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Probiotics in cardiovascular care: Mechanisms and future potential

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ABSTRACT

Cardiovascular diseases (CVD) remain a leading cause of global mortality, with coronary artery disease (CAD) being among the most prevalent conditions. Recent research indicates that probiotics play a role in modulating gut microbiota, offering potential therapeutic benefits in CVD management. Probiotics have demonstrated efficacy in reducing systemic inflammation, lowering cholesterol levels, and improving insulin sensitivity, which are key contributors to cardiovascular health. This review draws on peer-reviewed clinical studies focusing on strains such as *Lactobacillus reuteri* and *Bifidobacterium longum* to explore their role in improving lipid profiles, regulating blood pressure, and enhancing endothelial function. Studies were selected based on randomized controlled trials and observational data that examined the effect of probiotic interventions on cardiovascular outcomes. Results indicate significant reductions in low-density lipoprotein (LDL) cholesterol and improvements in vascular health through modulation of gut dysbiosis and reduction in oxidative stress. While probiotics offer promising benefits, safety concerns exist, particularly for immunocompromised patients, necessitating careful strain selection and monitoring. Moreover, individual variability in response to probiotics highlights the importance of personalized therapeutic approaches. Future research should focus on developing standardized clinical protocols, optimizing dosages, and conducting long-term studies to validate sustained benefits. In conclusion, probiotics represent a complementary strategy for managing CVD by addressing modifiable risk factors. However, further research is needed to refine personalized probiotic therapies and integrate them with pharmacological interventions. With robust clinical validation, probiotics could become an integral part of preventive cardiology, contributing to comprehensive cardiovascular care through targeted modulation of the gut microbiome.

KEYWORDS

Cardiovascular diseases; Bifidobacterium longum; Coronary artery disease; Gastrointestinal microbiome; Oxidative stress; Insulin resistance

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Introduction

Cardiovascular diseases (CVDs) are a leading cause of death globally, posing a significant public health burden. Among these, coronary artery disease (CAD) stands out due to its high prevalence and association with atherosclerotic plaque growth in arterial walls, which impairs blood flow and can lead to severe complications. Despite advancements in medical treatments, the global burden of CVDs continues to rise, necessitating novel strategies for prevention and treatment [1].

In recent years, the role of the gut microbiome in cardiovascular health has gained increasing attention. Research indicates that imbalances in gut microbial populations can influence the development of CVDs through mechanisms such as systemic inflammation, oxidative stress, and metabolic dysfunction. Probiotics, live beneficial microorganisms that help restore gut microbial balance, are being explored as promising interventions for improving cardiovascular health [2]. Probiotic strains such as Lactobacillus and Bifidobacterium have demonstrated the potential to lower cholesterol levels, reduce hypertension, and improve insulin sensitivity, all of which are critical risk factors for cardiovascular diseases.

Clinical evidence supports the use of probiotics in reducing low-density lipoprotein (LDL) cholesterol and managing blood pressure in individuals with hypercholesterolemia and hypertension. Additionally, probiotics have demonstrated beneficial effects in modulating gut dysbiosis and enhancing vascular function [3]. These findings highlight the potential role of probiotics in mitigating cardiovascular risk factors through non-invasive means. Despite promising findings, standardization of probiotic interventions remains a challenge due to variations in strain selection, individual response, and optimal dosage. Furthermore, the long-term cardiovascular benefits of probiotics require further investigation, emphasizing the need for more rigorous studies [4].

Current research suggests that probiotics could complement conventional cardiovascular therapies by reducing inflammation, improving metabolic function, and modulating blood pressure. Further research into the mechanisms of probiotic efficacy is needed to design targeted interventions [5]. This review aims to explore the cardioprotective potential of probiotics by analysing their mechanisms of action, evaluating clinical evidence, addressing challenges, and identifying future research directions to establish their role in cardiovascular health management.

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Mechanisms of Cardioprotective Effects of Probiotics

Reduction of cholesterol and lipid levels

Probiotic supplementation has demonstrated significant potential in lowering low-density lipoprotein (LDL) cholesterol and improving the high-density lipoprotein (HDL) to LDL ratio. These improvements reduce the formation of atherosclerotic plaques, which are critical risk factors for coronary artery disease (CAD) [6]. Probiotics achieve this effect by regulating cholesterol metabolism through the action of bile salt hydrolase (BSH) enzymes. These enzymes deconjugate bile salts, reducing their reabsorption and enhancing cholesterol excretion through faeces. Consequently, the overall cholesterol pool in circulation is diminished, promoting cardiovascular health [7].

Strains such as Lactobacillus and Bifidobacterium have shown efficiency in lipid modulation. Clinical studies and animal models report significant reductions in LDL cholesterol, triglycerides, and total cholesterol levels following probiotic administration. In hyperlipidemic subjects, probiotic supplementation improved lipid profiles, demonstrating its utility as an adjunct to conventional lipid-lowering therapies. Fermented foods enriched with *Lactobacillus reuteri* and *Bifidobacterium longum* have further confirmed these cholesterol-lowering benefits, making them a viable dietary intervention for at-risk individuals [8].

Probiotic-mediated lipid control also extends to cellular function, where cholesterol is assimilated into plasma membranes, further preventing its growth in circulation. These findings underscore the role of probiotics in addressing dyslipidemia, a major contributor to cardiovascular diseases, and suggest their potential to reduce dependence on pharmacological agents (Figure 1) [9].

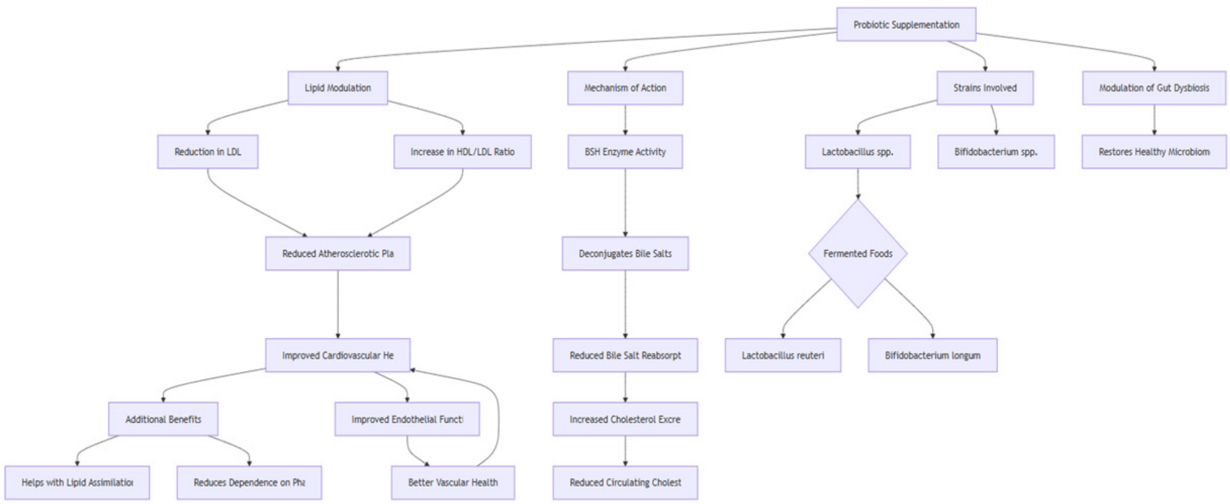

Figure 1. Detailed flowchart showing the role of probiotics in the reduction of cholesterol and lipid levels.

Anti-inflammatory and immunomodulatory effects

Chronic low-grade inflammation plays a central role in the pathogenesis of cardiovascular diseases. Elevated levels of pro-inflammatory cytokines such as tumour necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6) contribute to endothelial dysfunction and plaque formation. Probiotics mitigate these effects by modulating cytokine production and promoting immune homeostasis, creating a favourable environment for cardiovascular health [10].

Experimental evidence supports the use of specific probiotic strains, including *Bifidobacterium longum* and *Lactobacillus helveticus*, to reduce inflammatory markers. These strains enhance the function of regulatory T-cells (Tregs) and decrease the activity of pro-inflammatory cells, contributing to a balanced immune response. The modulation of gut microbiota by probiotics also enhances intestinal barrier integrity, preventing the translocation of lipopolysaccharides (LPS) into the bloodstream, a process linked to systemic inflammation and cardiovascular disease progression [11].

Probiotics indirectly influence endothelial function through their immunomodulatory effects. By reducing inflammatory markers, they help preserve endothelial integrity, maintaining optimal vascular function. This connection between gut health and systemic inflammation highlights the therapeutic potential of probiotics in managing cardiovascular risks beyond the gastrointestinal tract [12].

Blood pressure regulation and anti-hypertensive effects

Hypertension is a key modifiable risk factor for cardiovascular diseases, including stroke and myocardial infarction. Probiotics have shown promise in managing hypertension by inhibiting angiotensin-converting enzyme (ACE) activity. This inhibition limits the conversion of angiotensin I to angiotensin II, a potent vasoconstrictor, thus promoting vasodilation and reducing blood pressure [13].

Clinical studies indicate significant reductions in both systolic and diastolic blood pressure among hypertensive patients following probiotic supplementation. Multi-strain probiotics have proven particularly effective, with evidence suggesting that their ability to enhance nitric oxide (NO) availability plays a critical role in improving vascular function. NO, a potent vasodilator, relaxes vascular smooth muscles, reducing arterial stiffness and improving blood flow [14].

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The antihypertensive effects of probiotics are further supported by improvements in endothelial function and reductions in oxidative stress. This dual action of enhancing vasodilation and reducing oxidative damage makes probiotics a valuable adjunct to pharmacological therapies for hypertension, potentially lowering the burden of medication use in long-term management (Figure 2) [15].

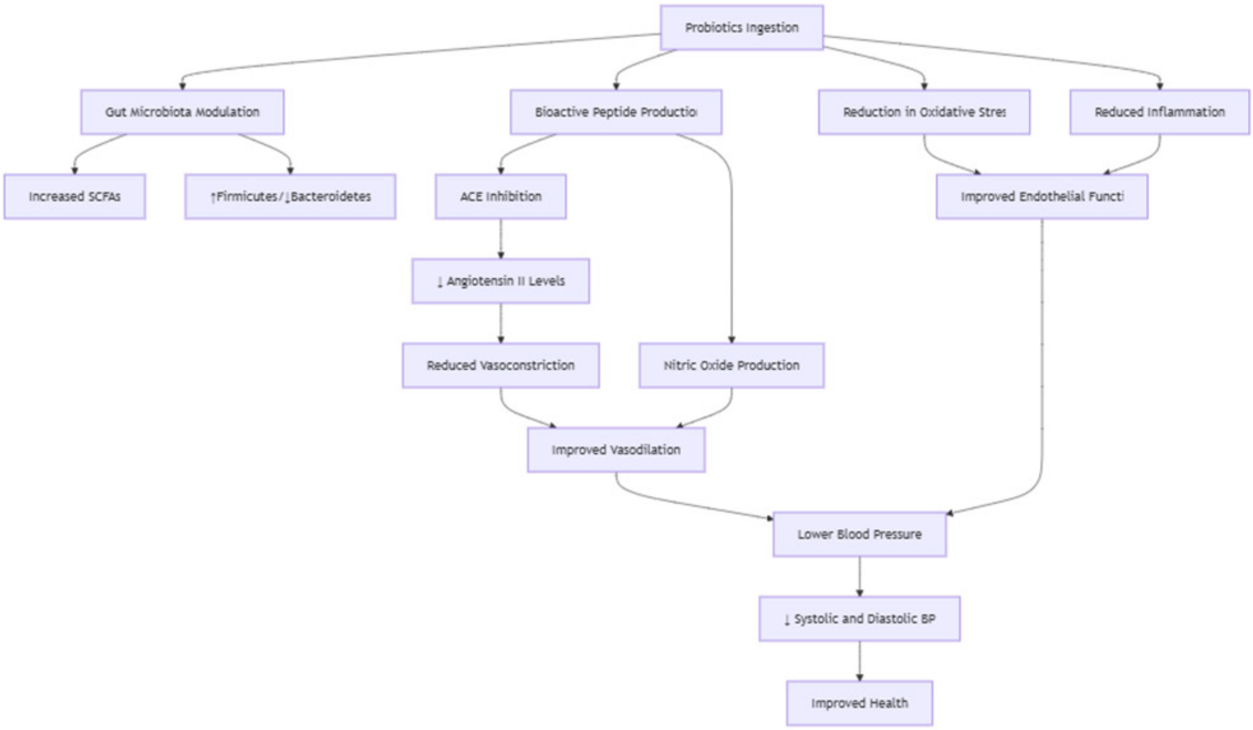

Figure 2. Flowchart showing the role of probiotics in the regulation of blood pressure and hypertensive effects.

Modulation of gut dysbiosis and endothelial function

Gut dysbiosis, or the imbalance of gut microbial populations, is increasingly recognized as a contributor to cardiovascular diseases. Dysbiosis impairs the intestinal barrier, allowing harmful substances such as LPS to enter the bloodstream. The resulting systemic inflammation exacerbates endothelial dysfunction, a precursor to hypertension and atherosclerosis [16]

Probiotics restore microbial balance and enhance intestinal barrier function, preventing the translocation of inflammatory molecules. This restoration reduces oxidative stress, preserving endothelial function and minimizing vascular damage. Improved gut integrity also ensures better regulation of metabolic processes, including lipid metabolism and insulin sensitivity, both of which are crucial in preventing metabolic syndrome and cardiovascular complications [17].

The production of short-chain fatty acids (SCFAs) by beneficial gut bacteria further contributes to cardiovascular health. SCFAs modulate insulin sensitivity and reduce inflammation, supporting vascular health and reducing the risk of type 2 diabetes. Clinical studies demonstrate that probiotic interventions enhance endothelial function, as evidenced by improved arterial elasticity and reduced vascular resistance. These findings suggest that probiotics can significantly impact vascular health by addressing both gut and systemic inflammation, offering a promising strategy for cardiovascular disease prevention and management (Figure 3) [18].

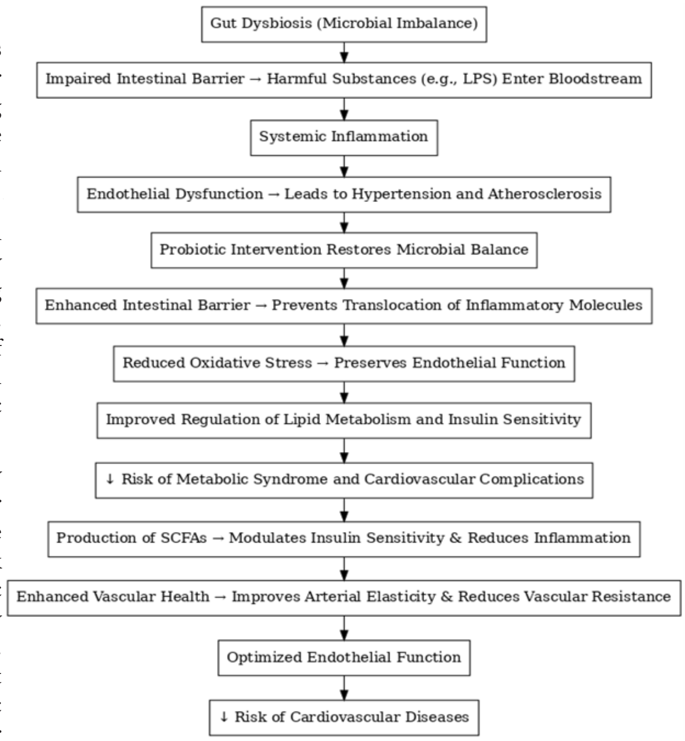

Figure 3. Flowchart explaining the probiotic modulation of gut dysbiosis and endothelial function.

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Clinical Evidences

Impact on coronary artery disease (CAD)

Probiotic supplementation has demonstrated significant benefits in managing coronary artery disease (CAD) by improving vascular health and modulating inflammation. Studies show that *Lactobacillus plantarum* 299v improves endothelial function through enhanced flow-mediated dilation and suppresses systemic inflammation by reducing levels of interleukin-6 (IL-6) and tumour necrosis factor-alpha (TNF-α). This indicates the potential of probiotics to restore vascular integrity, which is crucial in preventing the progression of CAD [19].

Additionally, *Lactobacillus rhamnosus* GG effectively reduces metabolic endotoxemia, a condition marked by endotoxins in circulation that drive chronic inflammation and impair vascular health. The administration of these probiotics improves the balance of gut microbiota, leading to reduced inflammatory markers and improved cardiovascular outcomes by targeting lipid metabolism and immune regulation [20].

Animal studies further reinforce these findings, revealing that *Bifidobacterium longum* and *Lactobacillus helveticus* exert anti-inflammatory effects by lowering the production of pro-inflammatory cytokines. These probiotics also promote bile salt hydrolase activity, reducing cholesterol absorption and lowering low-density lipoprotein (LDL) cholesterol levels. Clinical interventions using a combination of probiotics and prebiotics have shown additional benefits, such as alleviating anxiety and depression symptoms in CAD patients by reducing oxidative stress [21].

Benefits in stroke and hypertension management

Probiotic use has shown promise in stroke recovery by addressing gut dysbiosis, a condition that exacerbates systemic inflammation and worsens stroke outcomes. Restoring microbial diversity through probiotic supplementation enhances gut barrier integrity, preventing the translocation of harmful bacteria and reducing the severity of systemic inflammatory response syndrome (SIRS). In elderly patients recovering from ischemic stroke, the restoration of gut microbiota has been associated with cognitive improvements and enhanced vascular health, underscoring the role of the gut-brain axis in stroke management [22].

In hypertension management, probiotics act as adjunct therapies by modulating the renin-angiotensin system. Strains such as *Lactobacillus fermentum* and *Bifidobacterium breve* inhibit angiotensin-converting enzyme (ACE) activity, leading to vasodilation and reduced blood pressure. These probiotics have also been found to prevent endothelial dysfunction by decreasing oxidative stress and restoring the balance between T-helper 17 (Th17) cells and regulatory T (Treg) cells, thereby improving immune homeostasis [23].

Clinical studies indicate that long-term probiotic use results in significant reductions in both systolic and diastolic blood pressure, contributing to better vascular health. These findings are especially relevant for individuals with conditions like systemic lupus erythematosus, where vascular inflammation plays a critical role in hypertension development [24].

Effects on hypercholesterolemia and obesity

Probiotics have been extensively studied for their impact on lipid metabolism, with positive outcomes in hypercholesterolemia management. Specific strains, including *Enterococcus faecium* and *Lactobacillus paracasei*, reduce total and LDL cholesterol levels by modulating cholesterol metabolism-related genes. These probiotics also promote the production of short-chain fatty acids (SCFAs), such as acetic and propionic acid, which improve insulin sensitivity and decrease liver fat accumulation [25].

In obesity management, probiotics contribute by altering gut microbiota composition, reducing systemic inflammation, and preventing insulin resistance. Clinical trials have shown that consuming probiotic-rich soy milk containing *Lactobacillus plantarum* significantly reduces systolic and diastolic blood pressure in prediabetic patients, suggesting a dual benefit in managing hypertension and obesity. These findings highlight the comprehensive role of probiotics in reducing cardiovascular risks associated with obesity and metabolic disorders [26].

Probiotic interventions, therefore, offer a multi-faceted approach to cardiovascular health by regulating inflammation, improving lipid profiles, and restoring microbial balance. With further research, these strategies could become integral components of non-invasive cardiovascular disease management. Table 1 briefly describes the types of probiotics used in cardiovascular research [27].

Table 1. Types of probiotic strains used in cardiovascular research and their potential benefits.

Probiotic Strain	Potential Usage	Dose Range	Mode of Administration
Lactobacillus plantarum	Reduces LDL cholesterol and blood pressure	10^9 - 10^{10} CFU/day	Capsules, yoghurt
Lactobacillus reuteri	Lowers serum cholesterol, inflammation	1.25×10^{10} CFU/day	Fortified drinks
Bifidobacterium longum	Modulates lipid profiles, reduces triglycerides	10^8 - 10^9 CFU/day	Capsules, sachets
Lactobacillus acidophilus	Decreases blood glucose and improves HDL levels	10^9 CFU/day	Tablets, fortified milk
Lactobacillus casei	Lowers BMI, improves vascular function	1×10^9 CFU/day	Yoghurt, capsules
Lactobacillus rhamnosus	Enhances anti-inflammatory responses	10^9 - 10^{10} CFU/day	Tablets, yoghurt
Streptococcus thermophilus	Supports gut-heart axis, reduces hypertension	10^9 CFU/day	Yoghurt

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Challenges and Limitations

Variability in strain-specific effects

The therapeutic benefits of probiotics vary considerably between strains, complicating their use in cardiovascular therapies. For example, some strains, such as *Lactobacillus fermentum* and *Bifidobacterium breve*, demonstrate cholesterol-lowering properties, while others exhibit immunomodulatory effects. However, clinical studies in humans have yielded inconsistent outcomes compared to animal models, reflecting challenges in translating these effects across diverse populations [28]. Variability arises due to differences in gut microbiota composition, health conditions, and individual responses, complicating the standardization of probiotic treatments. Furthermore, there is limited data on optimal combinations of strains and the appropriate dosages required to achieve consistent therapeutic outcomes.

Addressing these inconsistencies requires targeted research into strain-specific mechanisms and developing personalized treatment approaches tailored to individual gut profiles. Personalized therapies can leverage advancements in microbiome profiling, potentially optimizing probiotic use to meet specific cardiovascular health needs. Clear clinical guidelines for healthcare providers are essential to ensure effective probiotic interventions that reflect these complexities [29].

Lack of long-term data and uncertainty in mechanisms

Most research on probiotics focuses on short-term clinical outcomes, limiting the understanding of their long-term effects on cardiovascular health. While several short-term studies have documented benefits—such as improved lipid profiles, better blood pressure regulation, and reductions in inflammatory markers—questions remain about the sustainability of these outcomes over time. The absence of long-term data restricts the ability to determine whether probiotics can offer durable protection against cardiovascular events, such as myocardial infarction or stroke [30].

The underlying mechanisms through which probiotics exert their cardioprotective effects are also not fully understood. Although probiotics are believed to regulate gut dysbiosis and influence immune pathways, definitive conclusions about these mechanisms are still pending. Further research is needed to explore how probiotics interact with the cardiovascular system, including the modulation of endothelial function and immune responses. Expanding mechanistic studies will enhance confidence in probiotics as a long-term adjunctive therapy for cardiovascular diseases [31].

Potential risks in immunocompromised individuals

Although probiotics are generally considered safe, their use in immunocompromised individuals presents potential risks. In rare cases, certain strains, such as Lactobacillus, have been associated with systemic infections, including bacteraemia. Vulnerable populations—such as patients undergoing chemotherapy, organ transplant recipients, and those with chronic conditions—are particularly susceptible to infections from probiotic use. These cases underscore the importance of carefully evaluating patient suitability before recommending probiotics.

To mitigate risks, healthcare providers must consider screening and monitoring protocols when prescribing probiotics to immunocompromised individuals. Developing guidelines that specify safe strains, dosages, and administration practices for high-risk populations is essential. These safety measures will enable clinicians to maximize the benefits of probiotics while minimizing potential risks [32].

Future Directions

Multi-centre trials are essential to validate the efficacy of specific probiotic strains and determine optimal dosages. Although probiotics have shown promise in reducing cardiovascular risks such as hypertension, hypercholesterolemia, and systemic inflammation, the variability in study outcomes—likely due to differences in strains, dosages, and patient profiles—emphasizes the need for standardized research protocols. Long-term studies are critical to assess the sustainability of these effects, ensuring that benefits persist across diverse patient populations [33].

Advancing personalized probiotic therapies represents a pivotal step in optimizing cardiovascular care. Given that interactions between gut microbiota and cardiovascular systems are influenced by individual microbiome compositions and genetic predispositions, tailored interventions are likely to yield better outcomes. High-throughput sequencing can map an individual's microbiome in detail, allowing healthcare providers to design specific probiotic treatments based on personal health profiles and cardiovascular risks. Personalized therapies could therefore enhance the therapeutic impact of probiotics, ensuring more precise management of cardiovascular conditions [34].

The integration of probiotics with existing pharmacological treatments also offers significant potential. Conventional therapies, such as statins and antihypertensive medications, have demonstrated efficacy but are often associated with side effects and, in some cases, resistance. Combining probiotics with these treatments could address underlying issues like inflammation, oxidative stress, and endothelial dysfunction, enhancing patient outcomes. Initial evidence suggests that probiotic supplementation might reduce the required dosage of these medications, potentially minimizing side effects, though further clinical validation is necessary [35].

The role of probiotics in modulating the gut-brain-cardiovascular axis presents another promising area for research. Evidence indicates that probiotics may influence not only cardiovascular health but also metabolic and mental health, offering a more integrated approach to disease management. Understanding the complexities of host-microbe interactions will be essential to develop comprehensive therapies. With a more robust scientific foundation, probiotics could become a key component in both preventive care and adjunctive treatments for cardiovascular diseases [36].

Conclusions

Probiotics offer a promising approach to managing cardiovascular diseases (CVD) by modulating key physiological pathways. Research demonstrates their ability to reduce hypertension, lower cholesterol, and mitigate systemic inflammation, improving endothelial function and metabolic regulation. Specific strains like *Lactobacillus reuteri* and

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Bifidobacterium longum have shown efficacy in lowering low-density lipoprotein (LDL) cholesterol, reducing the risk of atherosclerosis and coronary artery disease (CAD).

In addition to their lipid-lowering effects, probiotics promote blood pressure regulation through short-chain fatty acids (SCFAs) that inhibit angiotensin-converting enzyme (ACE), enhancing vascular health and reducing oxidative stress. These findings highlight the potential of probiotics to prevent vascular dysfunction and hypertension. However, safety concerns arise for immunocompromised individuals, where rare cases of infections have been reported. Careful strain selection and monitoring are essential to minimize such risks. Moreover, most studies focus on short-term outcomes, with limited data on the long-term impact of probiotics on cardiovascular health, necessitating further research.

The gut microbiome's complexity also presents challenges, as individual responses to probiotics vary. Personalized probiotic therapies tailored to individual microbiome profiles could optimize cardiovascular outcomes, emphasizing the need for future research into targeted interventions. In conclusion, probiotics represent a valuable adjunct to traditional cardiovascular treatments by addressing modifiable risk factors through non-invasive means. With further validation and careful consideration of safety, probiotics may become an integral part of personalized and preventive cardiology, complementing pharmacological therapies and lifestyle interventions to reduce the burden of cardiovascular diseases.

Disclosure statement

The authors declare that there are no conflicts of interest that could affect the results or conclusions of this study.

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