Activity Test of Cinnamon Bark Extract (*Cinnamomum Burmannii*) Nanoemulsion Preparation on Reducing Urea, Creatinine, and Kidney Histopathology in Male Rats Induced by Alloxan

Andi Masrayani Ahdanisa[1], Alinapiah Nasution[2], Maya Sari[3]
[1,2,3]Faculties Medicine , Dentistry and Knowledge Health , Universitas Prima Indonesia , North Sumatra

*E-mail : masrayaniahdanisa@yahoo.com

ABSTRACT
This study aims to test the activity of a nanoemulsion preparation of cinnamon bark extract (*Cinnamomum burmannii*) in reducing urea and creatinine levels, and evaluating the histopathological features of the kidneys in alloxan-induced male rats. Rats were divided into several groups, including a control group and a group treated with a nanoemulsion preparation of cinnamon bark extract. Urea and creatinine levels were measured to assess kidney function, while histopathological analysis was performed to evaluate changes in kidney tissue morphology. The results showed that treatment with a nanoemulsion preparation of cinnamon bark extract significantly reduced urea and creatinine levels and improved the histopathological features of the kidneys compared to the control group. Nanoemulsion of cinnamon bark extract (Cinnamomum burmannii) was proven to be effective in reducing blood glucose, urea, and creatinine levels in male white rats (Rattus norvegicus) of the Wistar strain induced by alloxan. The treatment group given nanoemulsion with a concentration of 20% showed the most optimal results, with a significant decrease in blood sugar, urea, and creatinine levels, approaching the values shown by the negative control group. In histopathological examination of the kidneys, the 20% treatment group also showed minimal tissue damage, characterized by only mild thickening of the glomerular basement membrane, compared to the other groups. These findings suggest the potential of cinnamon bark extract as a nephroprotective agent in the management of diabetes-induced kidney damage.

Keywords: *Nanoemulsi Extract Skin Wood Sweet, Urea, Creatinine*

INTRODUCTION

Diabetes mellitus is a common metabolic disease, characterized by high blood glucose levels. Hyperglycemia affects body cells directly and through alternative glucose metabolism pathways (Harreiter & Roden, 2019). Hyperglycemia results from abnormalities in insulin secretion, insulin action, or both, and manifests chronically and heterogeneously as dysfunctions in carbohydrate, fat, and protein metabolism (ADA, 2014). Hyperglycemia and the associated dysfunctions in carbohydrate, fat, and protein metabolism affect many organs and disrupt their normal function. These disorders develop gradually and are largely due to the detrimental effects of hyperglycemia and its associated metabolic abnormalities on the normal structure and function of the micro- and macrovascular vasculature, which is central to organ structure and functions throughout the body. Structural and functional disorders of the blood vessels of the organ system lead to micro- and macrovascular complications. Organ damage, dysfunction, and, ultimately, organ failure characterize these complications, affecting organs, including, in particular, the kidneys (Banday et al., 2020).

The kidneys are paired organs located retroperitoneally in the lumbar region. They maintain fluid and acid-base balance, remove nitrogenous waste products, and synthesize hormones such as renin, erythropoietin, and active vitamin D3. The functional unit of the kidney is the nephron, which is responsible for ultrafiltrate formation, reabsorption, and secretion of electrolytes and water, as well as acidification and concentration of urine. When the kidney structure is disrupted by a pathological process, markers of kidney function such as urea and creatinine levels increase (Reddi, 2020). Urea and creatinine are waste products of metabolism.

Urea is a product of protein metabolism. It is considered a non-protein nitrogenous waste product. Amino acids derived from protein breakdown are deaminated to produce ammonia. Ammonia is then converted to urea by liver enzymes. Therefore, urea concentration depends on protein intake, the body's capacity to break down protein, and adequate urea excretion by the renal system. Elevated urea levels can be caused by a high-protein diet or decreased renal excretion. Creatinine, also a renal waste product, is produced from the breakdown of creatine and phosphocreatine and can also serve as an indicator of kidney function. Creatine is synthesized in the liver, pancreas, and kidneys from the transamination of the amino acids arginine, glycine, and methionine. Creatine then circulates throughout the body and is converted to phosphocreatine through phosphorylation in skeletal muscle and the brain (Salazar, 2014). Correction of urea and creatinine levels must be addressed before kidney function deteriorates.

Long-term use of synthetic drugs can have adverse health effects. Therefore, the search for new phytotherapeutic agents from natural sources in the form of bioactive compounds has become crucial. In this regard, herbs and spices have emerged as potential remedies for many ailments arising from lifestyle changes. One such plant is cinnamon (*Cinnamomum burmannii)* .

Cinnamon has been used as a culinary spice for thousands of years. It has been shown to have several potential health benefits, including anti-inflammatory, antioxidant, anti-neuroinflammatory, neuroprotective, insulin sensitivity-enhancing, and anti-obesity properties (Bagherniya et al., 2018). Cinnamaldehyde, a major component of cinnamon, has previously been shown to have potent neuroinflammatory properties and may protect against early brain injury caused by hemorrhage (Gürer et al., 2019).

Identification of compounds using chromatography techniques shows that eugenol and cinnamaldehyde compounds are the metabolites that play the most role as mediators of the biological effects of cinnamon. This study tested mint leaf nanoemulsion preparations to improve kidney function in alloxan-induced white Wistar rats. The advantages of nanoemulsions are that they can increase absorption, are effective transport systems, require relatively little energy, and are thermodynamically stable (Kumar & Soni, 2017).

Objective study This is To determine the characteristics of the nanoemulsion preparation of cinnamon bark extract (*Cinnamomum burmannii)* through phytochemical tests , to observe kidney function by examining urea and creatinine levels in male white rats (*Rattus norvegicus*) of the Wistar strain induced by alloxan after administration of the nanoemulsion preparation of cinnamon bark extract (*Cinnamomum burmannii)* and to observe the histopathological picture of kidney tissue in white rats given the nanoemulsion preparation of cinnamon bark extract (*Cinnamomum burmannii)* with concentrations of 10% and 20% .

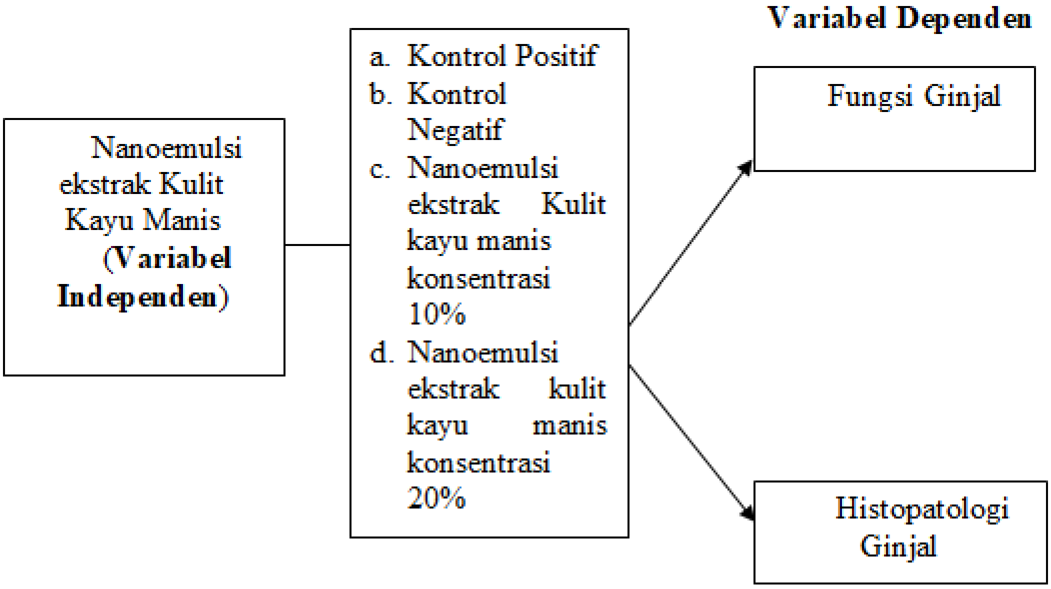

Figure 1. Framework Conceptual

METHODS

The type of research used in this study was quantitative experimental, employing *a true experiment* or laboratory experimental design. Experimental research is conducted by controlling all external variables that could influence the experimental activities. This study used *a post-test only control group design* .

This research was conducted in the Department of Pharmaceutical Pharmacology Laboratory, Faculty of Medicine, University of North Sumatra, and the Anatomical Pathology Laboratory, University of North Sumatra, from June to August 2025.

Based on the calculations above, the minimum number of test animals per group was 6. In this study, researchers used 24 Wistar rats for each experimental group. The test animals were randomly assigned to four groups.

The kidney function parameters in this study were urea and creatinine levels. Elevated blood urea levels are an indication of kidney damage. If the kidneys are unable to excrete enough urea, blood urea levels will rise above normal levels because glomerular filtration must decrease by 50% before blood urea levels can rise.

Kidney function examination follows the following steps: Step 1: On the 21st day, the rats were anesthetized for further blood sampling through the orbital vein with a capillary pipette of 3 cc collected into an EDTA (EthylenediamineTetraacetic Acid) tube and placed in a cool box. The blood sample was then examined at the University of North Sumatra Laboratory to determine amylase and lipase levels. Step 2: Using a pipette, blood was taken according to the pipette size and then the blood was dripped into the Creatinine (CREA) test kit to check creatinine levels and Blood urea nitrogen (BUN) to check urea levels in the blood. Step 3: Insert the Creatinine (CREA) and Blood urea nitrogen (BUN) test kits into the Reflovet Plus measurement chamber and close the measurement chamber cover. Step 4: Reflovet Plus displays and prints the results, after 2-3 minutes.

Data from histopathological observations through microscopic examination were collected and then scored. The research data were tabulated, then the changes found were analyzed and presented descriptively. The observation data were analyzed using SPSS *(Statistics of Package for Social Science)* 25.0 *for Windows* . The normality test for the data was analyzed using *the Kolmogorov-Smirnov test approach* (p > 0.05). To test the significance between the experimental groups, a one-way analysis of variance technique or *One Way ANOVA was used* at a 95% confidence level (p < 0.05). Further analysis or testing was carried out using *the Post Hoc Test* with the LSD technique.

RESULTS AND DISCUSSION

Phytochemical Test Results

Phytochemical testing was carried out to identify the content of secondary metabolite compounds contained in nanoemulsions of cinnamon bark extract (*Cinnamomum burmannii).* which is suspected to have potential as a natural therapeutic agent. The following are the screening results obtained:

Table 1. Test Phytochemicals

Secondary Metabolites	Color	Results	Note
Flavonoid	Pink	+	It is indicated that there is
Saponin	Yellow and foamy	+	It is indicated that there is
Tannin	turquoise	+	It is indicated that there is
Alkaloid	Yellow sediment	+	It is indicated that there is
Steroids/Triterpenoids	Green	+	It is indicated that there is

Information: (+) = Contain group compound Which tested
(-) = Does not contain the tested compound

Blood Sugar Level Observation Results

In this study, the test animals received preconditioning treatment in the form of alloxan induction to induce diabetes mellitus. Alloxan induction was performed on each test animal. The first stage involved fasting the mice for 18 hours and then inducing them with alloxan at a dose of 150 mg/kg body weight, administered via intraperitoneal injection. After 5 days, blood sugar levels were measured. The purpose of alloxan administration was to induce diabetes in the mice. Blood sugar levels were measured using a glucometer.

Blood sugar levels were measured by drawing 1 mL of blood from the rat's tail after first cleaning it with alcohol. The blood was then dripped onto a glucometer strip, which was then inserted into the device to read the results. Successful induction was indicated by a blood sugar level of 200 mg/dL or greater. Blood sugar levels were measured on days 1, 14, and 21. The changes observed were as follows:

Table 2. Results of Blood Sugar Level Observations

No	Group	Blood Sugar Level (mg/dL) Mean ± SD		
		Day 1	Day 14	Day 21
1	Negative Control	97.5 ± 6.50	98.66 ± 6.25	99.66 ± 6.25
2	Positive Control	289.16 ± 7.35	215.83 ± 10.16	115.33 ± 7.50

3	Treatment 1	292.83 ± 4.57	244.33 ± 8.84	123.66 ± 5.85
4	Treatment 2	293.5 ± 7.96	183.33 ± 4.92	102.83 ± 8.35

Based on the table above, it can be seen that the positive control group, treatment 1, and treatment 2 showed blood sugar levels greater than 200mg/dL. The positive control group showed an average blood sugar level of 289.16 ± 7.35 mg/dL. Treatment group 1 had an average blood sugar level of 292.83 ± 4.57 mg/dl and treatment group 2, namely, 293.5 ± 7.96 mg/dl. The results of these blood sugar level measurements indicate that the test animals are included in the category of diabetes mellitus and are then given treatment according to their respective groups.

Treatment was administered daily at 10:00 a.m. On the 14th day, the blood sugar levels of the test animals were measured again to see the changes that occurred. The negative control group that was not induced by alloxan and was only given distilled water showed blood sugar levels with an average of 98.66 ± 6.25 mg/dL. The positive control group that was given metformin had an average of 215.83 ± 10.16 mg/dL. Treatment group 1 that was given cinnamon bark extract nanoemulsion with a concentration of 10% had an average of 244.33 ± 8.84 mg/dL. Treatment group 2 with a concentration of 20% cinnamon bark extract nanoemulsion had an average of 183.33 ± 4.92 mg/dL. On the 14th day, the average blood sugar levels in the positive control group, treatment group 1, and treatment group 2 decreased but were not yet included in the normal blood sugar category.

On the 21st day, the rats' blood sugar levels were measured again to see the changes that occurred in all treatment groups. The negative control group obtained an average result of 99.66 ± 6.25 mg/dL. The positive control group obtained an average result of 115.33 ± 7.50 mg/dL. Treatment group 1, which was given a 10% concentration of cinnamon bark extract nanoemulsion, obtained a result of 123.66 ± 5.85 mg/dL. Treatment group 2, which was given a 20% concentration of cinnamon bark extract nanoemulsion, obtained an average result of 102.83 ± 8.35 mg/dL.

Based on the results of blood sugar level measurements on the 21st day, it can be concluded that the positive control group given metformin, treatment group 1 given nanoemulsion of cinnamon bark extract (*Cinnamomum burmannii*) with a concentration of 10%, and treatment group 2 given nanoemulsion of cinnamon bark extract (*Cinnamomum burmannii*) with a concentration of 20% experienced a decrease so that blood sugar levels returned to normal, namely below 135 mg / dL. Treatment group 2 experienced the most significant decrease and approached the negative control group compared to the other groups. Treatment group 1 given nanoemulsion of cinnamon bark extract (*Cinnamomum burmannii*) with a concentration of 10% was the group with the least decrease compared to the other groups but was still in the normal category.

Urea Level Observation Results

Observations of changes in urea levels were carried out after alloxan induction, namely on day 1, day 14, and day 21.

Table 3. Results of Observation of Urea Levels After Treatment

		Ureum Levels (mg/dL) Mean ± SD		
No	**Group**	**Day 1**	**Day 14**	**Day 21**
1	Negative Control	15.95 ± 0.65	15.97 ± 0.65	16.00 ± 0.64
2	Positive Control	41.12 ± 0.73	33.43 ± 0.98	17.99 ± 0.64

3	Treatment 1	41.43 ± 0.78	36.21 ±1.19	22.50 ± 1.06
4	Treatment 2	41.17 ± 0.78	32.65 ± 1.00	16.42 ± 0.86

Based on the results of urea level measurements on the 21st day, it can be concluded that the positive control group given metformin, treatment group 1 given nanoemulsion of cinnamon bark extract (*Cinnamomum burmannii*) at a concentration of 10%, and treatment group 2 given nanoemulsion of cinnamon bark extract (*Cinnamomum burmannii*) at a concentration of 20% experienced a decrease. Treatment group 2 experienced the most significant decrease and was closer to the negative control group compared to the other groups. Treatment group 1 given nanoemulsion of cinnamon bark extract (*Cinnamomum burmannii*) at a concentration of 10% was the group with the least decrease compared to the other groups.

Creatinine Level Observation Results

Observations of changes in creatinine levels were carried out after alloxan induction, namely on day 1, day 14, and day 21.

Table 4. Results of Creatinine Level Observations After Alloxan Induction

		Creatinine Levels (mg/dL) Mean ± SD		
No	**Group**	**Day 1**	**Day 14**	**Day 21**
1	Negative Control	0.26 ± 0.04	0.27 ± 0.04	0.29 ± 0.06
2	Positive Control	1.16 ± 0.12	0.86 ± 0.06	0.44 ± 0.09
3	Treatment 1	1.15 ± 0.10	0.87 ± 0.08	0.46 ± 0.06
4	Treatment 2	1.15 ± 0.10	0.81 ± 0.07	0.35 ± 0.08

Based on the results of creatinine level measurements on the 21st day, it can be concluded that the positive control group given metformin, treatment group 1 given nanoemulsion of cinnamon bark extract (*Cinnamomum burmannii*) at a concentration of 10%, and treatment group 2 given nanoemulsion of cinnamon bark extract (*Cinnamomum burmannii*) at a concentration of 20% experienced a decrease. Treatment group 2 experienced the most significant decrease and was closer to the negative control group compared to the other groups. Treatment group 1 given nanoemulsion of cinnamon bark extract (*Cinnamomum burmannii*) at a concentration of 10% was the group with the least decrease compared to the other groups.

Histopathological Observation Results

Histological examination of the kidneys evaluated the shape and changes in the glomerulus. The glomerulus is a dense, branching network of capillaries -, surrounded by Bowman's space and Bowman's capsule. Capillary endothelial cell nuclei, mesangial cells, and podocytes can be observed scattered throughout the glomerulus. The control group, which was not induced by alloxan and only given distilled water, had normal kidney histology because there were no changes in the glomerulus. In this group, there was no apparent dilation of the glomerular cells. The glomerular diameter also appeared normal. The kidney histopathology in the control group was normal, thus serving as a reference for describing the other groups and as a comparison with the treatment group induced by alloxan and given cinnamon bark extract (*Cinnamomum burmannii*).

Nomor ISSN: 3124-1115

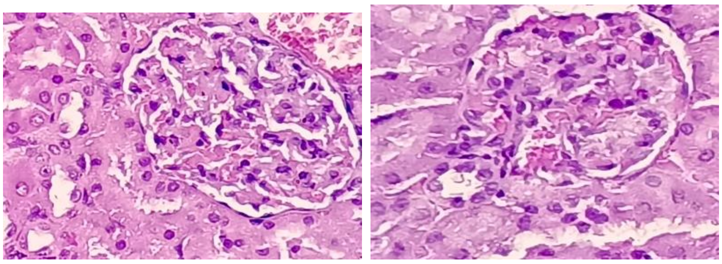

Figure 2. Histopathology of the Kidneys of the Negative Control Group

The positive control group was given alloxan and metformin induction. Glomerular basement membrane thickening and slight mesangial proliferation were observed. Glomerular cell dilation resulted in adhesions between the glomerulus and Bowman's capsule. This condition is related to the effects of the previous alloxan induction. The kidney histology in the positive control group differed slightly from the negative control group due to glomerular thickening.

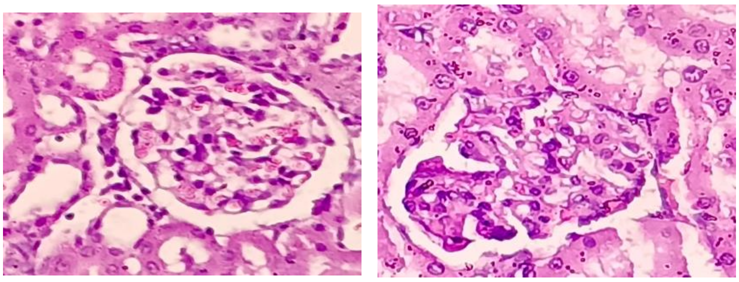

Figure 3. Histopathology of the Kidneys of the Positive Control Group

Treatment group 1 was induced by alloxan and a 10% concentration of cinnamon bark extract nanoemulsion. Glomeruli exhibited hypertrophy and hypercellularity, characterized by an increase in the number of mesangial and endothelial cells. Furthermore, there was thickening of the glomerular basement membrane. This dilation of glomerular cells resulted in adhesions between the glomerulus and Bowman's capsule. This condition is related to the effects of alloxan induction.

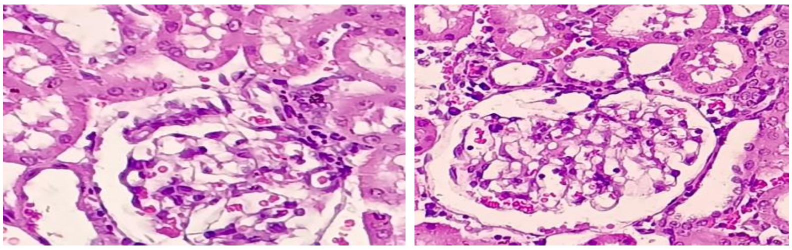

Figure 4. Kidney Histopathology of Treatment Group 1

Treatment group 2 was induced by alloxan and a 20% concentration of cinnamon bark extract nanoemulsion. The glomeruli experienced slight thickening of the glomerular basement membrane. This dilation of the glomerular cells resulted in adhesions between the glomeruli and Bowman's capsule. This condition is related to the effects of alloxan induction during preconditioning. However, this dilation was smaller than that of treatment group 1 and the positive control group.

Nomor ISSN: 3124-1115

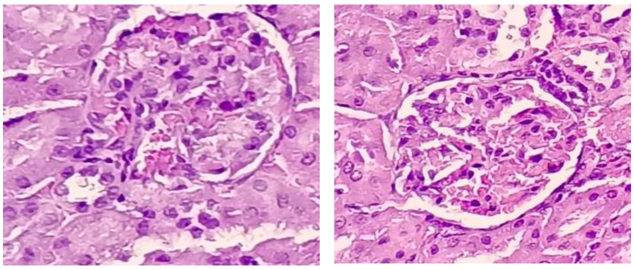

Figure 5. Kidney Histopathology of Treatment Group 2

The results of histopathological observations of the kidneys in the negative control group, positive control, treatment 1, and treatment 2 were then scored. The scoring system used was based on glomerular cell damage, namely: score 0 = no histopathological damage, score 1 = focal (mild) damage, score 2 = multifocal (moderate) damage, and score 3 = diffuse (severe) damage.

Table 5. Renal Histopathology Score

Group	Mean Score ± SD	Interpretation
Negative Control	0.1 ± 0.4	No damage
Positive Control	1.5 ± 0.8	Minor damage
Treatment 1	2.0 ± 0.6	Moderate damage
Treatment 2	1.3 ± 0.8	Minor damage (structural repairs)

Based on the results of observations on renal glomerular cells in each group, it can be concluded that the negative control group did not experience cell damage so it received a score of 0. The positive control group given metformin experienced mild thickening of the glomerular basement membrane and slight mesangial proliferation so it was included in the score 1, which is focal (mild) damage. Treatment group 1 which was given a nanoemulsion of cinnamon bark extract with a concentration of 10% experienced thickening of the glomerular basement membrane, an increase in the number of mesangial cells and endothelial cells, so it was included in the score 2, which was multifocal (moderate) damage. Finally, treatment group 2 which was given a nanoemulsion of cinnamon bark extract with a concentration of 20% experienced slight thickening of the glomerular basement membrane so it was included in the score category 1, which was focal (mild) damage.

DISCUSSION

This research was conducted to tested and analyzed the effectiveness of nanoemulsion preparation of cinnamon bark extract (*Cinnamomum burmannii*) on reducing urea, creatinine, and histopathological features in alloxan-induced male white rats (*Rattus norvegicus) of the Wistar strain.* Researchers used 24 male white rats (*Rattus norvegicus*) of the Wistar strain for each experimental group. The test animals were randomly assigned into 4 test groups. The groups consisted of a negative control group that was not induced by alloxan and given distilled water, a positive control group that was given alloxan and metformin induction, treatment group 1 that was given nanoemulsion of cinnamon bark extract (*Cinnamomum burmannii*) with a concentration of 10% and treatment group 2 that was given nanoemulsion of cinnamon bark extract (*Cinnamomum burmannii*) with a concentration of 20%.

The experimental animals were induced with type 2 diabetes mellitus by inducing alloxan. Alloxan was administered in a single dose via the intraperitoneal route to ensure rapid systemic distribution. The dose used in this study was 150 mg/kg body weight, which, according to the literature, has been shown to be effective in producing a type 2 diabetes model in mice without causing high mortality.

Diabetes mellitus is a common metabolic disease, characterized by high blood glucose levels. Hyperglycemia directly affects body cells and can also affect alternative glucose metabolism pathways (Harreiter & Roden, 2019). Hyperglycemia results from abnormalities in insulin secretion, insulin action, or both, and manifests chronically and heterogeneously as dysfunction in carbohydrate, fat, and protein metabolism (ADA, 2014). Long-term use of synthetic drugs can have adverse health effects. Therefore, the search for new phytotherapeutic agents from natural sources in the form of bioactive compounds has become crucial. In this regard, herbs and spices have emerged as potential remedies for many lifestyle-related diseases. One such plant is cinnamon (*Cinnamomum burmannii)* .

Cinnamon can also treat mouth ulcers, coughs, shortness of breath, stomach ache, flatulence, diarrhea, rheumatism, and cancer. Many chemicals, including cinnamaldehyde, cinnamic acid, coumarin, tannins, and flavonoids, are found in cinnamon bark (Sirait et al., 2023). Cinnamaldehyde found in cinnamon bark has demonstrated glucolipid-lowering effects in diabetic animals by improving glucose uptake and insulin sensitivity. Cinnamaldehyde exerts these effects through its actions on several signaling pathways, including the PPARγ, AMPK, PI3K/IRS-1, RBP4-GLUT4, ERK/JNK/p38MAPK, TRPA1-ghrelin, and Nrf2 pathways (Zhu et al., 2017).

Researchers then conducted phytochemical tests on cinnamon bark extract (*Cinnamomum burmannii)* . Phytochemical tests included tests for flavonoids, tannins, saponins, alkaloids, and steroids/triterpenoids. Based on the results of the phytochemical tests, it can be concluded that cinnamon bark extract (*Cinnamomum burmannii)* contains secondary metabolites in the form of flavonoids, saponins, tannins, alkaloids, and triterpenoids. The results of this study are in line with previous research conducted by Sirait et al., (2023) who conducted phytochemical tests on cinnamon bark extract. The results of phytochemical screening of cinnamon bark extract showed the presence of alkaloids, saponins, tannins, triterpenoids, and flavonoids. Antioxidant activity was obtained with an IC50 value of 25.35 ppm. Based on these results, cinnamon extract has a very strong antioxidant activity value.

Based on the results of blood sugar level measurements on the 21st day, it can be concluded that the positive control group given metformin, treatment group 1 given nanoemulsion of cinnamon bark extract (*Cinnamomum burmannii*) with a concentration of 10%, and treatment group 2 given nanoemulsion of cinnamon bark extract (*Cinnamomum burmannii*) with a concentration of 20% experienced a decrease so that blood sugar levels returned to normal, namely below 135 mg / dL. Treatment group 2 experienced the most significant decrease and approached the negative control group compared to the other groups. Treatment group 1 given nanoemulsion of cinnamon bark extract (*Cinnamomum burmannii*) with a concentration of 10% was the group with the least decrease compared to the other groups but was still in the normal category.

post hoc test on blood sugar levels was used to determine whether the groups had significant differences from the other groups. The results of the analysis showed that the significance value of the negative control group with the positive control was 0.003. The negative control group with treatment group 1 was 0.004. The negative control group with treatment group 2 was 0.544. Based on these data, it can be concluded that the negative control group and treatment group 2 were not significantly different. Meanwhile, the negative control group with treatment groups 1 and 2 were significantly different ($p < 0.05$).

Based on the results of urea level measurements on the 21st day, it can be concluded that the positive control group given metformin, treatment group 1 given nanoemulsion of cinnamon bark extract (*Cinnamomum burmannii*) at a concentration of 10%, and treatment group 2 given nanoemulsion of cinnamon bark extract (*Cinnamomum burmannii*) at a concentration of 20% experienced a decrease. Treatment group 2 experienced the most significant decrease and was closer to the negative control group compared to the other groups. Treatment group 1 given nanoemulsion of cinnamon bark extract (*Cinnamomum burmannii*) at a concentration of 10% was the group with the least decrease compared to the other groups.

post hoc LSD test on urea levels was used to determine whether the groups had significant differences compared to the other groups. The analysis results showed a significant difference between the negative control group and the positive control group (p = 0.000) and treatment group 2 (p = 0.000). There was no significant difference between the negative control group and treatment group 1 (p = 0.397).

Based on the results of creatinine level measurements on the 21st day, it can be concluded that the positive control group given metformin, treatment group 1 given nanoemulsion of cinnamon bark extract (*Cinnamomum burmannii*) at a concentration of 10%, and treatment group 2 given nanoemulsion of cinnamon bark extract (*Cinnamomum burmannii*) at a concentration of 20% experienced a decrease. Treatment group 2 experienced the most significant decrease and was closer to the negative control group compared to the other groups. Treatment group 1 given nanoemulsion of cinnamon bark extract (*Cinnamomum burmannii*) at a concentration of 10% was the group with the least decrease compared to the other groups.

The LSD post hoc test was used to determine whether the groups had significant differences compared to the other groups. The analysis results showed a significant difference between the negative control group and the positive control group (p = 0.004) and treatment group 2 (p = 0.001). There was no significant difference between the negative control group and treatment group 1 (p = 0.155).

Based on the observation results of the renal glomerular cells in each group, it can be concluded that the negative control group did not show any cell damage, thus obtaining a score of 0. The positive control group that received metformin treatment showed mild thickening of the glomerular basement membrane and slight proliferation of mesangial cells, so it was categorized in a score of 1 which indicates focal (mild) damage. In treatment group 1 which was given a cinnamon bark extract nanoemulsion with a concentration of 10%, there was observed thickening of the basement membrane, an increase in the number of mesangial and endothelial cells, so it was included in a score of 2 which reflects multifocal (moderate) damage. Meanwhile, treatment group 2 which received a concentration of 20% only experienced slight thickening of the glomerular basement membrane, so it was included in a score of 1, namely focal (mild) damage.

Improvements in kidney function and glomerular histology are inextricably linked to the active role of flavonoid compounds contained in cinnamon bark extract nanoemulsions. Flavonoids are known to possess antioxidant and anti-inflammatory properties that can reduce oxidative stress and prevent kidney cell damage. This mechanism contributes to inhibiting degenerative processes in kidney tissue, improving the integrity of the glomerular basement membrane, and reducing excessive mesangial cell proliferation, thus significantly supporting the overall recovery of kidney structure and function.

CONCLUSION

1. Nanoemulsion of cinnamon bark extract (Cinnamomum burmannii) was proven to be effective in reducing blood glucose, urea, and creatinine levels in male white rats (Rattus norvegicus) of the Wistar strain induced by alloxan.
2. The treatment group given nanoemulsion with a concentration of 20% showed the most optimal results, with a significant decrease in blood sugar, urea, and creatinine levels, approaching the values shown by the negative control group.
3. In histopathological examination of the kidneys, the 20% treatment group also showed minimal tissue damage, characterized by only mild thickening of the glomerular basement membrane, compared to the other groups.

ACKNOWLEDGEMENT

The Faculty of Medicine, Dentistry, and Health Sciences, as well as the directors of study programs, are acknowledged by the authors for their support of this research at Universitas Prima Indonesia. Additionally, we appreciate the supervisors' insightful comments. The University of North Sumatra, the Faculty of Pharmacy, the Pharmacology Laboratory, and the Nanomedicine Laboratory are all acknowledged by the authors for their invaluable support of this study.

REFERENCES

Banday MZ, Sameer AS, Nissar S. Pathophysiology of diabetes: An overview. Avicenna J Med. 2020 Oct 13;10(4):174-188. doi: 10.4103/ajm.ajm_53_20. PMID: 33437689; PMCID: PMC7791288.

Fernandez I, Vidueiros SM, Ayerza R, Coates W, Pallaro A. Impact of chia (Salvia hispanica L. (on the immune system: preliminary study. Proc Nutr Soc. 2008; 67: E12.

Grancieri M, Martino HSD, Gonzalez de Mejia E. Chia seed (Salvia hispanica L.) as a source of proteins and bioactive peptides with health benefits: a review. Compr Rev Food Sci Food Saf. 2019; 18: 480-99.

Grancieri, M. , Martino, H. S. D. , & Gonzalez de Mejia, E. (2019). Chia seed (*Salvia hispanica* L.) as a source of proteins and bioactive peptides with health benefits: A review. Comprehensive Reviews in Food Science and Food Safety, 18(2), 480–499. 10.1111/1541-4337.12423

Gürer, B., Kertmen, H., Bektas¸oglu, P.K., Öztürk, Ö. Ç., Bozkurt, H., Karakoç, A., … Çelikoglu, E. (2019). The effects of Cinnamaldehyde on early brain injury and cerebral vasospasm following experimental subarachnoid hemorrhage in rabbits. Metabolic Brain Disease, 34(6), 1–10

Harreiter, J.; Roden, M. Diabetes mellitus-Definition, classification, diagnosis, screening and prevention (Update 2019). *Wien Klin Wochenschr.* **2019** , *131* , 6–15.

Lazaro, H. , Puente, L. , Zúñiga, M. C. , & Muñoz, L. A. (2018). Assessment of rheological and microstructural changes of soluble fiber from chia seeds during an in vitro micro-digestion. LWT, 95, 58–64. 10.1016/j.lwt.2018.04.052

Liang, Y., Li, Y., Sun, A., & Liu, X. (2019). Chemical compound identification and antibacterial activity evaluation of cinnamon extracts obtained by subcritical n-butane and ethanol extraction. *Food science & nutrition* , *7* (6), 2186-2193.

Muhammad, D.R.A., Tuenter, E., Patria, G.D., Foubert, K., Pieters, L., & Dewettinck, K. (2021). Phytochemical composition and antioxidant activity of Cinnamomum burmannii Blume extracts and their potential application in white chocolate. *Food Chemistry* , *340* , 127983.

Menggala, SR, Vanhove, W., Muhammad, DRA, Hendri, J., Speelman, S., & Van Damme, P. (2019). Sustainable Harvesting of *Cinnamomum burmannii* (Nees & T. Nees) Blume in Kerinci Regency, Indonesia. *Sustainability* , *11* (23), 6709. https://doi.org/10.3390/su11236709

Reddi, AS (2020). Kidney function in health and disease. In *Nutrition in Kidney Disease* (pp. 39-50). Cham: Springer International Publishing.

Scott, R.P., & Quaggin, S.E. (2016). Formation and maintenance of a functional glomerulus. In *Kidney Development, Disease, Repair and Regeneration* (pp. 103-119). Academic Press.

Sirait, TS, Arianto, A., & Dalimunthe, A. (2023). Phytochemical Screening of Cinnamon Bark (Cinnamomum burmanii)(C. Ness & T. Ness) C. Ness ex Blume Ethanol Extract and Antioxidant Activity Test with DPPH (2, 2-diphenyl-1-picrylhydrazyl) Method. *International Journal of Science, Technology & Management* , *4* (1), 254-259.

Ullah R, Nadeem M, Khalique A, Imran M, Mehmood S, Javid A, et al. Nutritional and therapeutic perspectives of Chia (Salvia hispanica L.): a review. J Food Sci Technol. 2016; 53: 1750-8.

Walsh T, Worthington HV, Glenny AM, Marinho VC, Jeroncic A. Fluoride toothpaste of different concentrations for preventing dental caries. Cochrane Database Syst Rev. 2019 Mar 04;3(3):CD007868.