by 15-33% of TC	Rats	High lipid and High cholesterol	4 weeks	(Fukushima et al., 1999)
L. acidophilus L1	yoghurt containing *L. acidophilus* L1	Reduced by 2-3% of TC	Human	n/a	4 weeks	(Anderson & Gilliland, 1999)

Note: CFU (colony forming units), TC (total cholesterol), TG (triglycerides), HDL (high-density lipoprotein), LDL (low-density lipoprotein).

3.6. Probiotic Cholesterol Reduction in Animal Studies

Probiotics have been widely used in creating functional foods and beverages because of their various health benefits. Among lactic acid bacteria (LAB), the genera Lactobacillus and Bifidobacterium are well-known for their probiotic properties, including *Lactobacillus plantarum*, *L. reuteri*, *L. fermentum*, *L. acidophilus*, *L. kefiri*, *Bifidobacterium longum*, *B. lactis*, *B. breve*, and *B. pseudocatenulatum*. This mini-review examines explicitly the potential role of probiotics and their metabolic products in lowering blood pressure via in vivo cholesterol-lowering mechanisms. An increasing amount of evidence suggests that probiotics may help prevent the risk of cardiovascular disease. Numerous studies have investigated the potential benefits of probiotic consumption on various aspects of cardiovascular health (**Table 3.4**).

The ability of probiotics to lower cholesterol levels in animal models shows considerable variability across different cases strains. As summarized in **Table 3.2**, several *in vivo* studies have investigated the impact of specific probiotic strains on cholesterol metabolism. For instance, oral administration of a *Lactobacillus plantarum* CAAS 18008 suspension to hamsters for four weeks resulted in notable reductions of 28.8% in LDL cholesterol, 21.7% in total serum cholesterol (TC), and 30.9% in liver cholesterol (Ma et al., 2019). Similarly, Kim *et al.*, (2017) reported that a probiotic mixed culture containing *Bifidobacterium longum* CBG-C11, *B. lactis* CBG-C10, *B. breve* CBG-C2, *Lactobacillus reuteri* CBG-C15, and *L. plantarum* CBG-C21 was effective in increasing HDL cholesterol levels and decreasing total cholesterol, LDL cholesterol, and triglyceride (TG) levels in mice.

A study by Zheng *et al.*, (2013) demonstrated that administering *Lactobacillus acidophilus* LA15, *L. plantarum* B23, and *L. kefiri* D17 to mice on a high-cholesterol diet for four weeks significantly reduced LDL, TC, and TG levels. Furthermore, the use of double-coated Lactobacillus plantarum KCTC3928 in mice fed a high-fat diet for four weeks led to a 31% decrease in serum total cholesterol, a 2% decrease in LDL cholesterol, and a 32% decrease in triglycerides (Jeun et al., 2010). Several other lactic acid bacteria strains have also been documented to influence serum lipid profiles in mice, including *Lactobacillus kefiri* DH5 (Kim et al., 2017), *L. plantarum* MA2 (Wang et al., 2009), *L. acidophilus* ATCC 4356 (Huang et al., 2010), *L. plantarum* K21 (Wu et al., 2015), *B. pseudocatenulatum* SPM 1204, B. *longum* SPM 1205, and *B. longum* SPM 1207 (An et al., 2011).

In another study evaluating the cholesterol-lowering potential of *Lactobacillus acidophilus* KBc and *Lactobacillus brevis* KBa, isolated from wild horses' milk, Antara et al. (2019) orally administered these strains (at 10^{11} CFU/mL per rabbit daily) to male hypercholesterolemic rabbits for four weeks. Their findings demonstrated a significant reduction in blood serum cholesterol levels, ranging from 51.70% to 53.74%. Sindhu and Khetarpaul (2003) investigated the effects of *Lactobacillus casei* NCDC-19, derived from a fermented food mixture supplemented with 1% cholesterol. In this six-week study involving twenty young Swiss mice, the administration of *L. casei* NCDC-19 significantly lowered low-density lipoprotein (LDL) cholesterol by 37%. However, it did not significantly affect high-density lipoprotein (HDL) or triglyceride (TG) levels.

Taranto et al. (1998) reported that administering Lactobacillus reuteri CRL 1098 at a dose of 10^4 cells daily to hypercholesterolemic mice for one week caused a significant 38% decrease in total cholesterol, a 40% reduction in triglycerides, and a 20% increase in HDL cholesterol. Nguyen et al. (2007) isolated *Lactobacillus plantarum* PH04 from infant feces and administered it to hypercholesterolemic mice (at a dose of 10^7 CFU/mL per mouse daily) for two weeks. The results of this study indicated that *L. plantarum* PH04 could reduce total cholesterol by 7% and triglycerides by 10%.

Other studies have also explored the cholesterol-lowering effects of various lactic acid bacteria, including *Bifidobacterium longum* Bb-46 (Abd El-Gawad et al., 2005), *Lactobacillus acidophilus* (Fukushima et al., 1999), and *L. acidophilus* L1 (Anderson & Gilliland, 1999) identifying them as potential probiotics with this beneficial property. While the evidence gathered from these animal studies is promising, further research, particularly well-designed human clinical trials, is warranted to elucidate the potential benefits of probiotics on cardiovascular health. Nevertheless, the current evidence suggests that incorporating probiotics into a healthy dietary regimen may represent a simple and effective adjunctive strategy for reducing the risk of cardiovascular disease.

4. CONCLUSIONS

Probiotics show significant promise in improving cholesterol profiles, consistently reducing total and LDL cholesterol, liver cholesterol, and triglycerides while boosting HDL. However, their impact is highly variable, influenced by strain, dosage, and individual factors. For Indonesian fermented foods, harnessing this potential for cardiovascular health demands a deeper understanding of the unique strains present and their optimal application within the local dietary landscape.

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