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*by* Rinita Amelia

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# The Potential of West Sumatran *Dadiah* as The Novel to Alleviate Hyperglycemia, Hypercholesterolemia, and Reducing NF-kB Expression in Nephropathy Diabetes Rat Model

**Rinita Amelia[1,*], Faridah Mohd Said[2], Farzana Yasmin[3] and Harnavi Harun[4]**

[1]*Department of Histology, Faculty of Medicine, Universitas Baiturrahmah, Sumatera Barat 25586, Indonesia*
[2]*Postgraduate Nursing Studies, Faculty of Nursing, Lincoln University, Kelana Jaya 47300, Malaysia*
[3]*Faculty of Biotech, Lincoln University, Kelana Jaya 47300, Malaysia*
[4]*Department of Internal Medicine, Faculty of Medicine, Universitas Andalas, West Sumatra 25175, Indonesia*

**([*]Corresponding author's e-mail: rinitaamelia@fk.unbrah.ac.id)**

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**Abstract**

Diabetic nephropathy (DN) is the most common microvascular complication in diabetes mellitus (DM) patients. The main mechanism for the development of DN is an inflammatory reaction as indicated by increased expression of NF-kB in kidney tissue due to chronic hyperglycemia and hypercholesterolemia. Hyperglycemia is related to changes in the composition of the microbiota which cause dysbiosis. The therapeutic approach in DM sufferers using probiotics needs attention. *Dadiah* is a naturally fermented buffalo milk product in bamboo tubes. Even though this probiotic has health benefits, its mechanism as an antidiabetic is not widely known. This study aims to reduce blood sugar, cholesterol, and inflammatory marker NF-kB levels after Dadiah treatment. This study was an experimental animal study using 7 groups, each group of 6 rats, 8 weeks of intervention, and evaluation of serum glucose and cholesterol every 2 weeks. NF-kB expression in kidney tissue was examined after 8 weeks of the termination phase. We examined their effect on blood glucose levels, serum cholesterol, and NF-kB antibody expression in kidney tissue using immunohistochemical assays. probiotic metabolites in intraperitoneal Alloxan-induced diabetic rats 100 mg/kg b. w. The results showed the potential of *Dadiah* and its metabolites to significantly (one-way ANOVA test) reduce hyperglycemia and serum cholesterol and inhibit oxidative stress by reducing NF-kB expression in kidney tissue after treatment. *Dadiah* probiotics should be considered as a nutritional companion in DN and as a future therapeutic target for DM patients to prevent the development of microvascular complications and hypercholesterolemia.

**Keywords:** Dadiah, hyperglycemia, Hypercholesterolemia, NF-kB, Diabetes neuropathy, Probiotic

## Introduction

Diabetes Mellitus (DM) is a cause of premature death, blindness, heart disease, and kidney failure for sufferers. According to the International Diabetes Federation (IDF), there were approximately 451 million diabetic patients worldwide in 2017, which is expected to rise to 693 million by 2045. Diabetic nephropathy (DN) is a significant complication of diabetes; it is a leading cause of death and end-stage renal disease (ESRD) in diabetic patients. Around 30 % of people with diabetes have renal disease, and most of them develop DN [1]. DM consists of 3 main types, namely, type 1 DM (T1DM) as a result of an autoimmune reaction to pancreatic cell proteins, and type 2 DM (T2DM) as a result of a combination of genetic factors and environmental factors, such as obesity, overeating, lack of food, exercise, stress, and aging. Type 3 is Gestational diabetes, which is the third main form and occurs when pregnant women without a previous history of diabetes develop a high blood glucose level [2]. Generally, patients with T2DM experience complications, and cardiovascular complications that cause morbidity and mortality. T2DM patients experience impaired insulin secretion and/or action, causing hyperglycemia and hyperinsulinemia. Carbohydrate-restricted diets have been used effectively for over a century for the treatment of obesity and T2DM. Its effectiveness may be due to lowering the dietary contribution to glucose and insulin levels, which reduces hyperglycemia and hyperinsulinemia. Treatments for T2DM that enhance glycemic control while decreasing blood insulin levels make sense from a pathophysiologic standpoint [3]. Theincreasing prevalence of T2DM is becoming a major cause of microvascular such as retinopathy and macrovascular

complications such as peripheral vascular disease, and diabetic nephropathy [4,25].

Diabetic nephropathy (DN) is a condition of decreased kidney function and the main cause of end-stage kidney disease [6]. DN is triggered by genetic, environmental, cellular, and molecular mechanisms that play a role in kidney damage in diabetes [7]. DN is a clinical syndrome characterized by persistent albuminuria and progressive decline in kidney function. 50 % of patients with DN will experience end-stage kidney disease (ESKD) requiring treatment with dialysis or kidney transplantation which is associated with significantly increased cardiovascular morbidity and mortality. The main risk factors for the development of DN are chronic hyperglycemia, hypercholesterolemia, and reduced expression of Nuclear Factor Kappa Beta (NF-kB).Chronic hyperglycemia in DM sufferers is followed by damage, and impaired function of the eyes, kidneys, nerves, heart, and blood vessels. The diagnosis of diabetes mellitus is made based on the high level of glucose in the blood plasma [8,9]. Hypercholesterolemia can lead to atherosclerosis, coronary heart disease, pancreatitis, thyroid disorders, liver disease & disease [10]. NF-kB plays a role in the developmentand various complications of DM for sufferers, such as diabetic cardiomyopathy, retinopathy, nephropathy, and DM neuropathy. NF-kB is a ubiquitously expressed transcription factor that has a role in inflammation, apoptosis, adhesion, angiogenesis, and cell cycle. Inflammation has a significant role in the development and progression of ND. NF-κB controls numerous proteins involved in inflammation. Many therapeutic approaches for DM sufferers have been developed, such as the useof several antioxidants, flavonoids, and probiotics [27]. Probiotics are promising candidates for improvingglycemic management, inflammation systems, and lipid profiles in individuals with type 2 diabetes [12]. Probiotic supplementation improves glycemic control and cardiometabolic risk markers. One possible mechanism for the hypocholesterolemia impact of probiotics has been suggested by direct cholesterolinteraction or assimilation by probiotics [11]. The effectiveness and safety of probiotics for glycemic control in patients with impaired glucose control, including prediabetes and T2DM [12].

Many studies have used experimental models to evaluate the impact of supplementation with probiotics and prebiotics on various risk factors for metabolic syndrome [13]. The search for safer non-pharmacological therapies with cholesterol-lowering effects continues to be carried out by utilizing bacteria. Probiotic bacteria from the lactic acid group and Bifidobacterium can regulate serum cholesterol potential [14]. The results of the study showed that Gaio was able to lower cholesterol. Gaio is a yogurt product that utilizes the ability of *Enterococcus faecium* strains and *Streptococcus thermophilus* strains [15]. Decreased serum lipid concentrations with probiotic intake based on studies of various bacterial strains [16]. Probiotics are one of the most commonly used nutritional supplements around the world. One of the probiotics, *Dadiah* comes from West Sumatra, Indonesia, which is known as a traditional food.

*Dadiah* is a type of fermented milk originating from West Sumatra, Indonesia. *Dadiah* is made from natural fermented buffalo milk which involves lactic acid bacteria. *Dadiah* has the potential to be developed as a functional food source of probiotics. The fermentation of the curd is carried out by microbes originating from bamboo, banana leaves, and milk [17]. Bamboo segments contain several microbes consisting of mold, yeast, lactic acid-forming microorganisms, protein breakers, and spore formers [18,19]. The use of antioxidants in DM cases needs to be considered to prevent the development of DM into diabetic nephropathy. Probiotics can enhance antioxidant absorption and antioxidant-related activity. Many studies have been conducted by local and national researchers regarding the nutritional components and their antimicrobial activity in *Dadiah*. However, only a few have studied clinically and scientifically confirmed its effects on various diseases, especially metabolic diseases. Although this probiotic has beneficial properties, its presumed anti-diabetic mechanism is unknown. This study aims to reduce blood sugar levels, cholesterol, and the inflammatory marker NF-kB.

## Materials and methods

### Instruments of research

The instruments of research digital scale (ACS) with 0.01 g accuracy to weigh rats. Experimental animal cages, food and water containers for experimental animals, sonde to inject Dadiah and LAB isolated sampled from Dadiah 1 and 2 mL/day. The tools used in this research are a luminometer, pipettes, microscope, microtome, slide glass, razor blades/scissors, aluminum foil, metal basket, rotary tissue processor, refrigerator, water heater, processor cassette, autoclave (Hirayama), incubator (Fisher), hot plate, Eppendrof, bunsen, vortex, Erlenmeyer tubes, glucometer (Glucose blood level and cholesterol) and urine protein stick (UriScan).

**Experimental animals**

Wistar-strain male white rats (*Rattus norvegicus*) aged 2 - 3 months with a weight of ± 300-g, standard feed as daily food, a40 Ad libitium drinking water. Dadiah. Lactic Acid Bacteria dan bacteriocin isolated sampled in Dadiah from Tanjung Bonai, Lintau Tanah Datar, West Sumatra. The examination results obtained information that Dadiah contained Lactic Acid Bacteria of 7,1 X 1010 CFU/g [20].

**Preparation of *Dadiah***

*Dadiah* dosage for rats = conversion value x *Dadiah* dosage for humans. The dosage of administration, based on the recommended dosage of fermented milk in humans with a body weight of 70 kg, was 100 - 200 mL per day. The density (ρ) of *Dadiah* was 1.04 g/mL. The recommended *Dadiah* dosage is 104 g/70 kg of human. The Laurence table (2008), the conversion value of 70 kg of Human weight to 200 g of Rat weight is 0.018. The calculation of *Dadiah* dosage for the rat is *Dadiah* dosage for rat = conversion value x *Dadiah* dosage for humans. The recommended *Dadiah* dosage is 104/70 kg of human. *Dadiah* dosage for rat = conversion value x *Dadiah* dosage for human = 0.018×104 = 1,87 g/200 g of rat weight. 1.87 g of *Dadiah*/200 g of Rat weight = 9.35 g/kg b. w. The weight of the male white rat (*Rattus norvegicus*) is ± 300 g = 0.3 kg *Dadiah* solution containing 1 g/mL was made by suspending *Dadiah* with aqua dest. The material in this experimental study is *Dadiah* 3 mL [21].

**Preparation of LAB**

Isolate *L. fermentum* is rejuvenated first, then propagated in the medium MRS broth at a temperature of 370 °C for 24 h, and calculated the number of bacterial cells is by diluting up to $10^8$ CFU/mL. Dilution results are calculated on the MRS medium so that it is included at a temperature of 37 °C for 2×24 h in the incubator to find out the number of LAB to be induced. Following previous *in vitro* research obtained for 1 g Dadiah, there is a LAB colony of $7.1\times10^{10}$ CFU/mL.

**Preparation of bacteriocin (production of crude bacteriocin)**

T5 LAB of Dadiah was cultivated in MRS broth (1,000 mL) seeded with 10 % inoculum of overnight culture and incubated at 37 °C for 24 h. Following incubation, the entire broth was centrifuged for 16 min at 10.000 X g find the cell-free supernatant was used as crude Bacteriocin [22]. The amount of LAB and Bacteriocin used in this study was 1 and 2 mL per day.

**Methods**

This research is an experimental study base on animal trials with a post-test-only control-group design. Male *Rattus norvegicus* strain wistar rats were procured from Pharmacology Department, Universitas Andalas, Padang, West Sumatra, Indonesia. The research samples have the criteria, healthy with glowing eyes, active and having a good appetite, 2 - 3 months old, and weigh 200 - 300 g. All rats were maintainedat 23 - 25 °C, with both a standard pellet diet and water ad libitum. After acclimatization for 2 weeks, except for the negative control group, all other groups were injected with alloxan 100 mg/Kg b. w. All groups of mice were fed with standard pellets. Furthermore, the treatment group will be given *Dadiah*, LAB, and Bacteriocin. The experiment was conducted with 5 treatment groups and 2 control groups. In this study, 28 rats were divided into 5 groups with the number of each group of 6 rats. So that 6 DN rats were treated with *Dadiah* 3 mL/day (P1 group) and isolated samples of LAB and Bacteriocin from*Dadiah* 1 and 2 mL/day (P2-P5 group). Control groups were 3 DN rats without being treated (Positive control/C+) and 3 normal rats (control negative/C−) who d4 not have DN (without alloxan injection). The minimum sample of this study was determined according to the formula Federer is (t-1) (n-1) ≥ 15, t is the number of treatment groups. This study was an experimental animal study using 7 groups, each group of 6 rats, 8 weeks of intervention, and evaluation of serum glucose and cholesterol every 2 weeks. NF-kB expression in kidney tissue was examined after 8 weeks of the termination phase. The number of samples obtained by 42 rats.

**Induction of diabetes and *in vivo* experimental**

Before the experiment began, all the rats were weighed, and measured blood glucose levels were cut off the rat's tail's 1 mm end. Tail is required to follow up glucose serum level and cholesterol every week, retro orbital has collected in the final experimental before termination ($8^{th}$ week). After that, the blood dropped on the glucose stick of the glucometer (OneTouchMerck; accuracy ISO 15197:2003) and the test of proteinuria by UriScan Test Strips (Biosys Laboratories, INC). After all the data have recorded, we had the first experiment that ma2e rats into clinically marked DN for hyperglycemia (> 200 mg/dL) and proteinuria. In a preliminary study, rats kept on fasting for 12 h received a single injection of freshly dissolved allo2an in 1.0 mL of sodium citrate buffer (0.1 M pH4.5) intraperitoneally (i. p), at a rate of 100 mg/kg b. w. The

blood was withdrawn from the tail vein of rats,then the measurement of fasting blood glucose concentration and cholesterol serum every 2 weeks along the experimental protocol (56 days/8 weeks). After 7 days of alloxan induction, animals with fasting glucose > 200 mg/dL and proteinuria were considered diabetic nephropathy and grouped accordingly withan average of 6 rats per group and orally administered with *Dadiah*, LAB, and Bacteriocin isolated from *Dadiah* for eight weeks or 56 consecutive days [23].

**The dissection of experimental animals**

Dissection was performed after 56 days of treatment is given where male white rats (*Rattus norvegicus*) were killed using Anesthesia with ether. The method was by mixing the concentrated ether solution with 2 % NaCl solvent or 10 - 25 % in NaCl and a dose of 300 mg/kg or 1 - 1.25 g/kg placed on the bottom of the desiccator. Then put the rat in a closed container, wait until it became immobile, and its pupillary mydriasis and eyes were closed. If the rat lost consciousness, then brought ride inside the container, then laparotomy and neck pressure were done to kill it while pulling it anteriorly (dislocation Atlanta-occipitalis. Identification and nephrectomy were carried out, then directly put in a 10 % BNF solution, after the kidney organ was removed. The experimental protocol complied with the Helsinki Declaration as revised in 2013 and ethics clearance was approved by the Ethics Committee No:001/Ethics-A/03/03/2021.

**Tissue processing**

Rat renal tissue was processed into paraffin blocks and cut with a microtome with a thickness of 4 mm. The preparations were stained with hematoxylin-eosin and Sirius red. Measurements were taken by photo-shooting hematoxylin-eosin preparations with Olympus BX 51 light microscope at 400x (objective 40x) and 1,000x (objective 100x) magnifications. Photomicrographs were taken in representative areas. The standard procedure followed the Pathology Anatomy Laboratory Andalas University protocol.

**The techniques of immunohistochemical preparations**

Kidneys were removed, trimmed, and weighed and the relative weight of the organ was calculated. The relative weight of the organ (%) was calculated as gram/100 g of body weight. Specimens from the kidney were fixated immediately in 10 % buffered formalin for immunohistochemical testing of NF-kB.

**Data analyze**

A comparison of the test was conducted using the average difference test, namely the one-way ANOVA test. Before the test, the underlying assumption was the normality of the data the Kolmogorov-Smirnov test. If the data used does not meet any or all of the assumptions, a replacement test will be conducted, that is the Kruskal Wallis test. If the results of the one-way ANOVA are significantly different, the Duncan test will be carried out, as well as the further test for the Kruskal Wallis test, that is, Mann-Whitney. If the notation of the results of the further test between the 2 treatments is different, then the 2 treatments are significantly different. Meanwhile, if the notation between the 2 treatments is the same, then the 2 treatments are not significantly different test between treatments. The technique of IHC preparation in this study used ScyTek Laboratories procedure with UltraTech HRP Anti polyvalent (DAB)Staining Complete System

**Results and discussion**

*Dadiah*, traditional food from West Sumatra, Indonesia has health benefits due to probiotics and peptides inhibiting NF-kB expression in rat kidney tissue modeled diabetic. *Dadiah*'s clinical efficacy in lowering blood sugar and serum cholesterol indicates that it may be used as a future therapy to prevent diabetic progression.

**The NF-kB expression with immunohistochemistry in the kidney**

The expressions of NF-kB appeared brown on the IHC staining and the staining pattern was mainly in the form of cytoplasmic staining (**Figure 1**). The microscopic assessment used the Olympus BX51 light microscope at 400x magnification (40x objective) by assessing the positive intracytoplasmic brown staining on the representative area. Each sample was observed in 5 different fields of view. In each field of view (40x objective).

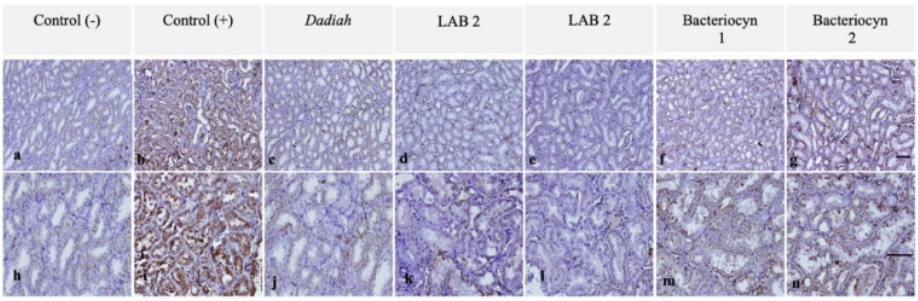


**Figure 1** The NF-kB expression with immunohistochemistry in the kidney.

The proportion of epithelial cells with positive intracytoplasmic brown staining was calculated, then compared to all epithelial cells per field of view. The staining intensity was reported in 4 intensity levels (negative, weak, moderate, and strong). The NF-kB immunohistochemical staining in the kidney of the animal model. The negative control group (a, h) and the positive control (b, i), the treatment with *Dadiah* (c, j), low-dosage lactic acid bacteria (d, k) and the high dosage (e, l), and low-dosage bacteriocin (f, m) and the high dosage (b, i). The NF-kB was intracytoplasmic expressed in a few tubular epithelial cells in the control animals with weak to moderate expressions, and some cells in the stroma and endothelium. The induction with alloxan showed an increase in the NF-kB expression with most of the tubular cells expressing moderate to strong. The treatment in the animal model showed a decrease in the NF-kB expression in the tissues compared to the positive control, both administered by *Dadiah*, lactic acid bacteria, and Bacteriocin. The NF-kB expression appeared to be lower in the treatment with *Dadiah* compared to other treatments. The immune peroxidase, using the low magnification with 10x objective lens (top) and the high magnification with 40x objective lens (bottom) at 200 µm scale.

**NF-kB expression numbers in each group**

NF-κB is a transcription factor that regulates the gene expression of several proinflammatory proteins. Based on **Figure 2**, the highest average of NF-kB expression in the C+ treatment (induced by alloxan+without any treatment) was 77.50 ± 8.80, and the lowest average of NF-kB expression was in the treatment (not induced by alloxan and not given a treatment), namely 20.83 ± 8.01. To prove whether there was a statistically significant difference the average number of NF-kBexpressions, the Kruskal Wallis statistical analysis would be carried out. Based on the results of the Kruskal Wallis test, the *p*-value was smaller than (0.000 < 0.050), so it can be concluded that there was a significant difference in the average NF-kB expression number between treatments. It was observed that the positive control groups had significantly higher averages of NF-kB expression than the C−, P1, P2, P3, P4, and P5 groups.

Conversely, the hostile control groups (C−) had considerably lower average NF-kB expression than the positive control groups (C+), P2, and P3 but were not significantly different from the P1, P4, and P5 groups. NF-kB is a core nuclear transcription factor in the inflammatory response, increasing the expression of various cytokines and chemical substances involved in the formation and development of DN, In addition, a more recent study found that antioxidan inhibited the activity of NF-kB and decreased the production of particular pro-inflammatory mediators, especially the Tumor Necrosis Factor and Interleukin-6 (TNF and IL-6) [24,25]. NF-kB is a ubiquitously distributed transcription factor that affectsinflammation, apoptosis, adhesion, angiogenesis, and cycle cells. Inflammation is one of the key mechanisms responsible for the development and progression of DN. Many inflammation-related proteinsare regulated by NF-kB. *Dadiah* is known to contain probiotics and antioxidants, so it has been proven that *Dadiah* can reduce oxidative stress and inflammation.

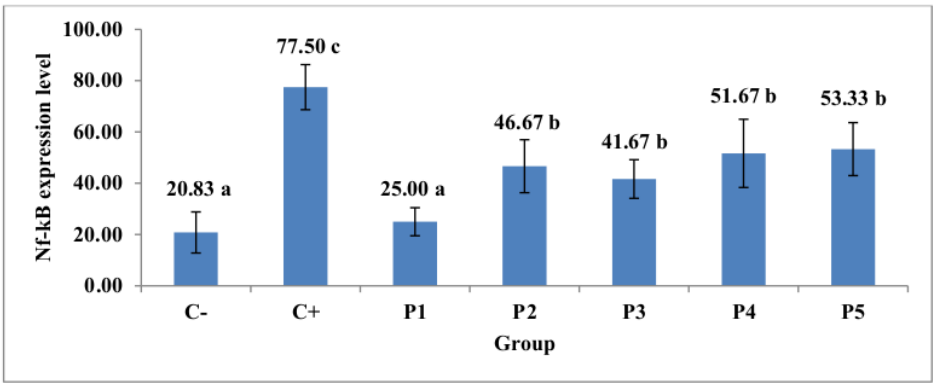


**Figure 2** NF-kB expression numbers in each group.

Even *Dadiah* itself contains a peptide that can stimulate endogenous antioxidants to inhibit the production of NF-kB. Administration of *Dadiah*, an isolateof lactic acid bacteria, and Bacteriocin has been shown to reduce macrophage activation in the production of proinflammatory cytokines. In addition, NF-kB expression shown in immunohistochemical examinationof kidney tissue decreases significantly close to the negative control [27].

**Blood glucose levels**

Blood sugar levels are an increase in glucose in the blood or an increase in serum glucose. Blood glucose levels in each treatment can be seen from the results of the research that has been carried out (**Figure 3**).

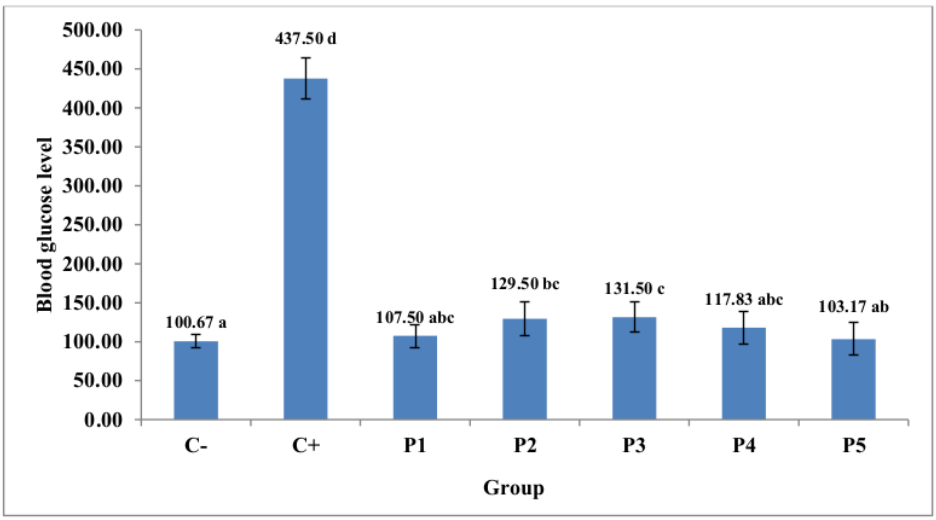


**Figure 3** Blood glucose levels in each treatment.

Based on **Figure 3**, it can be shown that the highest average blood glucose level in the C+ treatment (induced by alloxan+proteinuria) was 437.50 ± 26.70, and the lowest average blood glucose level was in the C− treatment (not induced by alloxan and not given any treatment), namely 100.67 ± 9.05. The highest average of blood glucose levels in the C+ treatment was significantly different from the C−, P1, P2, P3, P4, and P5 treatments. The lowest average of blood glucose levels in the C− treatment was significantly different from the C+, P2, and P3 treatments, but the C− treatment was not significantly different from the P1, P4, and P5 treatments. Hyperglycemia-induced oxidative stress has been linked to various diabetes

complications, including DN. There is significant evidence that oxidative stress and the inflammatory response have a role in DN development. Sustained hyperglycemia induces oxidative stress and generates substantial reactive oxygen species (ROS) in renal tissues, activating the nuclear transcription factor NF-kB and resulting in kidney inflammation. Probiotic-based antidiabetic therapy has been proposed, and its influence on glycation is being explored. *L. fermentum* ME-3 may be used therapeutically to inhibit the formation/accumulation of certain glycation products in the kidneys and to ameliorate certain frequent disease-related complications [28].

Probiotic-fermented blueberry juice protects mice fed a high-fat diet from obesity and hyperglycemia by altering the gut flora. In addition, in HFD-fed mice, blueberry juices markedly improved hyperlipidemia and insulin resistance. Another study found the effect of Yogurt containing *Lactobacillus bulgaricus* and *Streptococcus thermophilus* (LBST) on metabolic risk indicators is either beneficial or neutral. Increased blood pressure, increased blood glucose, abnormal blood lipids, subclinical inflammation (TNF and IL-6), overweight, and obesity are all metabolic indicators [29-30]. Similarly, Probiotic Yogurt significantly lowered fasting blood glucose ($p = 0.01$) and HbA1c ($= 0.05$) levels and boosted the activities of erythrocyte superoxide dismutase and glutathione peroxidase. Probiotic Yogurt made with *Lactobacillus acidophilus* and *Bifidobacterium lactis*. These data imply that probiotic Yogurt is a functional food with potential anti-diabetic and antioxidant effects. Furthermore, other research investigated whether giving probiotics and selenium to GDM patients for 6 weeks improved their hyperglycemic status and lipid profiles [31].

Several studies demonstrate treating diabetes patients with Voglibose (0.3 mg/kg) and probiotics (75 mg/kg) significantly decreased blood glucose and total cholesterol levels when compared to the diabetes group treated with only Voglibose (0.3 mg/kg). Similarly, research indicates that administering probiotic L sakei OK67 effectively prevents hyperglycemia development. the anti-diabetic effects of 14 probiotics in db/db mice resulted in improved intestinal barrier function and increased GLP-1 production, indicating that these probiotics may be suitable for preventing and treating diabetes. Other studies have discovered that consuming probiotic Yogurt can help lower fasting blood glucose levels. These findings suggest that consuming probiotic Yogurt regularly may have a beneficial effect on treating metabolic syndrome [32-31].

**Serum cholesterol levels**

The result of serum cholesterol levels showed that the C+ group has the highest average cholesterol of 166, while the P1 group as treated with *Dadiah* has the lowest average cholesterol of 116.2 (**Figure 4**). To prove a statistically significant difference in average cholesterol, a Kruskal Wallis statistical analysis will be performed. Based on the Kruskal Wallis test results, we obtained a *p*-value smaller than α ($0.003 < 0.050$), so it can be concluded that there is a significant difference in average cholesterol between treatments.

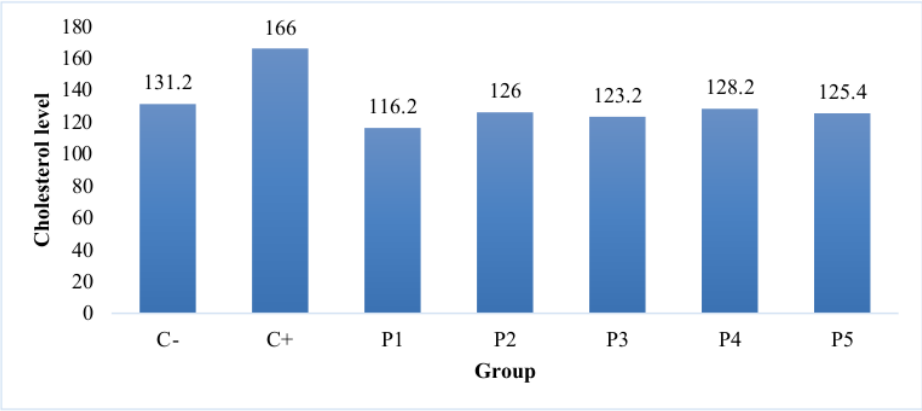


**Figure 4** Serum cholesterol levels in each group.

This study shows that the group of rats given the treatment of *Dadiah* can lower the cholesterol levels of mice-modeled DN compared to other groups. Lactobacillus species are the most often utilized bacteria probiotic treatments, and studies have shown that they can decrease cholesterol levels in humans. Consumption of probiotics may have a positive effect on managing cholesterol levels. The consumption of probiotic yogurt (300 g per day) containing *L. acidophilus* La5 (~$4.14\times10^6$ CFU/g) and *B.lactis* Bb12 (~$3.61\times10^6$ CFU/g) for 6 weeks significantly improved the lipid profile of type 2 diabetes mellitus (T2D) patients. In addition, the results suggested that the regular consumption of probiotic yogurtcould improve the cholesterol level of T2D patients.

The study concluded that probiotic consumption amended the glycemic control, inflammatory system, and lipid profile in T2D subjects [34-36]. *In vitro* studies have also shown that *L. acidophilus* and *B. lactis* can lower cholesterol absorption. Similarly, in a study obtained, after 4 weeks ofintake of *L. fermentum* ME3 containing food supplement probiotics, all subjects' LDL cholesterol, total cholesterol, and ox-LDL levels reduced dramatically, while HDL cholesterol showed a potential to improve. The activity of the bile salt hydrolase (BSH) enzyme can be utilized to screen new probiotics forfunctional properties such as hypocholesterolemia activity and colonization potential [37]. Accordingto a recent study, probiotics from fermented camel milk significantly improved blood glucose and lipid parameters and the morphological changes in the pancreas, liver, and kidney [38].

## Conclusions

The use of *Dadiah* containing *L. fermentum* strains has been demonstrated to reduce inflammatory reactions associated with diabetic complications (DN). This study can be observed in the lower expression of NF-kB antibodies as proinflammatory biomarkers that rise with hyperglycemia. The outcomes of providing *Dadiah* alone against probiotics alone or LAB metabolites such as bacteriocin revealed the same improvement in inflammation, blood glucose, and cholesterol. However, the gift of *Dadiah* had the most significant impact on the control group. These results demonstrate that *Dadiah* with a comprehensive composition has a more substantial effect on biomolecular and clinical outcomes. For this reason, probiotics, and new strategies from *Dadiah* need to prevent and treat metabolic diseases and prevent the progression of complications in DM. We suggested a clinical study for humans in a future study.

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# The Potential of West Sumatran Dadiah as The Novel to Alleviate Hyperglycemia, Hypercholesterolemia, and Reducing NF-kB Expression in Nephropathy Diabetes Rat Model

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