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ADVANCES IN SOCIAL HUMANITIES RESEARCH

Effectiveness Test of Bidara Leaf Ethanol Extract on Lipid Profile Changes in Streptozotocin-Induced Type 2 Diabetes Mellitus Rats

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Abstract

This research concluded that the declining construction performance and schedule delays in the Kucing Liar Fan 7 project, reflected by an average Project Performance Factor of 0.82 and a cost overrun of approximately 10% beyond the available contingency, resulted from the interaction of multiple factors, including design readiness, change control, material planning, communication and coordination, supervisory competency, and constrained underground working conditions. These issues were not caused by a single factor, as Management, Method, Material, People, and Environment collectively accounted for 84.93% of the prioritized relative importance among the six investigated factors. The identified lessons were documented in a Lesson Learned Register and translated into a proposed Controlling Project Management Office (PMO) implementation framework through a four-phase roadmap consisting of organizational assessment and preparation, PMO development and pilot implementation, organizational integration, and continuous improvement. The proposed PMO was designed to strengthen governance, standardization, coordination, and knowledge management without replacing the existing balanced-matrix authority structure of Project Managers and functional departments.It is recommended that PT Freeport Indonesia's Central Services Division prioritize design readiness and constructability reviews before construction authorization, strengthen project planning beyond analogous estimation through detailed work breakdown structures and integrated risk assessments, implement earned-value-based monitoring with standardized dashboards, and formally establish the proposed PMO to improve governance, communication, and knowledge management across future underground ventilation construction projects. Future research is recommended to evaluate PMO performance following organizational implementation, compare PMO maturity levels across other underground mining projects, and examine the integration of digital project management technologies, such as Building Information Modeling (BIM) and predictive analytics, into project governance.

INTRODUCTION

Diabetes mellitus (DM) is a metabolic disorder characterized by elevated blood glucose levels (hyperglycemia) resulting from impaired insulin secretion, insulin action, or both, particularly involving pancreatic β-cells. In individuals with hyperglycemia and insulin resistance, the translocation of GLUT4 from intracellular storage to the plasma membrane is impaired (Plasma, 2018), thereby disrupting glucose uptake into cells (Chen, 2018; Hasan, 2023; Luo, 2021). Diabetes mellitus is classified into several types, including type 1 diabetes,

which results from autoimmune or idiopathic destruction of pancreatic β-cells; type 2 diabetes, which is associated with insulin resistance and impaired insulin secretion; gestational diabetes, which develops during pregnancy due to increased insulin resistance; and other specific types caused by genetic disorders, endocrinopathies, or drug-related factors (Organization, 2016) .

One of the major complications of type 2 diabetes mellitus is dyslipidemia, characterized by abnormal lipid profiles, including increased triglyceride, total cholesterol, and low-density lipoprotein (LDL) levels, accompanied by decreased high-density lipoprotein (HDL) levels (Djasang, 2017). Dyslipidemia in type 2 diabetes mellitus contributes significantly to the development of atherosclerosis and coronary heart disease, which are among the leading causes of mortality in individuals with diabetes (Salem et al., 2018).

Streptozotocin (STZ) is a diabetogenic agent widely used to induce diabetes in experimental animal models through selective pancreatic β-cell damage. This model is relevant in preclinical research for evaluating the effects of pharmacological interventions on biochemical parameters, including lipid profiles (Martin-Sole, 2016).

The Ziziphus mauritiana plant (bidara leaves) contains bioactive compounds, including flavonoids, saponins, and tannins, which have demonstrated potential antioxidant, antihyperglycemic, and antidyslipidemic activities (Rais et al., 2018) . Therefore, this study aimed to evaluate the effectiveness of ethanol extract from bidara leaves on lipid profile changes in STZ-induced male Wistar rats as a model of type 2 diabetes mellitus.

The urgency of this research was supported by the increasing prevalence of type 2 diabetes mellitus and dyslipidemia globally and in Indonesia, along with the limitations and potential adverse effects associated with conventional pharmacological therapies (Perez, 2017) . Many communities in developing countries use traditional herbal medicine as complementary or alternative treatments; however, robust preclinical evidence supporting the therapeutic potential of many medicinal plants remains limited. This study provided novelty by systematically evaluating three doses of ethanol extract from Ziziphus mauritiana leaves (100 mg/mL, 200 mg/mL, and 300 mg/mL) over 42 days in an STZ-induced type 2 diabetes mellitus rat model, with comprehensive assessments of glycemic and lipid parameters (Organization, 2016) . The purpose of this study was to determine the effectiveness of bidara leaf ethanol extract in reducing blood glucose levels and improving lipid profiles, as well as to identify the most effective dose for potential therapeutic development (Khan, 2019) .

The objective of this research was to evaluate the antidiabetic and antidyslipidemic effects of ethanol extract from bidara leaves (Ziziphus mauritiana) in male Wistar rats induced by streptozotocin, specifically by measuring changes in blood glucose levels and lipid profile parameters, including triglycerides, total cholesterol, HDL, and LDL, across different dosage groups. The contribution of this research was twofold. Scientifically, it provided preclinical evidence regarding the dose-dependent effects of Ziziphus mauritiana leaf extract, supporting its potential as a source of bioactive compounds for antidiabetic and antidyslipidemic drug development. Practically, it provided a basis for developing standardized herbal products that may complement conventional type 2 diabetes mellitus therapy, particularly in resource-limited settings. The findings contribute empirical data for future clinical studies, support the rational utilization of medicinal plants, and contribute to efforts to identify affordable, accessible, and effective strategies for managing type 2 diabetes mellitus and its complications (Committee, 2025; Furman, 2021; Goyal, 2022) .

METHOD

Ethical Clearance and Extract Preparation

This research was conducted at the Ellio Medan Laboratory from February to May 2026, after obtaining ethical approval from the Health Research Ethics Commission (KEPK) of the University of Prima Indonesia (No. 100/KEPK/UNPRI/X/2026). The Ellio Science Pharmacy Research Laboratory was used for ethanol extraction of bidara leaves, in vitro testing through enzyme inhibition assays (α-amylase and α-glucosidase inhibition), and analysis of blood glucose levels and lipid profiles.

The Elio Science Center Experimental Animal Laboratory was used for the maintenance of experimental animals and the induction of type 2 diabetes mellitus using streptozotocin (STZ) in the rat model.

Experimental Animals

The population consisted of male Wistar rats (Rattus novergicus sp) (aged 6-12 weeks, weighing 150-200 g). All rats were kept in standard cages and were routinely given drinking water and pellet feed.

Experimental Procedures

The experimental animals were divided into 5 groups with 5 rats each. A type 2 diabetes rat model was prepared by intraperitoneal induction of 40 mg/kgBW of streptozotocin (STZ) (Ramalingam et al., 2020). Rats were declared to have DM if their blood sugar levels were more than or equal to 200 mg/dL. Bidara leaf extract was dissolved in. to obtain several concentrations and administered via gastric tube for 42 days. Blood sugar levels were measured periodically before and after treatment on days 7, 14, and 28. In addition, the rats' body weight was also measured daily. The test animal groups were:

Positive Control: DM rats (Metformin Administration)
Negative control: healthy mice (not given treatment)
Treatment 1: DM rats given 100 mg/ml extract
Treatment 2: DM rats given 200 mg/ml extract
Treatment 3: DM rats given 300 mg/ml extract
Treatment 4: DM rats given 400 mg/ml extract.

Examination of blood sugar levels in all treatment groups

Table 1. Analysis of Blood Sugar Level Data Distribution in All Treatment Groups

Parameter	Treatment Group	Data Distribution
Blood Sugar Levels Before Induction	Negative Control	Normal
	Positive Control	Normal
	Bidara Leaf Extract-1 100mg	Normal
	Bidara Leaf Extract-2 200mg	Normal
	Bidara Leaf Extract-3 300mg	Normal
	Bidara Leaf Extract-4 400mg	Normal
Blood Sugar Levels After Induction	Negative Control	Normal
	Positive Control	Normal
	Bidara Leaf Extract-1 100mg	Normal
	Bidara Leaf Extract-2 200mg	Normal
	Leaf Extract Bidara-3 300mg	Abnormal
	Bidara Leaf Extract-4 400mg	Normal
Blood Sugar Levels on Day 7	Negative Control	Normal
	Positive Control	Normal
	Bidara Leaf Extract-1 100mg	Normal
	Bidara Leaf Extract-2 200mg	Normal
	Bidara Leaf Extract-3 300mg	Normal
	Bidara Leaf Extract-4 400mg	Normal
Blood Sugar Levels on Day 14	Negative Control	Normal
	Positive Control	Normal
	Bidara Leaf Extract-1 100mg	Normal
	Bidara Leaf Extract-2 200mg	Normal
	Bidara Leaf Extract-3 300mg	Normal
	Bidara Leaf Extract-4 400mg	Normal
Blood Sugar Levels Day 28	Negative Control	Normal
	Positive Control	Normal
	Bidara Leaf Extract-1 100mg	Normal
	Bidara Leaf Extract-2 200mg	Normal
	Bidara Leaf Extract-3 300mg	Normal
	Bidara Leaf Extract-4 400mg	Normal

Table 1. shows that all blood sugar data tended to be normally distributed, except for post-induction blood sugar levels, which showed an abnormal distribution . Therefore, all blood sugar data were analyzed using a parametric statistical test in the form of a one-way ANOVA.

Simplasia Preparation

The samples were first determined in the Ellio Science Laboratory. Then, the bidara leaf samples were cleaned of any adhering dirt with running water. The samples were chopped and dried in the sun until dry. The samples were then powdered and stored (Mohamadou et al., 2021).

Making Bidara Leaf Extract

A 4.54 kg sample was macerated with 45.4 liters of 70% ethanol solvent at a ratio of 1:10 in a dark container for 4 days with occasional stirring. Then, the filtrate was filtered. The filtrate was concentrated using a rotary evaporator and its weight determined. The yield was calculated using the following formula (Mohamadou et al., 2021).

$$\text{Yield} = \frac{\text{Concentrated Extract Weight (Gr)}}{\text{Sample Material Weight (Gr)}} \text{ X } 100\%.$$

Phytochemical Screening (Rahmatullah et al., 2020)

The thick extract was tested using different reagents to determine its content.

1. **Alkaloid Test**

   A 2 mg extract was added to 5 ml of distilled water. 5 ml of 2% HCl and 2-3 drops of Dragendorff's reagent were added to the solution. The results were observed based on the changes that occurred (Patel et al., 2022).

2. **Flavonoid Test**

   A 2 mg sample was taken and 5 ml of 70% ethanol was added, then reacted with 0.05 mg of Mg powder and 1 ml of concentrated HCl. The presence of a red, orange, or yellow color in the solution indicates a positive result (Kumar et al., 2023).

3. **Saponin Test**

   The sample was mixed with 10 ml of distilled water. After shaking for 10 seconds, the presence of saponins was observed, indicated by foam that persisted for more than 10 minutes (Singh et al., 2020).

4. **Tannin Test**

   A mixture of 2 mg of sample and 5 ml of distilled water in a test tube is dripped with 1% FeCl3. A dark blue or blackish green color indicates a positive result (Sharma & Gupta, 2021).

RESULTS AND DISCUSSION

Table 2. Initial Body Weight Measurement of Mice in All Treatment Groups

Treatment Group	Body Weight (grams)			P value
	Median	Min	Max	
Negative Control	153	155	162	**< 0.001**
Control Positive	163	164	184	
Bidara Leaf Extract-1 100 mg	170	178	181	
Bidara Leaf Extract-2 200 mg	189	195	197	
Bidara Leaf Extract-3 300 mg	156	168	177	
Bidara Leaf Extract-4 400 mg	152	156	160	

The results of the data above show that there is a significant difference in the initial body weight of the mice used in this study, this can be seen from the P value <0.001. The highest

initial body weight tendency of mice was found in the 200mg Bidara Leaf Extract group, namely 189 grams and the lowest was found in the 400mg Bidara Leaf Extract group, namely 152 grams.

Table 3. Comparison of Initial Blood Sugar Levels of Mice in All Treatment Groups

Treatment Group	EARLY RAT KGD		P value
	Mean	Elementary School	
Negative Control	142.40	26,969	**< 0.001**
Positive Control	152.60	90,024	
Jujube Leaf Extract 100mg	131.20	17,254	
Bidara Leaf Extract 200mg	139.20	33,937	
Bidara Leaf Extract 300mg	125.00	21,095	
Jujube Leaf Extract 400mg	104.40	11,437	

The treatments had a normal data distribution. Therefore, the data analysis was then continued with parametric statistical analysis using the One-Way ANOVA test. The results of the One-Way ANOVA analysis can be seen in Table 4.

Table 4. Comparison of Blood Sugar Levels in Rats After STZ Induction

Treatment Group	Blood Sugar Level (mg/dl)		
	Mean	STD	P value
Negative Control	357.60	29,846	**< 0.001**
Positive Control	323.00	107,140	
Jujube Leaf Extract 100mg	261.40	39,463	
Bidara Leaf Extract 200mg	251.40	67,129	
Bidara Leaf Extract 300mg	339.60	55,202	
Bidara Leaf Extract 400mg	320.00	82,916	

The treatment of KGD mice after STZ induction showed a normal data distribution. Therefore, the data analysis was then continued with parametric statistical analysis using the One-Way ANOVA test. The results of the One-Way ANOVA analysis can be seen in Table 5.

Table 5. Comparison of Blood Sugar Levels in All Treatment Groups

Treatment Group	Blood Sugar Level (mg/dl)				
	Before Induction	After Induction	Day 7th	Day 14th	Day 28th
Negative control	26,969± 142.40	346 (252-306)	320.54± 175.89	435.66± 117.80	267.40± 138.74
Control Positive	175.89± 108.91	500 (405-500)	394.66± 186.88	119.03± 189.67	125.69 ±129.04
Bidara Leaf Extract-1 100mg	131.20± 17,254	261 (265-400)	355-50± 130.64	310.40± 212.40	360.65± 256-60
Bidara Leaf Extract-2 200mg	139.20± 33,937	320 (270-375)	365.34± 97.06	334.75± 168.05	209.62± 128.65
Bidara Leaf Extract-3 300mg	125.00± 21,095	402 (205-295)	345.19± 98.81	408.14± 271.06	256.24± 133.76

Bidara Leaf Extract-4 400mg	104.40± 11,437	415 (219-380)	389.60± 90.20	422.95± 217.05	244.10± 122.17
P value	**< 0.001**	**0.003**	**< 0.001**	**< 0.001**	**< 0.001**

Table 5 above shows a comparison of blood sugar levels in mice during treatment with bidara leaf extract. The results of this study indicate that before treatment, the mice's blood sugar levels showed a significant difference, as reflected by a P value <0.001 (P value: 0.001). Before treatment, the average blood sugar levels in mice tended to be normal, ranging from 139.20-131.20 mg/dl.

After being given induction in the form of Streptozotocin, the blood sugar levels of mice increased in all treatment groups (P value: 0.003), with a tendency for blood sugar levels in all treatment groups to increase in the range of 346-402 mg/dl. The blood sugar levels of mice tended to remain high even after 7 days of treatment.

This is reflected in the average blood sugar levels of mice which were still > 300 mg / dl (P value: 0.001). Interestingly, after 14 and 28 days of treatment, blood sugar levels began to decrease, but the decrease in blood sugar levels in the group receiving bidara leaf extract was still > 200 mg / dl and only the positive control group experienced a decrease < 200 mg / dl. Nevertheless, changes in blood sugar levels in mice receiving bidara leaf extract showed a significant decrease compared to the negative control group.

Table 6. Comparison of Lipid Profiles in Rats After Administration of Jujube Leaf Extract

Group Treatment	**Triglyceride Levels**		**Total Cholesterol**		**HDL**		**LDL**	
	Median	Range	Median	Range	Mean	Elementary School	Median	Range
Negative Control	86.00	34.00	120.00	12.00	60.00	8.33	53.00	27.00
Positive Control	76.00	32.00	135.00	15.00	66.00	2.57	43.00	53.00
Jujube Leaf Extract 100mg	1300	18.00	178.00	33.00	45.00	7.45	70.00	26.00
Bidara Leaf Extract 200mg	83.00	44.00	165.00	35.00	54.00	18.51	61.00	36.00
Bidara Leaf Extract 300mg	82.00	57.00	133.00	14.00	68.00	16.00	64.00	41.00
Jujube Leaf Extract 400mg	92.00	59.00	200.00	19.00	75.00	18.00	75.00	43.00
P value	**0.026**		**0.012**		**< 0.01**		**< 0.01**	

The comparative table data above shows that there are significant differences in Triglyceride, Total Cholesterol, HDL, and LDL levels in each treatment group (Hidayati et al., 2018). This can be seen from the P value for each lipid profile parameter which is <0.01. Meanwhile, the effect of administering Bidara Leaf Extract was significantly able to improve the lipid profile of respondents in this study. It can be seen from the results of further test analysis where each treatment group given Bidara Leaf Extract showed a significant difference compared to the control group. However, no significant differences were found in the Negative Control and normal groups. Except in the Bidara Leaf Extract group at a dose of 100 mg/kg BW, there was a significant difference with the Positive Control, Negative Control,

and control groups in the HDL level parameter. Therefore, it can be concluded that administering Bidara Leaf Extract at a dose of 100 mg/Kg BW is able to improve the lipid profile, except for improving HDL levels, a larger dose of 200 mg/kg BW is needed to obtain a significant anti-hyperlipidemic effect (Kurniawaty & Yanita, 2016) .

This study aims to evaluate the effectiveness of ethanol extract of bidara leaves (Ziziphus mauritiana) on changes in blood glucose levels and lipid profiles in male white Wistar rats induced by streptozotozin (STZ) as a model of Type 2 Diabetes Mellitus. STZ induction is used because it has the ability to damage pancreatic β cells through the GLUT-2 transporter, causing impaired insulin secretion, hyperglycemia, and dyslipidemia that resembles diabetes in humans. This animal model is widely used to assess the effectiveness of various antidiabetic and antidyslipidemic agents. (American Diabetes Association, 2025; Goldberg IJ, 2023).

Based on the research results, the initial blood sugar levels of all groups were still within the normal range, although there were statistically significant differences between treatment groups ($p<0.001$). After STZ induction, all groups experienced a significant increase in blood glucose levels, indicating that STZ successfully induced diabetes in the experimental animals. This increase in blood glucose levels occurs due to damage to pancreatic β cells, which causes reduced insulin production, disrupting glucose utilization by body tissues and increasing blood glucose levels. (Furman BL, 2021; Goyal SN et al., 2022).

The results of the data distribution analysis showed that almost all blood glucose levels had a normal distribution, so parametric analysis using One-Way ANOVA could be used to evaluate differences between treatment groups. The normal distribution of the data indicates that the research data meets the required statistical assumptions, so the analysis results obtained have good validity in explaining the effect of ethanol extract of bidara leaves on the observed parameters. (Abdel-Zaher AO et al., 2021; Alhakmani F et al., 2022).

7 days of treatment, blood glucose levels in most groups remained hyperglycemic. However, on days 14 and 28, a trend toward decreased blood glucose levels was observed in the group receiving bidara leaf extract. This decrease indicates that bidara leaf ethanol extract has antihyperglycemic activity that can improve glucose metabolism disorders in diabetic rats, although its effectiveness has not yet matched that of the positive control group receiving standard therapy. (Vergès B, 2020; Chukwuma CI et al., 2022).

The blood glucose-lowering effect demonstrated by bidara leaf extract is thought to be related to the flavonoids, saponins, tannins, and alkaloids contained in bidara leaves. Flavonoids are known to increase insulin sensitivity, reduce oxidative stress, and protect pancreatic β-cells from further damage. Furthermore, the antioxidant compounds in bidara leaves can reduce the formation of free radicals, which play a role in the progression of insulin resistance and diabetes complications (Luo J et al., 2021; Hasan MM et al., 2023).

In lipid profile parameters, this study showed significant differences in triglyceride, total cholesterol, HDL, and LDL levels between treatment groups. The p-value for triglycerides was 0.026, total cholesterol was 0.012, while HDL and LDL showed p-values less than 0.01. These results indicate that administration of bidara leaf ethanol extract significantly improved lipid profiles in type 2 diabetes mellitus rats (Mach F et al., 2020; Ference BA et al., 2022).

In the group receiving bidara leaf extract, there was a trend towards lower triglyceride levels compared to the diabetic group without therapy. This suggests that bidara leaf extract

can improve impaired lipid metabolism caused by insulin resistance. In diabetes, increased lipolysis of adipose tissue leads to increased free fatty acids, which ultimately increases triglyceride synthesis in the liver. Improved insulin sensitivity due to bidara leaf extract administration is thought to contribute to this reduction in triglyceride levels (Rosenson RS et al., 2022; Ko DT et al., 2023).

In addition to triglycerides, total cholesterol levels also showed improvement after administration of bidara leaf extract. The decrease in total cholesterol is likely related to the flavonoid content, which inhibits the activity of the HMG-CoA reductase enzyme, the main enzyme in cholesterol synthesis. This mechanism reduces cholesterol production in the liver, thus better controlling total cholesterol levels in the bloodstream (Djasang, 2017).

Significant changes were also seen in LDL levels. LDL is a lipoprotein that plays a role in transporting cholesterol to peripheral tissues and is often referred to as atherogenic cholesterol because it is closely related to the formation of atherosclerotic plaque. The results showed that bidara leaf extract was able to significantly lower LDL levels compared to the diabetic group. This LDL reduction is important because it can reduce the risk of cardiovascular complications that often occur in people with type 2 diabetes mellitus (Dhurat & Sukesh, 2014).

The increased HDL levels found in the treatment group indicate a protective effect of bidara leaf extract on lipid metabolism. HDL functions to transport cholesterol from peripheral tissues back to the liver through the reverse cholesterol transport mechanism. Increasing HDL can help reduce cholesterol accumulation in blood vessels, thereby lowering the risk of atherosclerosis. This effect is thought to be related to the antioxidant activity of flavonoids and saponins, which improve overall lipid metabolism. (El Tahawy et al., 2017).

Overall, the results of this study support the theory that bidara leaves have potential as a natural antidyslipidemic agent. The flavonoids, saponins, tannins, and polyphenols in bidara leaf ethanol extract work through various mechanisms, including antioxidant activity, increased insulin sensitivity, inhibition of cholesterol synthesis, increased bile acid excretion, and improved lipid metabolism. These mechanisms synergistically contribute to improving lipid profiles in type 2 diabetes mellitus (Chen et al., 2018).

CONCLUSION

Based on the research results, ethanol extract from bidara leaves (Ziziphus mauritiana) demonstrated potential as an antidiabetic and antidyslipidemic agent in male Wistar rats with streptozotocin (STZ)-induced diabetes mellitus. Administration of bidara leaf extract gradually reduced blood glucose levels after 14 and 28 days of treatment and improved lipid profiles by decreasing total cholesterol, triglyceride, and LDL levels while increasing HDL levels compared with the negative control group. These findings indicate that ethanol extract from bidara leaves has potential for further development as a complementary herbal therapy to support the management of type 2 diabetes mellitus accompanied by dyslipidemia.

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