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Therapeutic Potential of *Lactobacillus plantarum* DS1 in Modulating Hypertension, Blood Sugar and Inflammation via ACE-2 Expression in Diabetic Rats

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ABSTRACT

Hypertension and diabetes, two interrelated non-communicable diseases, contribute significantly to global morbidity and mortality and often trigger gut microbiota dysbiosis. Gut microbiota-based therapies, particularly probiotics, may serve as an alternative approach to managing hypertension and diabetes. This study aims to explore the therapeutic potential of *Lactobacillus plantarum* DS1 in modulating hypertension and inflammation by examining its effects on ACE-2 expression, providing a basis for developing probiotic therapy in chronic metabolic disorders. This study used male Wistar rats (*Rattus norvegicus*), which were maintained for 8 weeks. The *Rattus norvegicus* rats were split into three groups: group one (C-) was not treated with *Lactobacillus plantarum* DS1, group (C+) received a high blood sugar but was not given *Lactobacillus plantarum* DS1, and a treatment group (T) that received 1 mL of *Lactobacillus plantarum* DS1 every day per oral. *Lactobacillus plantarum* DS1 significantly reduced random blood sugar levels in the T group (from 241.17 mg/dl to 150.71 mg/dl). The T group showed stable systolic blood pressure (139.83 to 140.17 mmHg) and a slight decrease in diastolic blood pressure (80.33 to 78.50 mmHg), indicating that the treatment may help protect against high blood pressure. Treatment with *Lactobacillus plantarum* DS1 successfully lowered high ACE-2 levels in the T group, showing that it helps prevent this increase. Therefore, it is concluded that *Lactobacillus plantarum* DS1 effectively maintains blood pressure, lowers blood sugar, and controls inflammation in diabetic rats. *Lactobacillus plantarum* DS1 holds significant promise as a therapeutic agent for hypertension and inflammation in individuals with diabetes.

Keywords: *Lactobacillus plantarum*, *Lactobacillus plantarum DS1*, Probiotic, Hypertension, diabetes, ACE-2

Introduction

Hypertension and diabetes mellitus are two interrelated non-communicable disorders that substantially impact global morbidity and mortality rates.[1] These conditions often exist as comorbidities, increasing the chances of heart and kidney injuries, and are common around the world, especially in places like Asia. The combined impact of these diseases is intensified by common risk factors, such as obesity, poor nutrition, and sedentary lifestyles, which are prevalent in both high- and low- to middle-income nations.[2] Hypertension affects over 22% of the global population, whereas diabetes impacts approximately 9%.[3] In Southeast Asia, non-communicable diseases, such as diabetes and hypertension, constitute 55% of annual mortality.[4] The combination of these conditions increases the risk of small and large blood vessel pathologies, which can lead to heart disease and chronic kidney disease. The prevalence of both diseases continues to increase significantly, especially in developing countries, and they often occur together as metabolic comorbidities that worsen the patient's prognosis.[5]

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The complex relationship between insulin resistance, hyperglycemia, endothelial dysfunction, and oxidative stress is believed to be the pathophysiological basis of hypertension in diabetic patients.[6] Therapies based on gut microbiota, especially the application of probiotics, have emerged as a promising alternative method for the management of hypertension and diabetes.

Probiotics are bacteria that provide health benefits when ingested in sufficient quantities and have shown potential to alter the gut microbiota, thereby enhancing metabolic health.[7] This method is attracting interest because it effectively targets the fundamental gut dysbiosis associated with hypertension and diabetes. Probiotics help restore gut microbial balance, which is essential for mitigating chronic inflammation and improving insulin sensitivity. This process is especially advantageous for individuals with type 2 diabetes and hypertension, as it may result in improved glucose control and blood pressure management.[8] Probiotics influence the production of substances such as butyrate and acetate, which help control glucose and cholesterol levels, possibly reducing the risk of cardiovascular injury with diabetes. Probiotics have been shown to lower LDL cholesterol and increase HDL cholesterol levels, which are crucial in mitigating cardiovascular risk in individuals with diabetes. [9-10] Studies have shown that probiotics can help maintain stable blood sugar levels and blood pressure in individuals with type 2 diabetes and high blood pressure, highlighting their potential as a valuable addition to existing treatments.[11]

Lactobacillus plantarum is a probiotic that has been widely studied for its potential to improve metabolic health. This probiotic can lower both systolic and diastolic blood pressure, with a significant average decrease in blood pressure, and improve glucose metabolism.[12-13] This benefit helps prevent cardiovascular disease, control diabetes, and

treat obesity.[14] A review of several studies indicated that there was a notable drop in blood pressure, with an average decrease of -0.71 mmHg for systolic and −0.45 mmHg for diastolic blood pressure compared to a placebo.[15] *Lactobacillus plantarum* works by affecting GLP-1, fasting blood sugar, and insulin levels, which are essential for maintaining blood sugar balance. Several studies, including clinical trials, have demonstrated that consuming this probiotic can lower HbA1c levels in individuals with prediabetes, indicating improved blood sugar control.[16-17] Additionally, *Lactobacillus plantarum* also plays a role in reducing inflammation and oxidative stress, key factors in various metabolic diseases. Fermented foods often contain these probiotics, making them a convenient way to enhance overall health and alleviate symptoms of cardiovascular disease.[18]

Previous studies have shown that probiotics can help regulate the renin-angiotensin system (RAS) by reducing inflammation and oxidative stress, which in turn affects the function of angiotensin-converting enzyme (ACE) and ACE2 in various organs. Probiotics, particularly those modified to produce angiotensin, have shown promise in helping to control blood pressure and inflammation, both of which are key components of the RAS.[19] This control happens in several ways, like reducing oxidative stress and inflammation and increasing the gut bacteria, which together affect how ACE and ACE2 are expressed. Probiotics have been shown to reduce blood pressure by decreasing ACE activity.[19] ACE is a crucial element of the RAS that converts angiotensin I into the vasoconstrictor angiotensin II. This inhibition may lead to a reduction in blood pressure and an improvement in cardiovascular health.

Researchers have modified probiotics using gene cloning, gene identification, probiotic transformation, and gene expression to create angiotensin, targeting the ACE2/Ang (1-7)/Mas receptor system, which helps lower inflammation and widen blood vessels.[20] These probiotics have shown they can raise the levels of Ang(1-7) in the blood, which might help reduce inflammation and scarring in various tissues.[21] Probiotics can regulate inflammation by increasing the synthesis of anti-inflammatory cytokines such as IL-10 and TGF-β while simultaneously decreasing pro-inflammatory cytokines like TNF-α. This regulation helps sustain a balanced immune response and mitigate chronic inflammation.[22-23] The decrease in oxidative stress may additionally facilitate the modulation of ACE and ACE2 expression. Probiotics aid in restoring gut microbial diversity, which is frequently compromised in conditions such as hypertension. This repair can improve the gut's ability to protect itself and reduce harmful substances in the blood, both of which are important for overall health and managing the RAS. ACE2 expression is elevated in the gastrointestinal tract, rendering it a crucial target for probiotic therapies. Probiotics can alter the bacteria in the gut, which in turn affects the production of ACE2 locally and throughout the body, ultimately impacting how the RAS functions overall. Recent studies have demonstrated that probiotics can modulate the renin-angiotensin system by reducing inflammation and oxidative stress, and they can alter the levels of ACE and ACE-2 in various tissues.[24] However, there is still not much scientific proof about how *Lactobacillus plantarum* affects ACE-2 expression and blood pressure, particularly in diabetic rats with high blood pressure. This study aims to investigate how *Lactobacillus plantarum* DS1 may potentially modulate hypertension and inflammation by regulating ACE-2 expression, which could lay the groundwork for developing a probiotic therapy for chronic metabolic disorders.

Materials and Methods

Materials

Lactobacillus plantarum DS1, a strain isolated from Dadiah in Limapuluh Kota, West Sumatra, Indonesia, was used for this study. The bacteria were multiplied in de Man, Rogosa, and Sharpe (MRS) broth at 37°C for 24 hours, achieving a concentration of 3.8×10^{10} CFU/mL. Before its administration to the male Wistar *Rattus norvegicus* rats, the bacterial cell count was adjusted to a final concentration of 10^8 CFU/mL.

Research design

Healthy and active male *Rattus norvegicus* rats (18) were used for this 8-week experiment. The rats, weighing 250-300 g each, were divided into three groups of six: a negative control group (C-), a positive control group (C+), and a probiotic treatment group (T) (Table 1).

Diabetes adaptation

Before induction, *Rattus norvegicus* rats underwent a two-week phase. The rats were fed a high-fat diet pellet (a standard pellet with tallow) and water *ad libitum* (as much as they wanted) during this period to ensure consistent baseline conditions. The experimental animals (rats) were fasted for 12 hours before being administered freshly prepared streptozotocin (STZ) to induce diabetes. STZ was prepared just before use, dissolved in 0.01 M citrate buffer (pH 4), and injected intraperitoneally within 10-15 minutes to maintain its stability. The STZ dose was determined based on the rats' body weight, using a standard dose of 30 mg/kg body weight (BW). It should be noted that the dose of STZ can vary between 30 and 75 mg/kg BW, where a higher dose will affect the type of diabetes mellitus produced. For instance, giving 40 mg/kg BW of STZ will lead to lasting high blood sugar, a reduced ability to release insulin in response to glucose, and serious harm to the structure of pancreatic cells.

Blood sugar measurement

At the onset of the study, the random blood sugar levels of the *Rattus norvegicus* rats were measured using a glucometer. The method involves snipping a small portion of the mouse's tail tip (approximately 1 mm) and then attaching the glucometer strip to the drop of blood that emerges. The glucometer (Gluko-Dr®) reading is then recorded immediately. The Gluko-Dr glucometer operates using an enzymatic method. Glucose oxidase (GOD) in the strip will react with glucose in the blood, producing an electronic signal that is proportional to the blood sugar level. For this measurement, only about 2.5-4.0 µL of blood was required, which was placed on the right side of the strip and absorbed automatically. The measurement results appear after eleven seconds in mg/dL units. Normal blood sugar conditions in rats in this study ranged from 50 to 135 mg/dL.[25]

Blood pressure measurements

The tail cuff, a noninvasive and non-injurious device, was used to measure blood pressure in rats. This method was preferred because it allows measurements without anesthesia, which is safer for the animal and does not affect the study's results. The equipment used is generally a system for monitoring blood pressure, such as CODA®, which is specifically designed for rodents. Measurements were taken periodically, twice a week. This system works with two types of tail cuffs: a volume pressure recorder (VPR) cuff to record changes in blood volume and an occlusion cuff to temporarily stop blood flow. The rat was placed in a special restraint device before the measurement process to limit its movement. A heating pad was used to warm the rat to an ideal temperature of 37°C. The purpose of this heating is to dilate the blood vessels in the tail, enabling more accurate and consistent blood pressure measurements.

ACE-2 expression

Kidney tissue was placed on a glass slide with a special coating and treated with xylol for a total of 10 minutes, followed by a 10-minute soak in pure alcohol. The tissue on the slide was washed twice with phosphate-buffered saline (PBS) to adjust its pH to 7.2. Antigen retrieval was accomplished by microwaving the tissue at 95°C for 20 minutes in a citrate buffer with a pH of 6.0. After chilling the tissue, we washed it twice for two minutes in PBS. Finally, the tissue was washed twice for 2 minutes with PBS after a 30-minute endogenous peroxidase blocking step using 3% H_2O_2. The tissue was flooded with primary antibodies at a specific dilution and incubated for 18 hours at 4°C. After two 2-minute washes in PBS, the tissue was saturated with Histofine® Simple StainTM MAX PO (MULTI) for 1 hour at room temperature. Five 5-minute periods of PBS washing were followed by the addition of diaminobenzidine (DAB) as a substrate. After 5 minutes, the DAB reaction was terminated by rinsing the tissue under running water. Counterstaining was done by staining with Meyer's hematoxylin for 3 minutes. The tissue was washed once for 2 minutes with PBS and then continued with dehydration using absolute ethanol twice, each for 5 minutes. It was then cleaned with xylol for 2 × 5 minutes and mounted with Entellan. Positive cells or tissues are characterized by the presence of a brown color in their bluish-purple

cell nuclei, while negative results indicate the absence of this color. We interpret Image J by tallying the proportion of positive to negative cells.

Data analysis and ethical consideration

The research data were processed comprehensively using univariate and bivariate statistical approaches. The entire analysis process was conducted using SPSS version 26 software. This processing enables the analysis of the characteristics of each variable individually (univariate) and the identification of relationships or correlations between two variables (bivariate), allowing for valid and reliable conclusions to be drawn from the collected data. This study received ethical clearance from the Ethics Committee of the Faculty of Medicine, Universitas Baiturrahmah, Padang, Indonesia, under the ethical clearance number: 002/ETIK-FKUNBRAH/03/05/2021.

Results and discussion

This study isolated a total mass of *Lactobacillus plantarum* DS1 from Dadiah Limapuluh Kota, West Sumatra, Indonesia, which reached a concentration of 38×10^{10} CFU/mL. It has a strong probiotic potential, as the FAO/WHO recommends at least 10^6–10^9 CFU/mL for a probiotic to exhibit significant health benefits. Thus, the amount of *Lactobacillus plantarum* DS1 obtained in this study was far above the minimum limit, confirming its potential as a superior probiotic candidate. This high number of lactic acid bacteria is also relevant in the context of its use as a therapeutic probiotic. To receive the best health benefits, the probiotic should be ingested in sufficient quantities to improve the digestive system and produce bioactive substances, such as short-chain fatty acids (SCFAs), which help regulate blood pressure and balance metabolism.[26] Thus, the high population of *Lactobacillus plantarum* DS1 in this study shows enormous potential in clinical applications. The *Rattus norvegicus* rats were observed under diabetic conditions to determine the effects of *Lactobacillus plantarum* DS1 on blood sugar levels. This observation is crucial to understanding whether this specific probiotic can help stabilize or lower high blood glucose levels, a significant challenge in diabetes management (Table 2). Based on Table 2, it is evident that there was a significant increase in blood sugar levels in the C+ group compared to the C- group. After eight weeks of treatment, the C+ group maintained the highest average. Therefore, we can conclude that *Lactobacillus plantarum* is the optimal choice for lowering blood sugar. The univariate analysis revealed that *Lactobacillus plantarum* DS1 could significantly lower blood sugar levels in type 2 diabetic rats within 8 weeks. The one-way ANOVA test to answer the hypothesis yielded a significant value of $0.000 < 0.05$, indicating that all treatments significantly reduced blood sugar levels within 8 weeks. The BNT test showed that all treatment groups performed better than the C+ group ($p = 0.000$), indicating that we accepted the alternative hypothesis; specifically, *Lactobacillus plantarum* DS1 significantly lowered blood sugar levels over an 8-week period. The BNT test between treatment groups was significantly different. Similarly, the bivariate analysis combined with the univariate analysis indicates that *Lactobacillus plantarum* DS1 can reduce blood sugar levels. The administration of the *Lactobacillus plantarum* DS1 strain significantly reduced blood glucose levels in *Rattus norvegicus* rats. This effect aligns with earlier research, which shows that some strains of *Lactobacillus plantarum* can help the body utilize glucose more efficiently by enhancing insulin's effectiveness and modifying gut bacteria. *Lactobacillus plantarum* is known to reduce the activity of genes that lead to insulin resistance and increase the production of short-chain fatty acids (SCFAs), which help manage glucose levels.[27] The significant reduction in blood glucose levels aligns with earlier research that suggests some strains of *Lactobacillus plantarum* can enhance the body's ability to utilize glucose more effectively by improving insulin function and modifying gut bacteria.[28] Also, *Lactobacillus plantarum* is known to lower the activity of specific genes that contribute to insulin resistance and boost the creation of short-chain fatty acids (SCFAs), which help manage blood sugar levels.[29] *Lactobacillus plantarum* has shown that it can improve how well the body uses insulin and processes sugar in mice that were fed a high-fat diet and had diabetes caused by streptozotocin. This goal is achieved by reducing blood glucose and HbA1c levels, increasing glucose tolerance, and improving homeostatic model assessment for insulin resistance (HOMA-IR) scores.[30] The probiotic strain *Lactobacillus plantarum* CNCM I−4459 was shown to help the body respond better to insulin by reducing fasting glucose and fructosamine levels and assisting in the regulation of the genes that control how the liver manages blood sugar.[31] A detailed review and analysis found that taking it was associated with lower fasting plasma glucose and hemoglobin A1c levels, indicating better sugar processing in people with type 2 diabetes and prediabetes. Taking *Lactobacillus plantarum* as a supplement alters the types of bacteria in the gut, increasing bacteria such as those belonging to the Akkermansiaceae and Bifidobacteriaceae families, which are associated with improved metabolic health. The probiotic reduces the prevalence of bacteria associated with obesity and inflammation, promoting a healthier gut environment and improving insulin sensitivity.[32] Research on prediabetic human patients has shown that taking Lactobacillus plantarum HAC01 alters the types of bacteria in the gut; however, these changes were not significant enough to be considered clinically important.[33] *Lactobacillus plantarum* enhances the synthesis of SCFAs, which are advantageous for glucose metabolism. SCFAs are recognized for their ability to improve insulin sensitivity and diminish inflammation, therefore, facilitating glucose homeostasis. A study found that the probiotic *Lactobacillus plantarum* LRCC5314 increased SCFA production, altered the gut bacteria, and improved the ability of rats with stress-related type 2 diabetes to process glucose.[35] A study found that the postbiotic *Lactobacillus plantarum* LRCC5314 increased the production of SCFAs, altered the gut bacteria, and enhanced glucose processing in rats with stress-related type 2 diabetes. The probiotic influences fat processing by lowering the activity of genes that produce fat and increasing the activity of genes that break down fat, thereby improving overall metabolic health. This study examined blood pressure in *Rattus norvegicus* rats, specifically systolic and diastolic blood pressure, and discovered that the T group, which received an extract of *Lactobacillus plantarum* DS1, showed a significant difference compared to the control group. This evidence suggests the potential of *Lactobacillus plantarum* in regulating blood pressure (Table 3). Table 3 shows that the C-group's systolic blood pressure naturally decreased from 115.58 to 108.25 mmHg. This decrease is normal for healthy animals that are not stressed or sick. In the C+ group, there was an increase in systolic blood pressure from 141.67 to 153.75 mmHg after 8 weeks, indicating hypertension progression without intervention. In the T group, systolic blood pressure remained relatively stable, ranging between 139.83 and 140.17 mmHg. This persistent increase is likely because hypertension was induced before probiotic treatment. Although *Lactobacillus plantarum* DS1 may exert beneficial effects, such as reducing vascular inflammation, improving endothelial function, and modulating the renin–angiotensin system, this probiotic is incapable of completely reversing the structural or functional changes in blood vessels that have occurred due to hypertension. Previous studies have shown that *Lactobacillus plantarum* can activate the endothelial nitric oxide synthase (eNOS) enzyme through the PI3K/Akt pathway, thereby increasing the production of nitric oxide (NO) and facilitating blood vessel dilation.[36] The diastolic blood pressure in the C- group showed a slight decrease from 58.70 to 56.25 mmHg, suggesting a state of physiological stability. In the C+ group, the diastolic blood pressure increased significantly from 75.46 to 87.50 mmHg. This finding supports that hypertension is not controlled without treatment. In contrast to the T group, there was a slight decrease in diastolic from 80.33 to 78.50 mmHg, indicating the possibility of antihypertensive effects from the treatment. Therefore, we can conclude that the C+ group exhibited both systolic and diastolic hypertension progression. This conclusion is based on the consistent increase observed in both systolic and diastolic blood pressure values over the 8-week period. The absence of any treatment allowed hypertension to worsen naturally, thereby validating the model of uncontrolled hypertension used in this study. The T group managed to handle the rise in blood pressure (with systolic staying about the same and diastolic going down somewhat), which suggests that the tested compound might have a favorable effect.

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Table 1: Division of model rat groups

Control group		Treatment (T)
Negative control (C−)	**Positive control (C+)**	
Without the administration of *Lactobacillus plantarum* DS1	STZ-induced without the administration of *Lactobacillus plantarum*	Administration of *Lactobacillus plantarum* 1ml/head/day orally

Table 2: Results of blood sugar measurement in mg/dL

Group	Before treatment (mg/dl)	Week 8 care (mg/dl)
C-	91.25	98.00
C+	250.00	405.75
T	241.17	150.17

Table 3: Blood pressure of *Rattus norvegicus* rats

Groups	Systolic		Diastolic	
	Before treatment	**Weeks-8 treatment**	**Before treatment**	**Weeks-8 treatment**
Control -	115.58	108.25	58.70	56.25
Control +	141.67	153.75	75.46	87.50
T	139.83	140.17	80.33	78.5

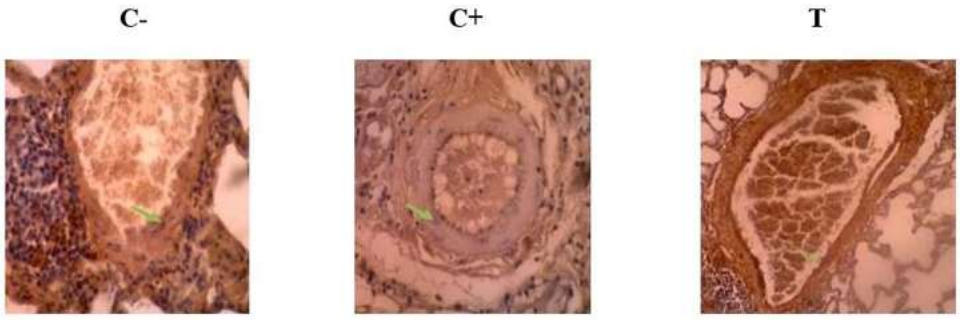

Figure 1: ACE-2 expression
Negative control (C-): Positive control (C+); Treatment (T)

The effectiveness of the treatment appeared better than no treatment, but it still did not normalize blood pressure to the level of group C-. In short, the extremely small p-values (1.36×10^{-17} for systolic blood pressure and 4.95×10^{-13} for diastolic blood pressure) indicate a highly statistically significant difference in both types of blood pressure between the treatment groups. This means that the treatments given do affect changes in systolic and diastolic blood pressure.

The consumption of beverages containing *Lactobacillus plantarum* has been shown to have beneficial effects on blood pressure and cardiovascular health. This probiotic strain can help regulate blood pressure, particularly diastolic pressure, and maintain blood vessel flexibility by producing angiotensin-converting enzyme (ACE) inhibitor peptides. Research indicates that Lactobacillus plantarum can help lower systolic blood pressure, fibrinogen levels, and interleukins in healthy individuals, thereby protecting against high blood pressure. Lactobacillus-containing probiotics have been shown to significantly reduce both systolic and diastolic blood pressure. The aggregated standardized mean difference for systolic blood pressure was −0.71 mmHg, whereas for diastolic blood pressure, it was −0.45 mmHg, indicating a significant effect compared to the placebo.[37] Probiotic intake resulted in a decrease in systolic blood pressure by -3.56 mmHg and diastolic blood pressure by -2.38 mmHg. The benefit was more significant with various probiotic species and when the intervention persisted for a minimum of 8 weeks.[38] *Lactobacillus plantarum* makes ACE inhibitory peptides while fermenting and can play a role in lowering blood pressure by inhibiting the activity of the ACE enzyme, which is key in the body's system for regulating blood pressure, important for controlling blood pressure by blocking the change of angiotensin I into angiotensin II, a strong substance that narrows blood vessels.[39] *Lactobacillus plantarum*-fermented milk significantly lowers blood pressure in rats that naturally have high blood pressure. This drop in blood pressure was associated with an increase in short-chain fatty acids and a resetting of the renin-angiotensin system.[40] People with hypertension often have compromised gut microbiota, which probiotics like *Lactobacillus plantarum* can influence. This modification may enhance cardiovascular health by improving intestinal barrier function and diminishing inflammation.[36] Drinking probiotic fermented milk has been associated with lower blood pressure in people who are pre-hypertensive and hypertensive,

suggesting it could be a valuable part of a diet for managing hypertension.[41]

In the C- group, there was a decrease in ACE-2 expression compared to the positive group with diabetes and hypertension (Figure 1). Having diabetes along with hypertension raises ACE-2 expression in the blood vessel lining, which suggests that this combination can make blood vessel reactions worse and possibly lead to more organ damage. The study showed that *Lactobacillus plantarum* DS1 significantly suppressed ACE-2 expression in *Rattus norvegicus* rats with diabetes and hypertension after 8 weeks. Although the visual difference in ACE-2 expression in Figure 1 is not always significant, the data indicate that the T group has lower ACE-2 expression compared to the C+ group with diabetes and hypertension. The lower ACE-2 levels in the C- group compared to the C+ group indicate that diabetes and hypertension raise ACE-2 levels in the blood vessel lining, confirming that the T group successfully reduces ACE-2 expression. IHC staining in group C- showed that ACE-2 was typically present in the lining of the coronary arteries, which matched with normal levels of blood pressure, blood sugar, and cholesterol. However, ACE-2 expression was still found in group C- because the rats used were old, as indicated by the presence of foam cells in the HE preparation.[42] In group C+, IHC staining also showed ACE-2 expression in endothelial cells. In the T group, researchers observed and measured ACE-2 expression despite the presence of many more endothelial cells than in group C+, by calculating the percentage of endothelial cells with ACE-2 relative to the total number of endothelial cells.

The study highlights how *Lactobacillus plantarum* DS1 can reduce ACE-2 levels in rats with diabetes and high blood pressure, suggesting it may be a valuable treatment option. This finding is consistent with numerous studies indicating that *Lactobacillus plantarum* can help lower blood pressure by decreasing ACE activity, a key factor in regulating blood pressure.[43-44] *Lactobacillus plantarum* strains demonstrate considerable ACE inhibitory action, a crucial method for lowering blood pressure. Fermented milk containing *Lactobacillus plantarum* Y44 exhibited an ACE inhibitory efficacy of 53.56%. Likewise, other strains, such as SR37-3 and SR61-2, exhibited ACE inhibition rates of 70.5% and 68.9%, respectively.[45] The antihypertensive effects are associated with alterations in gut microbiota makeup. People with high blood pressure often reduce the variety and amount of gut bacteria, which probiotics, such as Lactobacillus plantarum, can help increase. This modification may result in enhanced metabolic profiles and decreased blood pressure. The synthesis of advantageous metabolites, including short-chain fatty acids (SCFAs), constitutes an additional pathway. These compounds are associated with improved cardiovascular health and reduced blood pressure.[46] Numerous studies have shown that *Lactobacillus plantarum* can reduce blood pressure in hypertensive rat models. Fermented milk containing *Lactobacillus plantarum* significantly lowered both the systolic and diastolic blood pressure in rats that naturally have high blood pressure. Alongside the lowering of blood pressure, alterations in biomarkers associated with hypertension occur. A study reported that fermented milk containing Lactobacillus plantarum K79 significantly reduced the levels of proteins associated with blood pressure.[47] The inclusion of *Lactobacillus plantarum* in functional foods, particularly fermented dairy products, is a viable strategy for hypertension management. These items offer nutritional benefits and support cardiovascular health due to their probiotic properties.[48] *Lactobacillus plantarum* may be utilized as a therapeutic agent for managing hypertension, especially in those with coexisting diabetes and hypertension.

Conclusion

Gut microbiota-based therapy, particularly probiotics, can serve as an alternative approach for managing hypertension and diabetes. This study focuses on exploring how *Lactobacillus plantarum* DS1 can help manage high blood pressure and inflammation by affecting ACE-2 expression, which could lead to new probiotic treatments for long-term metabolic issues. The results of this study indicated that *Lactobacillus plantarum* DS1 significantly maintained stable blood pressure, reduced blood sugar levels, and regulated ACE-2 expression. Therefore, it was concluded that *Lactobacillus plantarum* DS1 is effective in lowering blood sugar, maintaining blood pressure, and controlling inflammation in diabetic rats. The implications of this study suggest that *Lactobacillus plantarum* DS1 has significant potential as a therapeutic agent for treating hypertension and inflammation in individuals with diabetes. The study's limitations include the possibility that results obtained from diabetic mice may not be fully applicable to humans due to physiological differences. The 8-week study duration is less than ideal for observing long-term effects. The study hasn't explained the specific biological processes beyond ACE-2 expression, and it needs to provide more precise numbers on blood sugar reduction and inflammation for a better overall understanding. Future studies on *Lactobacillus plantarum* DS1 should focus on long-term studies to understand its chronic effects on hypertension and inflammation in diabetic mice. The specific biological processes at work in *Lactobacillus plantarum* DS1's reduction of hypertension and diabetes should be explored, not just in ACE-2 expression, but also in the interaction between inflammation and gut bacteria, which may be elucidated using advanced techniques. Dose-response studies and potential combinations with conventional therapies are of significant importance. Finally, identifying predictive biomarkers may pave the way for more personalized medicine.

Conflict of Interest

The author`s declare no conflict of interest.

Author's Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

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