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ORIGINAL ARTICLE

In vitro cholesterol-lowering activity of probiotics isolated from commercial products in Medan City

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ABSTRACT

Regular consumption of probiotic drinks has been shown to provide numerous benefits for human health. One of the primary benefits is boosting the immune system by promoting optimal digestive health. Five brands of probiotic milk were collected, and bacterial isolates were obtained through a series of isolation and purification steps. The characterization of these isolates involved morphological and biochemical tests, including Gram staining, catalase activity assessment, and tolerance testing under simulated gastric conditions. The cholesterol-lowering activity of the isolates was evaluated in vitro by assessing their ability to reduce cholesterol levels in a simulated intestinal environment. The results demonstrated the presence of potential probiotic strains with cholesterol-lowering activity, providing a foundation for further research into the development of functional dairy products with cholesterol-lowering properties. The results indicated that probiotic milk from commercial beverages demonstrated a favorable response to bile salts in individuals with high cholesterol levels. Probiotic bacteria, such as *Lactobacillus acidophilus*, can survive in bile, facilitating the deconjugation of bile salts. This suggests that regular consumption of probiotic milk may aid in managing cholesterol levels in individuals with unhealthy lipid profiles. A significant relationship exists between the tolerance of probiotic milk to the digestive environment and its effectiveness in managing cholesterol. Mechanisms including bile salt deconjugation, short-chain fatty acid (SCFA) production, and increased cholesterol excretion contribute to cholesterol management. With appropriate formulation, probiotic milk can effectively control cholesterol levels, particularly in individuals at risk for cardiovascular disease.

Keywords: probiotic milk, cholesterol-lowering activity, immune system, digestive health

Introduction

The increasing popularity of probiotic drinks represents a significant global phenomenon, driven by consumers' heightened awareness of digestive health. In 2019, the global probiotic drinks market was valued at USD 13.65 billion and is projected to grow at a compound annual growth rate (CAGR) of 6.1% through 2027.[1] Consumers increasingly recognize the benefits of probiotic drinks in maintaining a balance of beneficial gut bacteria, which is crucial for digestion and nutrient absorption. In particular, the younger generation is increasingly focused on health and wellness, driving demand for these products. Additionally, the availability of ready-to-drink products contributes significantly to market growth.[2,3] Busy consumers seeking practical health solutions often choose convenient probiotic drinks. The microbiota of the digestive tract comprises various types of bacteria, with beneficial bacteria playing a crucial role in maintaining

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microbial balance. Probiotic drinks are a major source of these beneficial bacteria that can help reduce the risk of digestive-related diseases. Research indicates that maintaining a balanced microbiota may significantly reduce the risk of various digestive diseases.[4,5]

Regular consumption of probiotic drinks provides a variety of significant health benefits. One primary benefit is the enhancement of the immune system, which is facilitated by improved digestive health.[6] Research indicates that microorganisms in the digestive tract can influence neurotransmitters linked to mood and brain function, thereby contributing to mental health.[7] Probiotic drinks have demonstrated effectiveness in treating various health conditions, including diarrhea, skin diseases, allergies, flu infections, and inflammatory bowel symptoms.[8] Some studies suggest that probiotics may have potential in preventing cancer growth.[9] Additionally, probiotics contribute to optimizing the enzyme lipoprotein lipase, which aids in reducing levels of bad cholesterol (LDL) while increasing good cholesterol (HDL).[10] In addition, the disorder also affects cholesterol metabolism, where an imbalance in the production or absorption of bile salts may increase the risk of high cholesterol. Moreover, this disorder impacts cholesterol metabolism; an imbalance in bile salt production or absorption may raise the risk of high cholesterol.[11] The ability to withstand stomach acid and bile salts is essential for the efficacy of probiotics. Probiotics equipped with protective mechanisms against stomach acid and bile salts are more likely to reach the lower gastrointestinal tract and deliver their anticipated health benefits.[12]

Expanding research on commercial beverage products is crucial for understanding the effects of probiotics on diabetes and cholesterol. An in-depth evaluation is necessary to assess the effectiveness of various brands of probiotic drinks in addressing digestive challenges, particularly those related to cholesterol. Additionally, this study could be expanded to investigate whether probiotic drinks consistently provide benefits in managing blood glucose and cholesterol levels across a broader population.

Method

This study employed an in vitro experimental method to assess the cholesterol-lowering activity of probiotics. The research samples consisted of five brands of commercial probiotic milk, which were obtained from various stores in Medan City using a purposive sampling technique. The entire research process was conducted at the Prima University Laboratory in Medan from April to August 2024.

Probiotic isolation was conducted by taking 1 mL of a liquid sample or 1 gram of a solid sample, which was then serially diluted using 9 mL of 0.85% sterile physiological NaCl to achieve a dilution of 10^{-6}. A total of 0.1 mL from each dilution was spread onto de Man, Rogosa, and Sharpe (MRS) agar media using the spread plate technique. The cultures were incubated at 37°C for 48 hours under anaerobic conditions. Round, milky-white bacterial colonies measuring 1-3 mm in diameter were selected for purification through a repeated scratching technique on fresh MRS agar medium until single colonies were obtained. These single colonies were then transferred to MRS agar slant media for storage and further testing. The bacterial isolates were identified morphologically and biochemically through methods including Gram staining, catalase testing, and acid production testing. This method successfully isolated potential probiotics from commercial dairy beverages, which will subsequently be tested for cholesterol-lowering activity in vitro.[13]

The characterization process was conducted using Gram staining, catalase testing, stomach acid simulation, and bile salt tolerance tests. The antibacterial activity was assessed by preparing test bacteria and probiotic isolates, followed by measurements using the disc diffusion method. To evaluate cholesterol activity, a 1000 ppm cholesterol solution was prepared and mixed with 0.30% ox bile, then sterilized using a 0.22 μm cellulose acetate filter. A 1% culture of 24-hour-old lactic acid bacteria isolate was inoculated into MRSB medium containing the cholesterol solution and 0.3% ox bile, and then incubated at 37°C for 24 hours.

After incubation, the culture was centrifuged at 10,000 g for 10 minutes at 4°C, and the cholesterol content in the supernatant was measured using a spectrophotometer at a wavelength of 550 nm. Cholesterol reduction was calculated based on the difference between the initial cholesterol concentration and the concentration remaining after incubation. As a positive control, 10 mg of simvastatin was added to the same cholesterol solution, homogenized, and incubated for 60 minutes at 37°C. Following this, centrifugation was performed, and cholesterol levels in the positive control supernatant were measured to calculate the percentage of cholesterol reduction compared to the probiotic sample.[14]

Results

Table 1 presents the results of probiotic isolation conducted in this study, identifying five distinct probiotic isolates: Acidhopillus, Rillus, Liprolac, Amannikmat, and Lacto b. This research aimed to isolate potential probiotic strains with antimicrobial properties. These strains offer various health benefits, including improved lactose digestion, pathogen control in the gastrointestinal tract, serum cholesterol reduction, inhibition of tumor and cancer growth, and antimutagenic and anticarcinogenic properties. Consuming beverages that contain probiotics can provide therapeutic effects on the body by improving microbial balance in the gut.

Table 1. Probiotic isolation results

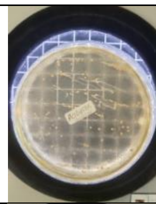
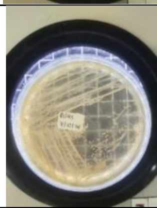
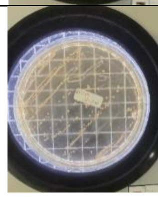
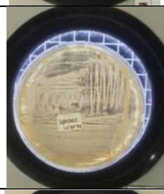
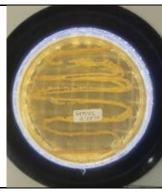
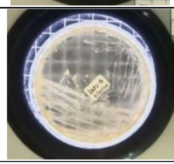
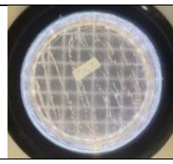
No.	Probiotic product	Sample code	Date		
			10/10/2024	11/10/2024	17/10/2024
1.	Acidhopillus	Pb 1			
2.	Rillus	Pb 2			
3.	Liprolac	Pb 3			
4.	Amannikmat	Pb 4			
5.	Lacto B	Pb 5			

Table 2 presents the results of the Gram staining of all probiotic isolates. The results indicate that all bacteria were Gram-positive with a bacillus morphology.

Table 2. Gram staining results

No.	Probiotic product	Gram stain result	Morphology	Sample Image
1	Acidhopillus	(+)	Basil	
2	Rillus	(+)	Basil	

3	Liprolac	(+)	Basil	
4	Amannikmat	(+)	Basil	
5	Lacto B	(+)	Basil	

Catalase testing of the probiotic isolates revealed that all isolates were catalase-negative. This finding is consistent with the characteristics of anaerobic bacteria, which typically do not produce catalase (see Table 3).

Table 3. Catalase test result

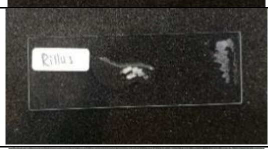
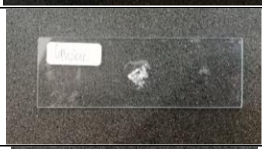
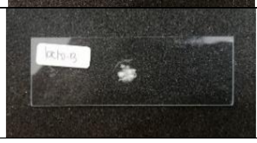
No.	Probiotic product	Gram staning	Catalase
1.	Acidhopillus	(-)	
2.	Rillus	(-)	
3.	Liprolac	(-)	
4.	Amannikmat	(-)	
5.	Lacto B	(-)	

Figure 1 presents the results of a study comparing isolate growth in media with normal pH and low pH. As shown in the figure, the Liprocal isolate exhibited the highest growth in the medium with a pH of 3, measuring 1.188, while the amannikmat isolate showed the lowest growth at the same pH, measuring 0.042. In the medium with a pH of 6, Lacto B demonstrated the highest growth at 0.426, whereas the amannikmat isolate again exhibited the lowest growth at 0.099.

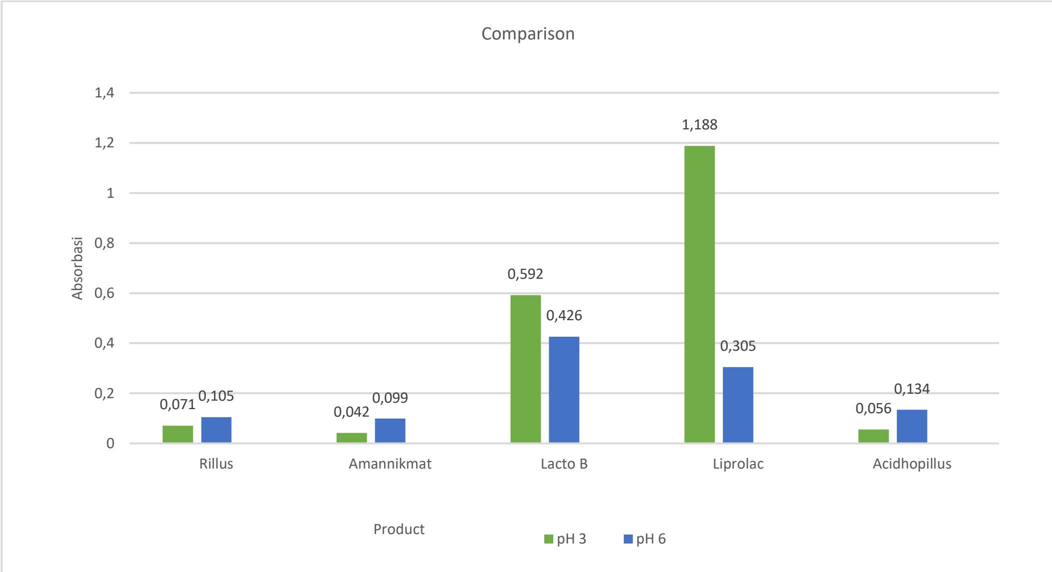


Figure 1. Comparison of isolate growth on media with normal pH versus media with low pH

Figure 2 presents the results of a study on bacterial growth percentages obtained through acid tolerance testing. The highest growth percentage was observed in the Acidhopillus isolate (239.29%), followed closely by Amannikmat (235.71%), Rillus (147.89%), and Lacto B (71.96%). In contrast, the lowest growth percentage was recorded for the Liprolac isolate (25.67%).

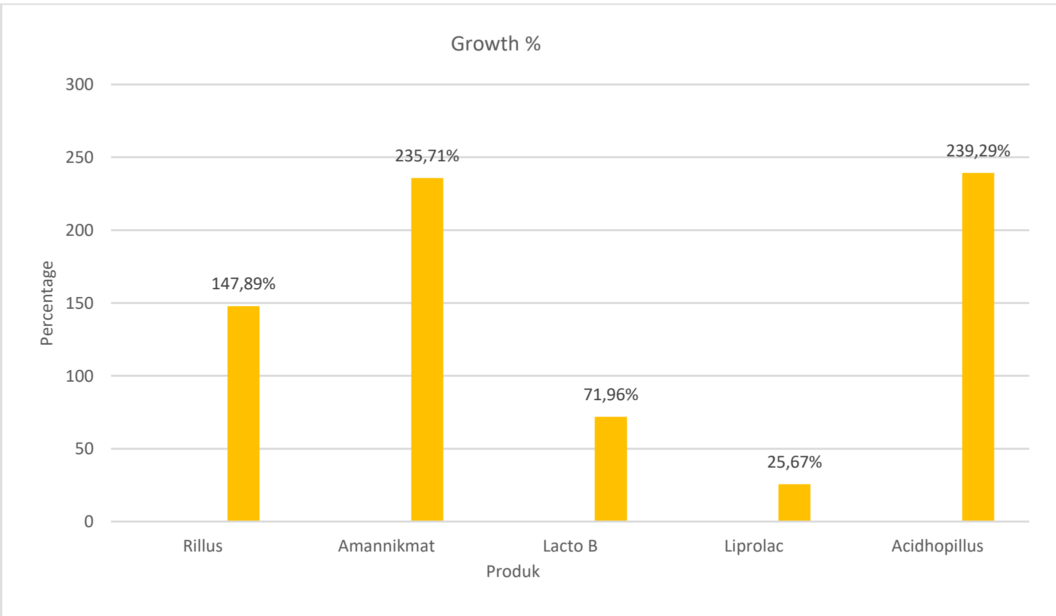


Figure 2. Percentage of bacterial growth via acid assay (%)

Figure 3 presents the research findings on the growth comparison of isolates using a bile salt assay in both normal MRS and 0.3% MRS media. As illustrated in the figure, the Lacto B isolate exhibited the highest growth in normal MRS medium, measuring 0.461, while the amannikmat isolate demonstrated the lowest growth, at 0.168. In the 0.3% MRS medium, Lacto B also displayed the highest growth, recording a value of 0.414, whereas the amannikmat isolate again showed the lowest growth, at 0.352.

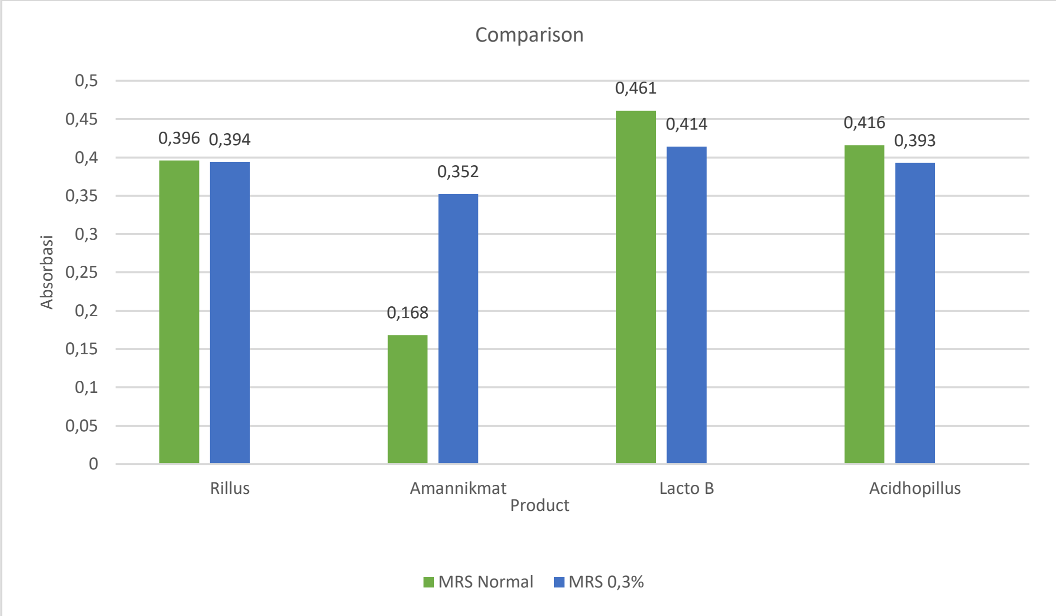


Figure 3. Comparison of isolate growth using bile salt assay on normal MRS and 0.3% MRS

Figure 4 illustrates the results of the study on bacterial growth percentages obtained from the bile salt tolerance test. The findings show that the highest growth percentage was observed in the Amannikmat isolate, reaching 209.52%, followed by the Rillus isolate at 99.49%, and the Acidhopillus isolate at 94.47%. The lowest growth percentage was recorded in the Lacto B isolate, at 89.80%.

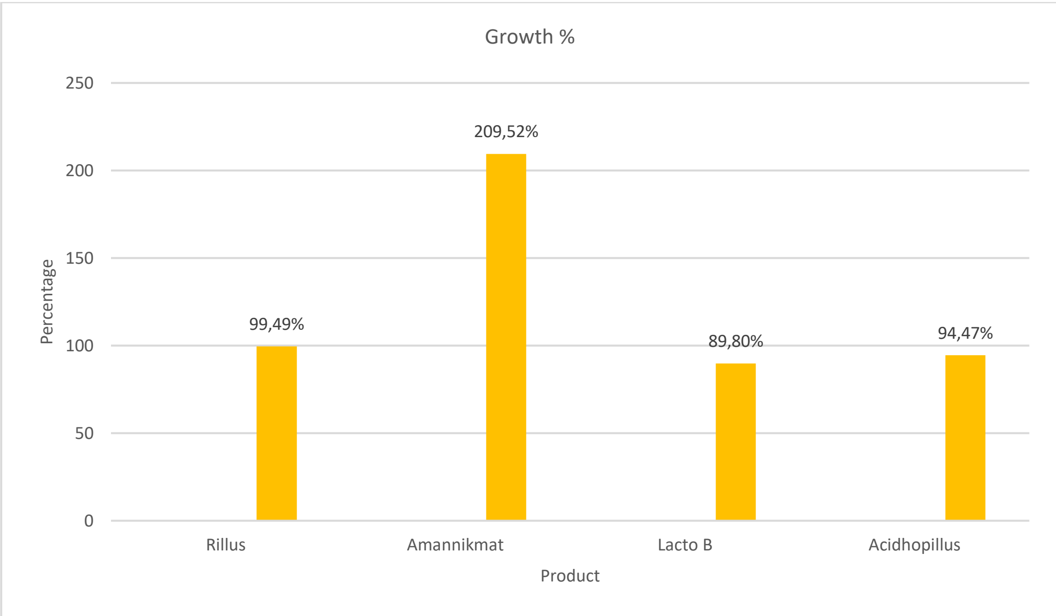


Figure 4. Bacterial growth in bile salt assay

Figure 5 presents the results of the antimicrobial assay conducted in this study. The results demonstrate antimicrobial activity against the bacterial strains tested in this study.

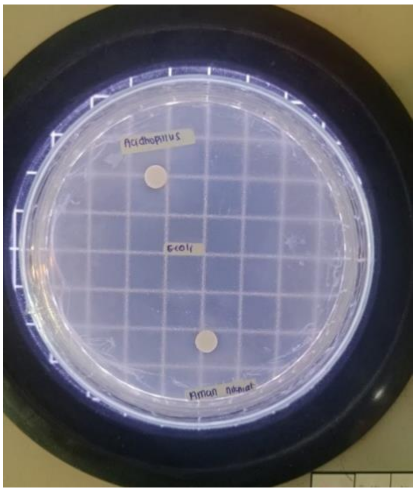


Figure 5. Antimicrobial assay

Table 4. Results of cholesterol reduction assay by isolates

No.	Probiotic product	Code	Abs	Conc. (mg/ml)	%
1.	Amannikmat	An	0.109	1.0890	24,77%
	Amannikmat Cholesterol	AnK	0.082	0.8210	
2.	Rillus	R	0.068	0.6760	7,35%
	Rillus Cholesterol	RK	0.063	0.6260	
3.	Acidhopillus	Ac	0.211	2.1110	14,69%
	Acidhopillus Cholesterol	AcK	0.180	1.7980	
4.	Simvastatin 10 mg	K+	1,097		80,03%
	Simvastatin 10 mg Cholesterol	KK	0,219		

Among the isolates tested, Amannikmat exhibited the highest cholesterol-lowering activity, achieving a reduction in cholesterol levels of 24.77%. Acidhopillus and Rillus showed reductions of 14.69% and 7.35%, respectively. In comparison, the positive control demonstrated a more substantial decrease of 80.03%.

Discussion

Characteristics of commercial probiotic beverages

Characterization results revealed that all probiotic isolates were Gram-positive bacilli, consistent with the genus Lactobacillus. Negative catalase tests indicated the anaerobic nature of these bacteria. The isolates successfully passed simulated gastric conditions and bile salt tolerance tests, demonstrating their potential as probiotics. The Liprocal isolate exhibited optimal growth at pH 3, whereas Amannikmat showed the least growth at the same pH. At pH 6, Lacto B was the isolate with the highest growth. Overall, Acidhopillus experienced the most significant growth increase (239.29%), followed closely by Amannikmat (235.71%). Conversely, Liprolac displayed the lowest growth increase (25.67%). Lacto B thrived in normal MRS media, while Amannikmat exhibited the poorest growth under these conditions. In 0.3% MRS media, Lacto B continued to show the highest growth among the isolates, while Amannikmat demonstrated a significant growth increase of 209.52% under these conditions. Antimicrobial testing indicated that all tested bacteria exhibited antimicrobial activity.

Andriani et al.[15] highlighted that Gram-positive nature of bacterial isolates, including *Lactobacillus casei* and *Lactobacillus rhamnosus*, indicates their resistance to gastric acid and digestive enzymes, enabling them to reach the large intestine alive. This ability is crucial for the effectiveness of probiotics in modulating host health. Our Gram-positive staining results align with those of Prayoga et al. (2021), which demonstrated that anaerobic bacteria—indicated by the negative catalase test in our isolates—exhibit greater stability in the intestinal environment. This stability enables bacteria to interact effectively with bile salts, which play a key role in lowering cholesterol levels.

Anabanua et al.[16] explained that bile salt binding by probiotics is a primary strategy in modulating lipid metabolism. Probiotics bind bile salts, preventing their reabsorption and increasing excretion. This process forces the body to synthesize more bile salts from blood cholesterol, potentially reducing total cholesterol levels. This ability indicates that our Gram-positive and catalase-negative isolates may serve as effective cholesterol-lowering agents. Furthermore, Andriani et al.[15] emphasized the importance of probiotic adaptation to the dynamic gastrointestinal environment. Our results show that the tested bacterial isolates possess characteristics aligned with these requirements; resistance to gastric acid, survival in anaerobic conditions, and interaction with bile salts suggest that probiotics in commercial milk containing these isolates could play an integral role in cholesterol management strategies.

Nevertheless, further research, particularly human clinical trials, is needed to confirm the potential benefits of probiotic milk demonstrated in this in vitro study. As suggested by Brandvold et al.[17], future studies should identify optimal doses and durations of consumption for the most effective results. Additionally, involving a broader and more diverse population would provide a comprehensive picture of the effectiveness of probiotic milk. In conclusion, these promising initial findings highlight significant opportunities for developing probiotic milk products aimed at enhancing cardiovascular health.

The effectiveness of commercially available probiotic dairy drinks in reducing cholesterol levels

This study demonstrates the efficacy of commercial probiotic products in reducing cholesterol levels. Among the isolates tested, amannikmat proved to be the most potent, lowering cholesterol by 24.77%, followed by acidophillus (14.69%) and rillus (7.35%). For comparison, the positive control exhibited a cholesterol reduction of 80.03%. Commercial probiotics have emerged as a promising avenue for hypercholesterolemia management. Lactic acid bacteria, including *Lactobacillus* and *Bifidobacterium* commonly found in these products, possess the ability to bind and excrete bile salts. According to Brandvold et al.[17], this mechanism involves reducing intestinal reabsorption of bile salts, thus stimulating the synthesis of new bile salts from blood cholesterol. These findings underscore the significant potential of commercial probiotic products as an intervention for elevated cholesterol. The results corroborate previous research highlighting the role of probiotics in modulating lipid metabolism.

Previous studies have shown that probiotics, especially *Lactobacillus plantarum*, can reduce cholesterol levels. For example, Widajati et al.[18] reported decreased total cholesterol and LDL levels in experimental rats after administering *L. plantarum*. Although the effects varied with concentration, these findings suggest a mechanism involving cholesterol binding in the intestinal lumen and subsequent fecal excretion. This study indicates that consuming commercial probiotic milk containing lactic acid bacteria may help manage cholesterol levels through a bile acid binding mechanism. These findings support developing more targeted probiotic products for cardiovascular health. Therefore, probiotic milk could serve as a practical nutritional alternative for maintaining heart health.

The survival and metabolic activity of probiotic bacteria in the harsh gastrointestinal environment are crucial for their cholesterol-lowering efficacy. Research has shown that specific strains, such as *Lactobacillus acidophilus*, exhibit robust tolerance to gastric acid and bile, ensuring their viability upon reaching the intestines. This adaptive capacity allows probiotics to perform various metabolic functions, including cholesterol management.[19,20] Thus, gastrointestinal tolerance is a critical criterion for selecting probiotic strains used in dyslipidemia therapy.

The primary mechanism by which probiotic bacteria manage cholesterol levels is through bile salt deconjugation. This process transforms bile salts into a more easily excretable form, thereby reducing intestinal reabsorption and lowering blood cholesterol levels. A study by Yılmaz and Paula[20] demonstrated that kefir containing *Lactobacillus acidophilus* effectively reduced total and LDL cholesterol levels in both individuals with normal lipid profiles and those with dyslipidemia. These findings support the crucial role of bacterial bile salt tolerance in enhancing cholesterol metabolism.

Further research by Lee et al.[19] reinforced these findings by showing that *L. acidophilus* can decrease hepatic fat accumulation and lower triglyceride levels. Direct interactions between probiotics and lipids within the gastrointestinal tract are hypothesized to underlie this mechanism. However, the results of studies investigating the effects of probiotics on lipid profiles remain inconsistent. Setyaji and Setyani[21] reported that not all clinical trials have shown significant changes. Consequently, the ability of probiotics to tolerate gastrointestinal conditions remains a key focus of further research to optimize their use as an intervention for managing cholesterol levels.

Short-chain fatty acids (SCFAs), which are produced by probiotic bacteria, play a pivotal role in managing blood lipids, specifically cholesterol and triglyceride levels. Chaudhary and Mudgal[22] demonstrated that SCFAs can inhibit hepatic cholesterol synthesis and enhance fecal excretion. Additionally, Momin et al.[10] demonstrated that probiotics effectively reduce triglyceride and LDL levels. These effects occur due to the ability of SCFAs to regulate lipid metabolism. For probiotics to exert their beneficial effects, they must colonize the large intestine, the primary site of SCFA production. Furthermore, their ability to withstand both the acidic conditions of the stomach and the bile-rich environment of the small intestine is crucial for successful colonization. The appropriate formulation of dairy products containing probiotics can enhance the viability of these bacteria during digestion, thereby maximizing their health benefits.

Overall, the relationship between probiotic tolerance to the gastrointestinal environment and its efficacy in managing cholesterol levels underscores the crucial importance of selecting suitable bacterial strains. Probiotic dairy products containing *Lactobacillus acidophilus* hold promise as a natural solution for managing high cholesterol, particularly among individuals at risk of cardiovascular disease. In vitro studies demonstrate that probiotic bacteria derived from commercial dairy products exhibit potential as cholesterol-lowering agents. A primary mechanism behind this capability involves interactions between probiotics and bile acids. Specifically, research shows that probiotics can bind bile acids in the intestines, thereby preventing their reabsorption by the liver. Consequently, the body increases production of new bile acids, utilizing cholesterol from circulating blood streams, which ultimately leads to reductions in total and LDL cholesterol levels. Past investigations have revealed that *Lactobacillus acidophilus* and *Lactobacillus plantarum* are adept at effectively deconjugating bile acids—a process enabling probiotics to function both preventatively and adjuntively in managing blood cholesterol concentrations.

Moreover, in vitro experiments show that probiotics can reduce cholesterol levels in culture medium by binding cholesterol in the intestinal lumen. Comparative analyses with a simvastatin control group reveal that though less potent than synthetic medications, probiotic isolates still hold promise as safer natural alternatives. Furthermore, probiotics generate short-chain fatty acids (SCFAs), which are recognized for their capacity to suppress cholesterol synthesis in the liver and promote lipid elimination through feces. The fact that probiotics can produce SCFAs suggests that isolates from commercial dairy products not only offer cholesterol management but also provide extra advantages for those suffering from dyslipidemia. The robust relationship between probiotic resilience in the gastrointestinal environment and its effectiveness in managing cholesterol highlights the importance of choosing the correct strain. Probable bacteria capable of surviving gastric acidity and bile have greater chances of arriving in substantial numbers in the intestines, enabling them to achieve therapeutic outcomes. Consequently, strain selection plays a crucial role in creating efficacious probiotic products—especially commercial ones derived from dairy.

In conclusion, this research highlights the potential of probiotic dairy products as a natural strategy for managing cholesterol levels. Probiotic bacterial isolates obtained from commercial dairy products have been shown to lower cholesterol levels through mechanisms such as bile acid deconjugation and cholesterol binding. However, additional in vivo studies in humans are necessary to confirm these findings and assess their efficacy in complex physiological conditions. When formulated appropriately, probiotic dairy products could support heart health and lower the risk of cardiovascular disease.

Conclusion

Commercial probiotic milk products have shown a beneficial response to bile salts in individuals with elevated cholesterol levels. Probiotic bacteria, including Lactobacillus acidophilus, can survive in bile-rich environments, facilitating bile salt deconjugation. This mechanism reduces bile salt reabsorption, thereby lowering total and LDL cholesterol levels in the bloodstream. Regular consumption of probiotic milk is linked to better cholesterol management in individuals with dyslipidemia. Moreover, a significant correlation exists between a probiotic strain's tolerance to the gastrointestinal environment and its efficacy in cholesterol management. Probiotics that withstand gastric and bile acids are more likely to reach the colon and exert beneficial effects. Mechanisms including bile salt deconjugation, short-chain fatty acid production, and enhanced cholesterol excretion contribute to effective cholesterol management. With precise product formulation, probiotic milk products present a promising strategy for controlling cholesterol, especially in individuals at risk for cardiovascular disease.

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