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Antidiabetic Activity Test of Ethyl Acetate Fraction of Bengkal Leaves (*Nauclea orientalis* L.) on Male White Mice

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A B S T R A C T

Diabetes mellitus remains a major global health problem, driving the search for safe and effective natural antidiabetic agents. This quasi-experimental study evaluates the antidiabetic activity of the ethyl acetate fraction of bengkal leaves (*Nauclea orientalis* L.) and determines the optimal dose in alloxan-induced male mice. Using a completely randomized design, 30 mice were divided into six groups: negative control, positive control (glibenclamide 0.65 mg/kgBW), and treatment groups receiving 150, 300, 450, and 600 mg/kgBW of the ethyl acetate fraction. Blood glucose levels were measured on days 1, 3, and 7 and analyzed using ANOVA and Duncan's post hoc test. The results show a significant reduction in blood glucose levels ($p < 0.001$), with the 450 mg/kgBW dose being the most effective, producing a 49.53% decrease on day 7, comparable to the positive control. Higher doses showed lower effectiveness. The study concludes that the ethyl acetate fraction of bengkal leaves has strong antidiabetic activity and potential for development as a phytopharmaceutical candidate for diabetes management.

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INTRODUCTION

Diabetes mellitus is a chronic metabolic disease characterized by an increase in blood glucose levels due to impaired insulin secretion, insulin resistance, or a combination of both. The disease has become a global health problem as its prevalence increases significantly as lifestyles, urbanization, and consumption patterns of modern society change. Global reports show that diabetes mellitus not only increases morbidity and mortality rates, but also poses a huge economic burden on health systems in various countries (Zheng et al., 2021). This condition confirms that diabetes mellitus requires a comprehensive and sustainable therapeutic approach.

The management of diabetes mellitus currently generally relies on pharmacological therapies in the form of oral antidiabetic drugs and insulin, which work through various molecular mechanisms. Although conventional therapy is effective in controlling glycemia, its long-term use is often associated with side effects such as hypoglycemia, gastrointestinal disorders, and certain cardiometabolic risks (Davies et al., 2022). In addition, dependence on synthetic therapies can be an obstacle in developing countries due to limited access and the cost of treatment. Therefore, the search for safer and natural resource-based alternative antidiabetic agents is becoming an important focus in modern pharmaceutical research.

The use of medicinal plants as complementary therapy for diabetes mellitus is gaining attention due to their diverse secondary metabolite content and multitargeted mechanism of action. Various studies show that natural compounds such as flavonoids, alkaloids, and phenolics have hypoglycemic activity through inhibition of carbohydrate-digestion enzymes and increased insulin sensitivity (Dirir et al., 2022). In Indonesia, one of the plants empirically used to treat diabetes mellitus is the bengkal leaf (*Nauclea orientalis* L.). However, the use of this plant is still dominated by traditional experience and has not been fully supported by scientific evidence based on fractionation and standardized pharmacological tests.

The fractionation approach in pharmaceutical research aims to separate active compounds based on the degree of polarity in order to obtain fractions with more specific biological activity. The ethyl acetate fraction is known to be able to extract semipolar compounds such as flavonoids and phenols that have high potential as antidiabetics. These compounds work through the inhibition mechanisms of the enzymes alpha-glucosidase and alpha-amylase, as well as through antioxidant activity that protects pancreatic beta cells from oxidative stress (Pan et al., 2024). Therefore, the ethyl acetate fraction is an important focus in the development of antidiabetic phytopharmaceutical candidates.

Several previous studies have reported antidiabetic activity of various species within the genus *Nauclea*, but most studies still focus on coarse extracts or polar fractions without an in-depth evaluation of specific semipolar fractions (Gidado et al., 2021). Other studies have shown that the antidiabetic effectiveness of medicinal plants is strongly influenced by the dose and duration of administration, but data on the interaction of the two factors are still limited (Ngau et al., 2024). In addition, there have not been many studies that have

examined the ethyl acetate fraction of bengkal leaves using a quasi-experimental design with advanced statistical analysis. This gap suggests the need for more targeted research to determine the effectiveness and optimal dosage of the ethyl acetate fraction of the leaves of bengkal.

Based on the background and gaps of the study, this study aims to evaluate the antidiabetic activity of the ethyl acetate fraction of the leaf (*Nauclea orientalis* L.) in male aloxan-induced white mice. This study specifically aims to determine the dose of the ethyl acetate fraction that provides the optimal effect of reducing blood glucose levels. In addition, this study also evaluated the effect of observation time on the effectiveness of reducing blood glucose levels. Thus, this study is expected to provide a more comprehensive understanding of the pharmacological potential of the ethyl acetate fraction of bengkal leaves.

Theoretically, this study contributes to enriching pharmacognosy and pharmacological studies related to the use of semipolar fractions of medicinal plants as antidiabetic agents. Practically, the results of this research can be a scientific basis for the development of more effective and standardized leaf-based phytopharmaceuticals. The findings regarding optimal dosage also provide important implications for the formulation of safe and rational herbal preparations. Thus, this research contributes to bridging traditional knowledge and evidence-based scientific approaches in the management of diabetes mellitus (Kashtoh & Baek, 2022).

THEORETICAL REVIEW

Diabetes Mellitus as a Target of Modern Pharmaceutical Therapy

Diabetes mellitus is a chronic metabolic disease that is the main focus of pharmaceutical research due to its pathophysiological complexity and its systemic impact on various organs. Chronic hyperglycemia in diabetes mellitus is closely related to increased oxidative stress, inflammation, and pancreatic beta cell dysfunction that accelerates disease progression. Recent studies show that therapeutic approaches that target more than one molecular pathway are considered more effective in controlling diabetes mellitus than single therapy (DeFronzo et al., 2021). Therefore, the development of antidiabetic agents that have a multi-target mechanism is an important direction in global pharmaceutical research.

Limitations of Synthetic Antidiabetic Drugs

Although various classes of antidiabetic drugs have become available, their clinical effectiveness is often limited by side effects and long-term tolerability. Sulfonylurea and insulin drugs, for example, have a significant risk of hypoglycemia, while sodium-glucose cotransporter-2 inhibitors may increase the risk of urinary tract infections in some patients. Recent pharmacoepidemiological evaluations suggest that patient adherence to synthetic antidiabetic therapy remains a major challenge in clinical practice (Petersmann et al., 2020). This condition encourages the exploration of safer therapeutic alternatives, especially from natural sources.

The Role of Medicinal Plants in Antidiabetic Therapy

Medicinal plants have long been used as a source of bioactive compounds that have the potential to control blood glucose levels through a variety of mechanisms. Phytochemical compounds such as flavonoids, alkaloids, and phenolics are known to increase insulin sensitivity, inhibit intestinal glucose absorption, and reduce oxidative stress. Early experimental and clinical studies show that plant-based agents can provide synergistic effects through different metabolic pathways than synthetic drugs (Eddouks et al., 2021). This makes medicinal plants an important source in the development of antidiabetic phytopharmaceutical candidates.

Antidiabetic Activity of Flavonoid and Phenolic Compounds

Flavonoids and phenolic compounds are the most researched groups of secondary metabolites in the context of antidiabetics. This compound works by inhibiting the enzymes alpha-glucosidase and alpha-amylase, thereby slowing down the breakdown of complex carbohydrates into glucose. In addition, the antioxidant activity of flavonoids plays a role in protecting pancreatic beta cells from damage caused by free radicals (Rao et al., 2022). The combination of these mechanisms makes flavonoids a prime candidate in the development of diabetes therapies based on natural ingredients.

Fractionation as a Strategy for Optimizing Pharmacological Activities

Fractionation is an important approach in pharmaceutical research to improve the selectivity and biological potential of plant extracts. The ethyl acetate fraction is specifically known to be effective in extracting semipolar compounds that have high biological activity. Pharmacological research shows that the ethyl acetate fraction of various medicinal plants often exhibits stronger antidiabetic activity than crude extracts (Zhang et al., 2023). This approach allows the identification of the most active fractions as the basis for the development of more standardized phytopharmaceutical preparations.

Potential of Genus Nauclea as an Antidiabetic Agent

Genus *Nauclea.* It has been reported to have a wide range of pharmacological activities, including antidiabetic, anti-inflammatory, and antioxidant. Phytochemical studies show that plants of this genus are rich in indole alkaloids, flavonoids, and phenolic compounds that contribute to hypoglycemic activity. In vivo studies on the species *Nauclea* others showed an improvement in blood glucose levels and pancreatic tissue protection in diabetic model animals (Abubakar et al., 2022). These findings strengthen the scientific basis for the selection of bengkal leaves (*Nauclea orientalis* L.) as an object of antidiabetic research.

Research Gaps and Relevance of Current Studies

Although various studies have proven the antidiabetic potential of plants of the genus *Nauclea*, most studies still focus on coarse extracts or polar fractions without an in-depth evaluation of ethyl acetate fractions specifically. In addition, data on optimal dosage and the effect of duration of administration on the

effectiveness of lowering blood glucose are still limited. Recent studies emphasize the importance of dose-response approaches and timing analysis to ensure the effectiveness and safety of phytopharmaceutical candidates (Silva et al., 2024). Therefore, research on the antidiabetic activity of the ethyl acetate fraction of the leaves in male white mice is relevant and contributes importantly to the development of diabetes therapies based on natural ingredients.

METHODOLOGY

Research Type and Design

This research is an experimental quantitative research with a **quasi-experimental** design using the design **static-group comparison**. This design was chosen because it allows evaluation of the effects of pharmacological treatments through comparisons between control groups and treatment groups without full randomization, while still maintaining adequate internal validity for in vivo studies (Harris et al., 2020). This approach is commonly used in experimental pharmacological research to assess the biological activity of a compound or fraction of a medicinal plant against specific physiological parameters. The research will be carried out for approximately five months in 2025 at the Laboratory of Phytochemistry and Pharmacology, Department of Pharmacy, Health Polytechnic of the Ministry of Health, Jambi.

Research Ethics

All research procedures involving test animals have received ethical approval from the Health Research Ethics Committee of the Jambi Ministry of Health Polytechnic with a certificate number **LB.02.06/2/044/2025**. The implementation of the research follows the principles of welfare of test animals, including the principle of **Replacement, Reduction, and Refinement**, in order to minimize animal suffering during the study (Percie du Sert et al., 2020).

Population and Sampling Techniques

The population of this study was male white mice (*Sparrow muscle*) who are healthy, two to three months old, with a body weight between 20 and 30 grams. The sampling techniques used are **non-probability sampling and purposive sampling**, since the selection of test animals is based on certain biological and physiological criteria relevant to the purpose of the study. The number of test animals was determined using Federer's formula for experimental research, so that five mice were obtained in each treatment group. With six treatment groups, the total number of test animals used was 30 mice; this number was considered adequate for parametric statistical analysis (Charan & Kantharia, 2021).

Research Materials and Tools

The main ingredients used in this study include bengkal leaves (*Nauclea orientalis* L.), 70% ethanol, ethyl acetate, aqueous, aloxan monohydrate, glibenclamide, and tragacantha as suspension agents. The tools used include a Simplicia blender, a separation funnel, a rotary evaporator, an analytical scale,

an injection syringe, and a blood glucose level measuring device. All chemicals used have a pro-analysis degree to ensure the validity of the research results (OECD, 2022).

Extraction and Fractionation Procedure

Fresh bengkal leaves are sorted, washed clean, then cut into small pieces and dried by aerating until dry simplicia is obtained. Simplisia is then ground into a fine powder and macerated using 70% ethanol in a ratio of 1:10 for three days with periodic stirring. The obtained filtrate is filtered and evaporated using a rotary evaporator until a viscous extract is obtained. The ethanol extract was further fractionated using the liquid–liquid partition method with ethyl acetate solvent and water in a 1:1 ratio. The ethyl acetate fraction is collected and vaporized until a viscous fraction is obtained, which is used as a test material (Azwanida, 2021).

Animal Preparation Test and Treatment

The test animals were acclimatized for seven days with standard feeding and drinking water ad libitum. Diabetes induction was carried out by intraperitoneal administration of monohydrate alloxan at a dose of 175 mg/kgBW, except in the negative control group. After 24 hours, blood glucose levels are measured to confirm the occurrence of hyperglycemia. The test animals were then divided into six groups, namely negative control (0.5% tragacantha), positive control (glybenclamide 0.65 mg/kgBW), and four treatment groups of ethyl acetate fraction of bengkal leaves with doses of 150, 300, 450, and 600 mg/kgBW. Treatment was administered orally, and blood glucose levels were measured on the 1st, 3rd, and 7th days after treatment (Ayepola et al., 2022).

Data Collection and Analysis Techniques

The data collected were in the form of blood glucose levels of male white mice before and after treatment. The data is presented in the form of mean and standard deviation, then statistically analyzed using the test **Analysis of Variance (ANOVA)** one-way to find out the differences between treatment groups. If there are significant differences, the analysis is followed by the Duncan test to meaningfully determine the different groups. All statistical analysis was performed using standardized statistical software, with a confidence level of 95% and a significance value set at $p < 0.05$ (Field, 2020).

RESEARCH RESULTS

Yield of Extraction and Fractionation of Bengkal Leaves

The initial stage of this study focuses on the extraction and fractionation process of bengkal leaves as a basis for obtaining chemically and biologically representative test fractions. The maceration process of simplification of simplicia leaves using ethanol solvent produced a thick extract with a fairly high yield, showing that the extraction method used was able to extract bioactive compounds optimally from the plant matrix.

The fractionation process is carried out to separate compounds based on their polarity level, so that a more specific fraction is obtained and has the potential to have more directed pharmacological activity.

Table 1. Yield Determination Result Data

No.	Fraction Name	Extract Weight (g)	Fraction Yield (%)
1	Ethyl Acetate Fraction	0.34	3.40
2	Water Fraction	1.88	18.80

Based on **Table 1**, the water fraction shows the highest yield compared to the ethyl acetate fraction. These findings indicate that most of the chemical components of the Bengkal leaves are polar. However, the ethyl acetate fraction remains the main focus of research because the semipolar fraction generally contains compounds with stronger biological activity, although the amounts are relatively smaller. The low yield of the ethyl acetate fraction does not reflect the low biological potential, but rather indicates the selectivity of this fraction in attracting certain active compounds relevant to antidiabetic activity.

Phytochemical Characteristics of Bengkal Leaf Fractions

Identification of secondary metabolite content was performed to provide a chemical basis for the pharmacological activity observed in in vivo assays. The results of the phytochemical test showed the difference in the composition of the metabolites between the extract and each fraction.

Table 2. Phytochemical Screening Results of Bengkal Leaf Extract and Fractions

No.	Sample	Alkaloid	Flavonoid	Triterpenoid/Steroid	Tannin	Saponin
1	Ethanol Extract	+	+	−	+	+
2	n-Hexane Fraction	−	−	+	−	−
3	Ethyl Acetate Fraction	+	+	−	+	−
4	Water Fraction	+	+	−	+	+

Results in **Table 2** show that the ethyl acetate fraction contains alkaloids, flavonoids, and tannins, while saponins are not detected. This composition reflects the characteristics of the semipolar fraction that can extract bioactive compounds that play a role in the control of blood glucose levels. The presence of flavonoids and alkaloids in the ethyl acetate fraction provides a strong scientific basis that these fractions have the potential to modulate glucose metabolism through multiple mechanisms, making them worthy of further evaluation in antidiabetic assays.

Blood Glucose Reduction Profile after Alloxan Induction and Treatment

Induction of aloxan successfully created a hyperglycemia condition in mice, demonstrated by an increase in blood glucose levels above 200 mg/dL in all test groups after induction. This condition is the starting point to evaluate the effectiveness of the ethyl acetate fraction of bengkal leaves in lowering blood glucose levels.

Table 3. Percentage Reduction of Blood Glucose Levels in Test Animals

No.	Treatment Group	Fasting (mg/dL)	Diabetic (mg/dL)	Day 1 (mg/dL)	SD	%	Day 3 (mg/dL)	SD	%	Day 7 (mg/dL)	SD	%
1	Negative Control	126.2	210.5	193.4	6.878	8.12	195.0	6.205	7.36	195.8	6.301	6.98
2	Positive Control	110.5	219.7	131.2	7.294	40.28	113.4	8.142	48.38	100.4	4.393	54.30
3	Ethyl Acetate Fraction 150 mg/kgBW	111.5	208.5	175.2	13.293	15.97	147.6	19.139	29.20	109.4	11.371	47.52
4	Ethyl Acetate Fraction 300 mg/kgBW	121.5	213.5	182.0	6.325	14.75	174.2	6.301	18.40	167.2	6.380	21.68
5	Ethyl Acetate Fraction 450 mg/kgBW	107.3	204.5	133.6	7.635	34.66	115.8	8.319	43.37	103.2	4.658	49.53
6	Ethyl Acetate Fraction 600 mg/kgBW	113.5	209.5	192.6	5.941	8.07	186.8	6.723	10.83	181.8	7.328	13.22

Based on **Table 3**, the entire treatment group showed a decrease in blood glucose levels over the time of observation. However, the magnitude of the decrease is highly dependent on the dose of the ethyl acetate fraction administered. Dosage **450 mg/kgBW** shows the most consistent and significant decrease in blood glucose levels on the 1st, 3rd, and 3rd day until it reaches **49.53% on day 7**, close to the effectiveness of positive controls. Instead, the dosage **600 mg/kgBW** Instead, it showed a relatively small decline and was close

to the negative control group. These findings indicate that the ethyl acetate fraction of the leaves has an optimal therapeutic dose range, and increasing doses beyond the optimal point does not increase effectiveness, or even tends to decrease it.

Normality and Homogeneity of Blood Glucose Data

Before inferential analysis is performed, the data is tested to ensure that parametric statistical assumptions are met.

Table 4. Normality Test Results

Test	Statistic	df	Say.
Kolmogorov–Smirnov	0.091	90	0.065
Shapiro–Wilk	0.975	90	0.085

Results in **Table 4** indicate that the data is normally distributed because the significance value is greater than 0.05.

Table 5. Homogeneity Test Results

Test Basis	Levene Statistic	df1	df2	Say.
Based on Mean	2.821	17	72	0.101

The significance value in **Table 5** shows that the variance of data between groups is homogeneous. The fulfillment of the assumptions of normality and homogeneity ensures that the results of the ANOVA analysis obtained are valid and can be interpreted scientifically.

Effect of Dose and Observation Time on Blood Glucose Levels

Two-way ANOVA analysis was performed to evaluate the effect of ethyl acetate fraction dose, observation time, and the interaction of the two on blood glucose levels.

Table 6. Two-Way ANOVA Results

Source	df	F	Say.
Treatment Group	5	246.065	0.000
Observation Day	2	63.116	0.000
Treatment × Day	10	9.530	0.000

Results in **Table 6** show that fractional doses, observation time, and interactions all have a very significant influence on blood glucose levels. The effect of lowering blood glucose is not only influenced by the size of the dose, but also by the duration of administration, which confirms the importance of temporal evaluation in studies of antidiabetics based on natural ingredients.

Determination of Optimal Dose Based on Duncan Post Hoc Analysis

To determine the most effective dose, Duncan's further test was carried out.

Table 7. Duncan Post Hoc Test for Blood Glucose Levels

Treatment Group	Mean Blood Glucose (mg/dL)
Positive Control	115.00
Ethyl Acetate Fraction 450 mg/kgBW	117.53
Ethyl Acetate Fraction 150 mg/kgBW	144.07
Ethyl Acetate Fraction 300 mg/kgBW	174.47
Ethyl Acetate Fraction 600 mg/kgBW	187.07
Negative Control	194.73

Results in **Table 7** indicate that the dose **450 mg/kgBW** is in the same group as the positive controls, which signifies equal effectiveness in lowering blood glucose levels. Overall, this study proves that the ethyl acetate fraction of bengkal leaves has a pronounced and consistent antidiabetic activity, with an **optimal dose of 450 mg/kgBW** as the most effective dose, while higher doses show decreased effectiveness.

DISCUSSION

Induction of aloxan in male white mice in this study was shown to be successful in creating hyperglycemia, which was demonstrated by an increase in blood glucose levels to exceed 200 mg/dL in all test groups. According to recent experimental reports, aloxan acts as a diabetogenic agent by means of triggering the formation of excessive reactive oxygen species in the β pancreas, thereby causing impaired insulin secretion and dysfunction of glucose metabolism (Radenković et al., 2021). This diabetes model is widely used in pharmacological research to evaluate the antidiabetic potential of natural compounds, as they are able to represent oxidative stress conditions in diabetes mellitus. The successful formation of a hyperglycemia model became a strong methodological foundation for assessing the pharmacological response of the ethyl acetate fraction of Bengkal leaves. Thus, the change in blood glucose levels in the treatment phase can be ascertained to be directly related to the biological activity of the test compound, not to the result of spontaneous physiological adaptations of test animals.

Administration of the ethyl acetate fraction of bengkal leaves showed a pattern of decreased blood glucose levels that differed between doses and observation times. Gradually, the decrease in blood glucose became more pronounced from day 1 to day 7, which indicated the cumulative effect of bioactive compounds in the fraction. This phenomenon is in line with the concept of the pharmacodynamics of natural materials, where phytochemical compounds generally take a certain amount of time to achieve optimal biological effects through multiple mechanisms. Some recent research states that

phytochemicals work not only through a single target, but rather through simultaneous modulation of oxidative stress, insulin sensitivity, and peripheral glucose metabolism (Zhang et al., 2023). Therefore, the gradual response observed in this study reflects the typical characteristics of plant-based antidiabetic agents.

Of all the doses tested, the ethyl acetate fraction of bengkal leaves at a dose of 450 mg/kgBW showed the most optimal effect of reducing blood glucose levels, with a percentage reduction of 49.53% on day 7. These findings suggest a clear therapeutic dose range, where maximum effectiveness is achieved at a given dose before experiencing a decreased response. Theoretically, the optimal dose reflects the balance between the availability of active compounds and the body's biological capacity to respond to pharmacological stimulation. When the dose is at its optimal point, the active compound is able to work effectively without causing receptor saturation or disruption of homeostasis. This concept is in line with the finding that the antidiabetic effectiveness of natural ingredients does not necessarily increase linearly as doses increase (Al-Ishaq et al., 2022).

In contrast, an increase in dose to 600 mg/kgBW actually showed a decrease in effectiveness close to the negative control groups. This nonlinear response can be explained through the concept of hormesis, which is a biological phenomenon in which low to moderate doses provide therapeutic effects, while high doses decrease the response or are even counterproductive. According to a recent report, high doses of phytochemical compounds have the potential to trigger antagonistic interactions between components or increase metabolic load on target organs (Calabrese & Mattson, 2021). This condition confirms that the ethyl acetate fraction of bengkal leaves contains a mixture of compounds with biological effects that are sensitive to changes in concentration. Thus, these findings reinforce the importance of determining the optimal dosage in the development of phytopharmaceutical candidates.

The results of phytochemical tests showed that the ethyl acetate fraction of bengkal leaves contains alkaloids, flavonoids, and tannins, which are widely known to have antidiabetic activity. Flavonoids act as powerful antioxidants that can suppress oxidative stress and increase insulin sensitivity, while alkaloids are reported to affect insulin secretion as well as increase glucose uptake by peripheral tissues. In addition, tannins are known to inhibit the activity of carbohydrate-digestion enzymes such as α-glucosidase, thereby reducing glucose absorption in the gastrointestinal tract. The combination of these mechanisms explains why the ethyl acetate fraction shows significant biological activity despite its relatively low yield. These findings confirm that the quality and specificity of the active compounds determine the therapeutic potential more than the quantity of the extract alone (Saeedi et al., 2021).

The validity of the results of this study is strengthened by the fulfillment of statistical assumptions, namely the normality and homogeneity of the data, so that the two-way ANOVA analysis can be carried out validly. The results of the analysis showed that the dosage factor, observation time, and interaction of the two had a significant effect on the blood glucose level of mice. This indicates that the antidiabetic effects of the ethyl acetate fraction are not static, but dynamic and

depend on the duration of administration and concentration of the compound. Significant interactions between treatment groups and observation time confirm that the biological response to natural materials evolves progressively. These findings are consistent with recent research that emphasizes the importance of the time dimension in the pharmacological evaluation of natural materials (Liu et al., 2024).

Although it shows promising results, this study has some limitations that need to be critically observed. The study has not evaluated supporting parameters such as insulin levels, lipid profiles, and the histopathological picture of the pancreas that can strengthen the interpretation of the mechanism of action of the ethyl acetate fraction of bengkal leaves. In addition, the use of short-term animal models limits understanding of the chronic effects and safety of long-term use.

CONCLUSION AND RECOMMENDATION

Based on the results of the study and discussion, it can be concluded that the ethyl acetate fraction of bengkal leaves (Nauclea orientalis L.) has significant antidiabetic activity in male aloxan-induced white mice. This fraction is able to significantly lower blood glucose levels and show a response that is influenced by the dose and time of administration. The dose of 450 mg/kgBW is the most optimal because it results in the highest reduction in blood glucose levels and is comparable to the positive control of glibenclamide. These findings suggest a clear therapeutic dose range, where increasing doses above the optimal point do not increase effectiveness. Overall, the results of this study support the potential of bengkal leaves as a prospective source of natural materials to be further developed as a candidate for phytopharmaceuticals in the management of diabetes mellitus.

FURTHER STUDY

Therefore, further research is recommended to examine the molecular mechanism, subchronic toxicity assays, as well as the potential formulation of this fraction as a phytopharmaceutical. Overall, the findings of this study make a meaningful scientific contribution to the development of effective and rational local natural ingredients-based antidiabetic agents (Ogunyemi et al., 2022).

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