

Activity Test of Nano Emulsion Preparation of Star Anise (*Illicium Verum*) Extract on Reducing Urea and Renal Creatinine Levels in Male Rats Induced by Alloxan

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ABSTRACT

Diabetes mellitus is a disease that knows no boundaries, this disease appears when the body cannot control glucose levels. This study aims to test and analyze the effectiveness of the nanoemulsion preparation of star anise (*Illicium verum*) extract on reducing urea, creatinine, and kidney histopathology in male Wistar rats (*Rattus norvegicus*) induced by alloxan. The sample of rats used was 24 in 4 groups (positive and negative controls, treatments 1 and 2) where the extract preparation in the treatment was a nanoemulsion of star anise (*Illicium verum*) extract with a concentration of 10% and 20%. The results of this observation indicate that administration of star anise (*Illicium verum*) extract with a concentration of 20% can improve the histological structure of the kidneys in male Wistar rats (*Rattus norvegicus*) with diabetes.

Keywords: *Star anise, Nanoemulsion, Kidney, Urea - Creatinine, Diabetes*

INTRODUCTION

Diabetes mellitus is a disease that knows no boundaries. This disease occurs when the body cannot control the level of glucose (a type of sugar) in the blood, causing the kidneys to produce a lot of urine. This occurs when the body does not produce enough insulin or does not absorb it properly. This can be caused by impaired insulin secretion, resistance to peripheral insulin action, or both. Chronic hyperglycemia in synergy with other metabolic abnormalities in patients with diabetes mellitus can cause damage to various organ systems, leading to the development of disabling and life-threatening health complications. (Goyal, 2022).

Glucose has consequences in the form of oxidative stress. Chemically, glucose is an aldohexose, making it a fairly reactive molecule. Glycemia modulation and regulation of glucose uptake by cells are crucial for health. Hyperglycemia causes metabolic disorders by triggering abnormal pathways that increase oxidative stress in human tissues. (Furukawa, 2017).

Oxidative stress is a key factor in the pathogenesis and progression of diabetes and its related complications. An imbalance between reactive oxygen species (ROS) production and the body's antioxidant defense mechanisms leads to cell damage and dysfunction. In diabetes, elevated blood sugar and mitochondrial dysfunction contribute to increased ROS production, which further exacerbates oxidative stress. This oxidative burden negatively impacts various aspects of diabetes, including impaired beta-cell function and insulin resistance, leading to impaired glucose regulation. Furthermore, vascular damage from oxidative stress and impaired endothelial function contribute to the development of diabetic vascular complications such as nephropathy. (Caturano, 2023).

Diabetic nephropathy is characterized by a progressive decline in kidney function, hypertension, proteinuria, and other signs of chronic renal insufficiency. Glomerular

Filtration Rate (GFR) is a parameter used to assess kidney function and the progression of chronic kidney disease. A decrease in GFR is accompanied by an increase in blood urea and creatinine, as these two compounds can only be excreted by the kidneys (Lutfiana, 2019). The pathophysiology of diabetic nephropathy is characterized by chronic hyperglycemia, which results in progressive damage to the renal microvasculature. (Sugahara, 2021).

Type 2 diabetes mellitus can damage the small blood vessels in the kidneys, leading to diabetic nephropathy. This condition can reduce the kidneys' ability to filter blood, resulting in increased blood urea and creatinine levels. Blood creatinine and urea concentrations are the best guides for predicting the progression, prognosis, and establishing dietary restrictions for kidney disease in type 2 diabetes mellitus (Salazar, 2014).

Star anise is an important species widely used in traditional Chinese medicine. Both the fruit and its essential oil are pharmacopoeial ingredients and have been used for centuries to treat rheumatism, insomnia, and digestive disorders. The valuable properties of star anise fruit are attributed to its unique chemical composition, which contains abundant amounts of phenylpropanoids, mono- and sesquiterpenoids. Numerous scientific studies have shown that star anise fruit and essential oil exhibit potent biological activities such as antibacterial, antifungal, anti-inflammatory, and antioxidant effects. (Sharafan, M., Jafernik, K., Ekiert, H., Kubica, P., Kocjan, R., Blicharska, E., & Szopa, 2022).

LITERATURE REVIEW

The functional unit of the kidney is the nephron, which consists of the glomerulus and its associated tubule. Each kidney has approximately one million nephrons. Approximately 20% of cardiac output is channeled through the glomerulus. Water flow through the glomerulus is free, while the flow of electrolytes and solutes is determined by the size and charge of the nephron. (Amin, R., Ahn, SY, & Moudgil, 2021) The kidneys are mitochondria-rich, continuously active cellular organs, making them vulnerable to damage caused by oxidative stress caused by hyperglycemia. This condition is known to accelerate chronic kidney disease (Duni et al., 2019). Chronic kidney disease is a lifestyle-related disease that affected approximately 9% of the global population in 2017. Underlying causes include various conditions such as diabetes, hypertension, nephritis, polycystic kidney disease, transplantation, and unknown factors. (Katayama, K., & Dohi, 2024) Urea is a major metabolite derived from dietary protein and tissue protein turnover. Creatinine is a product of muscle creatine catabolism. Both are relatively small molecules distributed throughout the body (Hosten, 1990).

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.

The sample of this study was a Wistar rat (*Rattus norvegicus*) weighing 160-200 grams and aged 2-3 months with a total of 6 test animals per group. In this study, researchers used 24 Wistar rats for each experimental group. The experimental groups were divided into positive and negative control groups, treatment 1 and 2. The test animals were acclimatized for 7 days in the laboratory of the Department of Pharmacology and Therapeutics, Faculty of Medicine, University of North Sumatra. The research procedures included: acclimatization of test animals, preparation of star anise extract soaking star anise powder using 96% ethanol solvent with a concentration of 2000 ml for 3 days, phytochemical test of star anise extract to see the content of secondary metabolites in the extract, preparation of test animals, administration of treatment, treatment groups 1 and 2 were given extract doses with concentrations of 10% and 20%, for positive control not given anything, and negative control mice were induced by alloxan and given metformin. All test animals were given treatment for 21 days. Kidney function and histopathology were then observed. The data

from the study were tabulated and analyzed using SPSS (Statistical Package for Social Science).

RESULTS

Phytochemical testing was carried out to identify the content of secondary metabolite compounds contained in star anise extract. The results of the phytochemical tests carried out can be concluded that star anise extract contains secondary metabolites in the form of flavonoids, saponins, tannins, alkaloids, and triterpenoids.

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 was that the mice were fasted for 18 hours and then induced with alloxan at a dose of 150 mg/kgBW with a volume of 1 mL/300gBW administered via intraperitoneal injection. After 5 days, blood sugar levels were measured. The purpose of alloxan administration was to make the mice diabetic. Blood sugar levels were measured using a glucometer. Blood sugar levels were measured on days 1, 14, and 21. The changes that occurred were observed and the following results were obtained:

Table 1 Results of Blood Sugar Level Observations

No	Group	Blood Sugar Level (mg/dL) Mean \pm SD		
		Day 1	Day 14	Day 21
1	Negative Control	101.66 \pm 9.66	104.16 \pm 8.97	106 \pm 9.57
2	Positive Control	310.83 \pm 7.08	200.5 \pm 9.52	118.66 \pm 11.63
3	Treatment 1	314.16 \pm 11.49	214.83 \pm 6.43	129.33 \pm 7.20
4	Treatment 2	316.16 \pm 9.55	176.5 \pm 10.89	110.83 \pm 9.82

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 had an average result of 106 \pm 9.57 mg/dL. The positive control group had an average result of 118.66 \pm 11.63 mg/dL. Treatment group 1, which was given a 10% concentration of star anise extract nanoemulsion, had a result of 129.33 \pm 7.20 mg/dL. Treatment group 2, which was given a 20% concentration of star anise extract nanoemulsion, had an average result of 110.83 \pm 9.82 mg/dL.

Observations of changes in urea levels were carried out after alloxan induction, namely on day 1, day 14, and day 21. The following are the results of observations on the urea levels of test animals during the treatment process:

Table 2 Results of Observation of Urea Levels After Alloxan Induction

No	Group	Ureum Levels (mg/dL) Mean \pm SD	
		Before Induction	After Alloxan induction
1	Positive Control	16.92 \pm 0.44	41.5 \pm 0.91
2	Treatment 1	16.71 \pm 0.42	41.34 \pm 0.79
3	Treatment 2	16.74 \pm 0.48	42.60 \pm 0.77

Observations on urea levels showed that the positive control group initially had an average urea level of 16.92 \pm 0.44 mg/dL. After being induced with alloxan and left for 5 days, the level increased to 41.5 \pm 0.91 mg/dL. Treatment group 1 of 16.71 \pm 0.42 mg/dl to 41.34 \pm 0.79 mg/dl. Treatment group 2 from 16.74 \pm 0.48 mg/dl to 42.60 \pm 0.77 mg/dl.

Table 3 Results of Observation of Urea Levels After Treatment

No	Group	Ureum Levels (mg/dL) Mean \pm SD		
		Day 1	Day 14	Day 21
1	Negative Control	16.79 \pm 0.57	16.84 \pm 0.57	16.87 \pm 0.57
2	Positive Control	41.50 \pm 0.91	35.7 \pm 0.99	20.93 \pm 0.89

3	Treatment 1	41.34 ± 0.79	37.73 ± 0.64	23.49 ± 0.84
4	Treatment 2	42.60 ± 0.77	34.79 ± 1.07	17.51 ± 1.05

Observations on urea levels on the 14th day: The urea levels of the test animals were re-measured to observe any changes. On the 14th day, the average urea levels in the positive control group, treatment group 1, and treatment group 2 decreased.

On the 21st day, the rats' urea levels were measured again to observe the changes that occurred in all treatment groups. The negative control group had an average result of 16.87 ± 0.57 mg/dL. The positive control group had an average result of 20.93 ± 0.89 mg/dL. Treatment group 1, which was given a 10% concentration of star anise extract nanoemulsion, had a result of 23.49 ± 0.84 mg/dL. Treatment group 2, which was given a 20% concentration of star anise extract nanoemulsion, had an average result of 17.51 ± 1.05 mg/dL.

Observations of changes in creatinine levels were carried out after alloxan induction, namely on day 1, day 14, and day 21. The following are the results of observations on the creatinine levels of test animals during the treatment process:

Table 4 Results of Creatinine Level Observations After Alloxan Induction

No	Group	Creatinine Levels (mg/dL) Mean ± SD	
		Before Induction	After Alloxan induction
1	Positive Control	0.30 ± 0.07	41.5 ± 0.91
2	Treatment 1	0.27 ± 0.05	41.34 ± 0.79
3	Treatment 2	0.30 ± 0.07	42.60 ± 0.77

The results of observations on creatinine levels showed that the positive control group initially had an average creatinine level of 0.30 ± 0.07 mg/dL. After being induced with alloxan and left for 5 days, the levels rose to 41.5 ± 0.91 mg/dL. Treatment group 1 of 0.27 ± 0.05 mg/dl to 41.34 ± 0.79 mg/dl. Treatment group 2 from 0.30 ± 0.07 mg/dl to 42.60 ± 0.77 mg/dl. Based on these observations, it can be concluded that alloxan induction triggers an increase in creatinine levels to abnormal levels. After the increase in creatinine, the study was continued with the administration of star anise extract nanoemulsion preparations with concentrations of 10% and 20%.

Table 5 Results of Creatinine Level Observations After Alloxan Induction

No	Group	Creatinine Levels (mg/dL) Mean ± SD		
		Day 1	Day 14	Day 21
1	Negative Control	0.29 ± 0.06	0.30 ± 0.06	0.32 ± 0.07
2	Positive Control	1.21 ± 0.09	1.17 ± 0.10	0.52 ± 0.06
3	Treatment 1	1.15 ± 0.10	0.95 ± 0.07	0.48 ± 0.06
4	Treatment 2	1.15 ± 0.10	0.77 ± 0.09	0.36 ± 0.08

Observations on creatinine levels on the first day showed that the negative control group that was not alloxan induced had an average value of 0.29 ± 0.06 mg/dl. The positive control group showed an average value of 0.29 ± 0.06 mg/dL.

On the 21st day, the rats' creatinine levels were measured again to observe the changes that occurred in all treatment groups. The negative control group had an average result of 0.32 ± 0.07 mg/dL. The positive control group had an average result of 0.52 ± 0.06 mg/dL. Treatment group 1, which was given a 10% concentration of star anise extract nanoemulsion, had a result of 0.48 ± 0.06 mg/dL. Treatment group 2, which was given a 20% concentration of star anise extract nanoemulsion, had an average result of 0.36 ± 0.08 mg/dL.

Histopathological observations were performed using a light microscope at 400x magnification. The following is a histological image of the kidney tissue in each treatment group:

The glomerulus appears as a round-oval structure containing a dense network of fine capillaries. Capillary endothelial cell nuclei, mesangial cells, and podocytes can be observed scattered throughout the glomerulus. The control group that was not induced by alloxan and

only given distilled water had normal kidney histology and was categorized as 0, meaning there was no damage to the glomerulus. In this group, there was no glomerular cell dilation. 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 that was induced by alloxan and given star anise extract (*Illicium verum*).

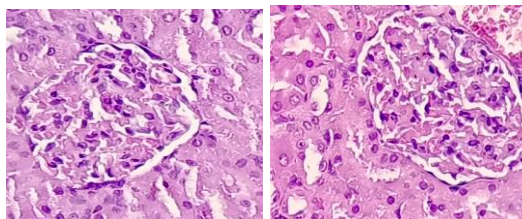


Figure 1 Histopathology of the Kidneys of the Negative Control Group

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.

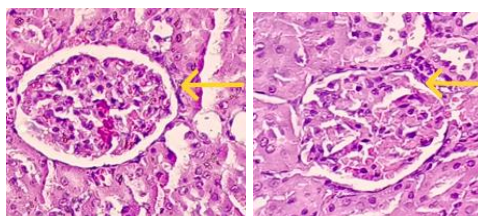


Figure 2 Histopathology of the Kidneys of the Positive Control Group

Treatment group 1 was given alloxan induction and a 10% concentration of star anise 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 widening of the glomerular cells resulted in adhesions between the glomerulus and Bowman's capsule. This condition is related to the effects of alloxan induction.

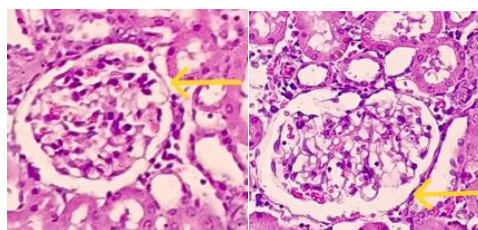


Figure 3 Kidney Histopathology of Treatment Group 1

Treatment group 2 was given alloxan induction and a 20% concentration of star anise extract nanoemulsion. The glomeruli experienced slight thickening of the glomerular basement membrane. This dilation of the glomerular cells resulted in adhesions between the glomerulus 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.

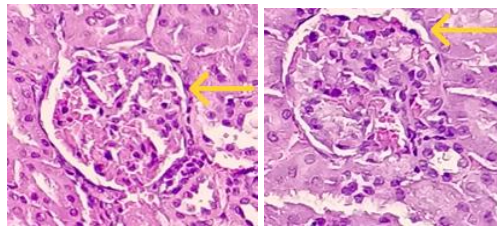


Figure 4 Kidney Histopathology of Treatment Group 2

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.

Then, we proceeded to the analysis. The results of the data normality test in this study can be seen in the following table:

Table 6 Results of Blood Sugar Level Normality Test

Group	df	Sig
Negative Control	6	.712
Positive Control	6	.960
Treatment 1	6	.988
Treatment 2	6	.774

Based on the results of the normality test conducted using the Shapiro-Wilk test, the data is said to be normally distributed if the p-value is > 0.05 . Therefore, it can be concluded that the data for the negative control group, positive control, treatment 1, and treatment 2 are normally distributed. After the data is known to be normally distributed, a homogeneity test is continued using the Levene test to determine whether each variant of this research group comes from the same or homogeneous population. The following results were obtained:

Table 7 Results of Blood Sugar Level Homogeneity Test

Levene static	df1	df2	Sig
.592	3	20	.628

The results of the homogeneity test using Levene's test can be seen in the table above. The significance value is 0.628. The significance value obtained is greater than 0.05, so it can be concluded that the negative control group, positive control group, treatment group 1, and treatment group 2 come from populations that have the same variance, or are homogeneous. Next, we test for significance to see the relationship between the variables studied. The following data is obtained from the one-way ANOVA test.

Table 8 Results of One Way ANOVA Test on Blood Sugar Levels

	Amount	df	Mean square	F	Sig
Intergroup	1868,458	3	622,819	6,635	.003
In Group	1877,500	20	93,875		
Total	3745.958	23			

The results of the One-Way ANOVA test in the table above show a significance value of 0.003, or < 0.05 . Based on these data, it can be concluded that there is a significant difference between the control group and the treatment group. A post hoc test concluded that there was

no significant difference between the negative control group and treatment group 2. Meanwhile, the negative control group and treatment groups 1 and 2 were significantly different ($p < 0.05$).

DISCUSSION

This study was conducted to test the effectiveness of a nanoemulsion preparation of star anise (*Illicium verum*) extract on reducing urea, creatinine, and kidney histopathology in male Wistar rats (*Rattus norvegicus*) induced by alloxan. Research conducted by Suarsana et al. (2010) explained that experimental diabetes induction using alloxan causes nephrosis in 40–50% of kidney damage. The damage found was in the number of glomeruli, glomerular diameter, and Bowman's capsule space distance.

Star anise (*Illicium verum*) is a plant that can be used as an alternative treatment. This plant contains bioactive compounds such as flavonoids and terpenoids, which have been shown to reduce oxidative stress caused by diabetes. Previous research by Dewajanthi et al. (2020) showed that star anise contains several compounds, one of which is flavonoids, which act as easily oxidized compounds (antioxidants), making it often used as a traditional medicine to treat many diseases.

Researchers then conducted phytochemical tests to identify the compounds contained in the star anise extract nanoemulsion. Based on the results of the phytochemical tests, it can be concluded that star anise (*Illicium verum*) extract contains various secondary metabolites, namely flavonoids, saponins, tannins, alkaloids, and triterpenoids. These compounds are important bioactive components that provide various pharmacological activities, including antioxidant, anti-inflammatory, antihyperglycemic, and nephroprotective, thus having great potential to overcome kidney tissue damage, especially due to chronic diseases such as diabetes mellitus.

This study used Wistar rats (*Rattus norvegicus*) as samples, weighing 160-200 grams and aged 2-3 months. Researchers used 24 Wistar rats for each experimental group. The test animals were randomly assigned to 4 test groups. The test animals were then given a preconditioning treatment in the form of alloxan induction at a dose of 150 mg/kgBW with a volume of 1 mL/300gBW administered via intraperitoneal injection. After 5 days, blood sugar levels were measured. Blood sugar levels were measured using a glucometer. Next, the rats' blood sugar, urea, and creatinine levels were measured to check for diabetes.

On the first day of the study (after 5 days of alloxan induction), it was seen that the positive control group, treatment 1, and treatment 2 showed blood sugar levels greater than 200 mg/dL. The positive control group showed an average blood sugar level of 310.83 ± 7.08 mg/dL. Treatment group 1 had an average blood sugar level of 314.16 ± 11.49 and treatment group 2, namely, 316.16. The results of these blood sugar level measurements indicate that the test animals are categorized as diabetes mellitus and are then given treatment according to their respective groups. The results of this study are in line with research conducted by Kim et al., (2024) which concluded that a dose of 150 mg/kg of alloxan is the most ideal for experimental diabetes models, because it offers a high induction rate, a lower risk of complications. Thus, this study confirms that alloxan effectively increases blood glucose levels in mice, with a dose of 150 mg/kg BW providing the best balance between the effectiveness of hyperglycemia induction and the safety of the test animals.

Observations on urea levels showed that the positive control group initially had an average urea level of 16.92 ± 0.44 mg/dL. After being induced with alloxan and left for 5 days, the level increased to 41.5 ± 0.91 mg/dL. Treatment group 1 of 16.71 ± 0.42 mg/dl to 41.34 ± 0.79 mg/dl. Treatment group 2 from 16.74 ± 0.48 md/dl to 42.60 ± 0.77 mg/dl. Meanwhile, the results of observations on creatinine levels showed that the positive control group initially had an average creatinine level of 0.30 ± 0.07 mg/dL. After being induced by alloxan and left for 5 days, the level rose to 41.5 ± 0.91 mg/dL. Treatment group 1 from 0.27 ± 0.05 mg/dl to 41.34 ± 0.79 mg/dl. Treatment group 2 from 0.30 ± 0.07 mg/dl to 42.60 ± 0.77 mg/dl. Based on these observations, it can be concluded that alloxan induction triggers an increase in creatinine levels to abnormal levels. All the data obtained were then processed

and tested first so that it was necessary to carry out several data analyses in the form of normality tests, homogeneity tests, and one-way ANOVA tests.

Based on these observations, it can be concluded that alloxan induction triggers an abnormal increase in urea and creatinine levels. These results align with previous research conducted by Qu et al. (2023) who conducted a trial on diabetic mice. Diabetic test animals were characterized by increased urea and creatinine levels. After the increase in blood sugar, urea, and creatinine levels, the study continued with the administration of a nanoemulsion of star anise extract at concentrations of 10% and 20%.

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 10% concentration of star anise extract nanoemulsion, and treatment group 2 given 20% concentration of star anise extract nanoemulsion 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 10% concentration of star anise extract nanoemulsion was the group with the least decrease compared to the other groups but still fell into the normal category.

The next observation is on kidney histology. Based on the results of observations on the kidney 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 so it was included in the score 1, which is focal (mild) damage. Treatment group 1, which was given a nanoemulsion of star anise 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 is multifocal (moderate) damage. Finally, treatment group 2, which was given a nanoemulsion of star anise extract with a concentration of 20%, experienced slight thickening of the glomerular basement membrane so it was included in the score category 1, which is focal (mild) damage.

Administering alloxan to mice can induce diabetes, which subsequently impacts the structure of glomerular tissue. This condition triggers glomerular hypertrophy due to increased pressure on glomerular cells. Research conducted by Handani et al. (2015) showed that mice receiving alloxan-induced glomerular cell dilation experienced adhesions between the glomerulus and Bowman's capsule.

The results of this observation indicate that administration of star anise extract (*Illicium verum*) with a concentration of 20% can improve the histological structure of the kidneys in male Wistar rats (*Rattus norvegicus*) with diabetes. This can be seen from the histopathological condition of the kidneys in the treatment group and the control group which show structural similarities, indicating the improvement of kidney tissue. This improvement effect is inseparable from the content of active compounds in star anise extract (*Illicium verum*), such as flavonoids, tannins, and other phenolic compounds, which are known to have antioxidant, antihyperglycemic, and anti-inflammatory activities. These compounds play a role in protecting and regenerating kidney cells that are damaged by oxidative stress and inflammation induced by chronic hyperglycemia in diabetic conditions. The improvement of the histological structure is inseparable from the content contained in star anise extract.

The results of this study align with previous research conducted by Khan et al. (2022), which found that star anise (*Illicium verum*) extract has the potential to lower blood glucose levels, inhibit oxidative stress, and reduce the glycation process and the formation of Advanced Glycation End Products (AGEs), both in vitro and in vivo. Therefore, this extract has the potential to be used as an additional agent to inhibit non-enzymatic glycation reactions associated with diabetes.

CONCLUSION

1. Star anise extract nanoemulsion contains secondary metabolites such as flavonoids, saponins, tannins, alkaloids, and triterpenoids. The antidiabetic activity of flavonoids supports the regulation of carbohydrate digestion, insulin signaling, and insulin secretion, thus helping to lower blood sugar levels in diabetic mice.
2. At a concentration of 20%, star anise extract nanoemulsion reduced blood glucose levels to below 135 mg/dL. A concentration of 10% produced a smaller reduction effect, but still within the normal threshold. Based on the results of one-way ANOVA ($p = 0.003$) followed by the LSD test, there were significant differences between the treatment groups, except between the negative control group and the 20% treatment group.
3. These observations indicate that administration of star anise (*Illicium verum*) extract at a concentration of 20% can improve the histological structure of the kidneys in male Wistar rats (*Rattus norvegicus*) with diabetes. This is evident from the histopathological condition of the kidneys in the treatment and control groups, which showed similar structures, indicating improved kidney tissue.

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