The Effect of Dragon Tail Leaf Extract (*Epipremnum pinnatum* (L.) Engl) on Blood Glucose in Rats with Diabetes Mellitus

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Abstract: Diabetes mellitus is a metabolic disorder characterized by elevated blood glucose levels exceeding normal limits (hyperglycemia) due to impaired insulin secretion by the pancreas. One alternative treatment being developed is the use of medicinal plants with antidiabetic activity. Dragon's tail leaf (Epipremnum pinnatum (L.) Engl.) is known to contain secondary metabolites such as flavonoids, alkaloids, saponins, and phenolics that have the potential to lower blood glucose levels. The purpose of this study was to determine the effect of dragon's tail leaf extract on blood glucose levels in rats with diabetes mellitus. This experimental study used a pre-test-post-test control group design. Thirty-six rats were divided into six groups: K(-) as normal controls, K(+) as diabetic controls induced by alloxan at 100 mg/kgBW, Kmet as a comparison group induced by metformin at 250 mg/kgBW, and treatment groups P1, P2, and P3, which were administered dragon's tail leaf extract at varying doses of 125, 250, and 375 mg/kgBW. Diabetes induction was performed using alloxan to induce hyperglycemia. Blood glucose levels were measured using the POCT method. The results showed that administration of dragon's tail leaf extract (Epipremnum pinnatum (L.) Engl.) reduced blood glucose levels in diabetic rats (p=0.001). Thus, dragon's tail leaf extract has potential as a natural antihyperglycemic agent in the management of diabetes mellitus.

Keywords: Diabetes Mellitus, Blood Glucose, Alloxan, Epipremnum pinnatum (L.) Engl

INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by elevated blood glucose levels due to impaired insulin secretion, insulin action, or both. Chronic hyperglycemia can cause damage to various organs, including the eyes, kidneys, nerves, and cardiovascular system (Soelistijo, 2021) (Shafriani, 2021). Globally, the prevalence of diabetes continues to increase and has become a major health problem, with the number of sufferers reaching 537 million people by 2022 (International Diabetes Federation (IDF)., 2021). The 2023 Indonesian Health Survey (SKI) report shows that the prevalence of diabetes mellitus (DM) in Indonesia has increased. According to doctors' diagnoses, the prevalence of DM has increased compared to the results of the 2018 Basic Health Research (Riskesdas), which was 1.5% in 2018, increasing from 2.0% to 2.2% in 2023. The prevalence of DM in West Sumatra according to the 2023 SKI is 1.6%. According to the 2023 SKI results, the prevalence of diabetes mellitus (DM) in women (2.0%) is higher than in men (1.3%). The prevalence of DM also increases with age, reaching its highest rate in the 65-74 age group (Tim Penyusun SKI 2023, 2023). References based on WHO (1999) and the American Diabetes Association (2003) are used, as quoted in the 2007 Basic Health Research (Ministry of Health,

2008) as follows: <140 mg/dl: No DM, 140 - <200 mg/dl: Impaired Glucose Tolerance (IGT) and ≥ 200 mg/dl: Diabetes Mellitus (DM) (Gayatri et al., 2019).

Blood glucose refers to the concentration of glucose in the bloodstream. Glucose levels are tightly regulated because they serve as the primary energy source for cells. Generally, normal blood glucose levels range from 70–110 mg/dL. After meals, glucose levels increase, while they are typically lowest in the morning before meals. Blood glucose levels below 70 mg/dL are called hypoglycemia, while levels above 110 mg/dL are called hyperglycemia. Blood glucose monitoring plays a crucial role in clinical practice, particularly in patients with diabetes mellitus, for diagnostic purposes, determining therapy, and evaluating treatment effectiveness (Endiyasa et al., 2019). Alloxan is an organic compound derived from urea that is structurally similar to glucose and is carcinogenic and cytotoxic. This compound has the molecular formula $C_4H_2N_2O_4$ and a relative molecular mass of 142.06. In diabetes-related research, alloxan is widely used as a diabetogenic agent to evaluate the antidiabetic potential of both pure compounds and plant extracts (Ighodaro et al., 2018).

Alloxan-induced diabetes falls under the category of insulin-dependent diabetes mellitus, which occurs as a result of administering the compound to test animals. Alloxan can be administered through various routes, such as intraperitoneal, intravenous, or subcutaneous, in either single or repeated doses. However, a single intraperitoneal administration is the most commonly used method. Doses used in various studies range from 90 to 200 mg/kg body weight, with 150 mg/kg being the most commonly used dose. Factors such as animal species, route of administration, and nutritional status play a role in determining the optimal dose for diabetes induction. However, a single intraperitoneal administration in the range of 170–200 mg/kg body weight has been reported to be more effective (Ighodaro et al., 2018). Animals that are fed or have high blood glucose levels tend to show resistance to the toxic and diabetogenic effects of alloxan. Therefore, test animals are generally fasted for at least 12 hours before alloxan administration. This fasting state causes a decrease in blood glucose levels, which in turn increases the uptake of alloxan by β-cells in the pancreatic islets of Langerhans, thus enhancing the compound's diabetogenic effect (Ighodaro et al., 2018).

Diabetes cases continue to increase due to unhealthy lifestyles such as high-sugar diets and sedentary lifestyles, which exacerbate insulin resistance and systemic inflammation despite effective metformin therapy. Metformin therapy has limitations, such as the risk of lactic acidosis in patients with impaired kidney function (Rena et al., 2017). Indonesia has a rich biodiversity, including medicinal plants with potential antidiabetic properties. One such plant is the dragon's tail leaf (*Epipremnum pinnatum* (L.) Engl.). The dragon's tail plant is a climbing plant containing secondary metabolites, including alkaloids, flavonoids, saponins, tannins, glycosides, and steroids/triterpenoids (Sani K et al., 2022). Dragon's tail leaf extract (*Epipremnum pinnatum*) has been shown to suppress the production of pro-inflammatory cytokines such as TNF-α, IL-6, and IL-1β in LPS-stimulated human PBMC cells, through regulation of the NF-κB pathway, which plays a key role in the inflammatory mechanism. Active compounds such as flavonoids, lignans, and phenylpropanoid glycosides in these leaves contribute to immunomodulatory and antioxidant activities that can improve insulin sensitivity and reduce oxidative stress, two key factors in the pathogenesis of diabetes mellitus (Pan et al., 2019).

This has prompted the search for adjuvant therapies such as dragon's tail leaf extract (*Epipremnum pinnatum* (L.) Engl.), which contains organic compounds such as flavonoids, alkaloids, saponins, tannins, and glycosides (Masfria et al., 2017). The combination of these two compounds has the potential to create a synergistic effect in suppressing inflammation, increasing autophagy, and protecting pancreatic β-cell function, opening up significant opportunities for the development of new, specifically targeted drugs for the prevention and treatment of diabetes (Antar et al., 2023). However, further research into the effects of dragon's tail leaf extract on blood glucose levels requires further investigation, particularly regarding the effective dosage and in vivo mechanism of action. This study was conducted to evaluate the effects of *Epipremnum pinnatum* (L.) Engl. leaf extract on blood glucose levels in rats with diabetes mellitus.

RESEARCH METHODS

Types and Design of Research

This study is an experimental laboratory study using a Pretest–Posttest Control Group Design. This design was used to evaluate changes in blood glucose levels before (pretest) and after (posttest) administration of dragon's tail leaf extract to alloxan-induced rats.

Time and Place of Research

This research was conducted from March to August 2025. This research will be conducted at the Non-Infectious Biomedical Laboratory of the Faculty of Medicine, Andalas University to conduct extraction and examination of blood glucose levels in mice, as well as the Animal House of the Faculty of Pharmacy, Andalas University for the treatment of mice.

Tools and materials

The tools used in this study include a glucometer (Glukocheck), glucose strips (Autocheck), injection syringes, oral probes, analytical scales, animal cages, and laboratory glassware.

The materials used include alloxan monohydrate (Sigma-Aldrich) as a diabetes inducer, 96% ethanol (Merck) as an extraction solvent, distilled water (Aquabidest), sterile water for injection (Otsu-WI), 70% alcohol, povidone iodine (Betadine), and ethanol extract of dragon's tail leaves (*Epipremnum pinnatum* (L.) Engl).

Test Animals

The test animals used were male white rats (*Rattus norvegicus*) of the Wistar strain weighing approximately 150–250 grams and aged 2–3 months. The rats were acclimatized for 7 days under controlled environmental conditions (temperature 22–25°C, 12-hour light–dark cycle), and given standard feed and drinking water ad libitum.

Extract Preparation

Dragon's tail leaves (*Epipremnum pinnatum* (L.) Engl) were dried, then powdered and extracted using a maceration method with 96% ethanol solvent for 5 × 24 hours. The filtrate obtained was filtered and evaporated using *a rotary evaporator* until a thick extract was obtained.

Research Procedures

A total of 36 mice were randomly divided into five groups (n=6), namely:

K- : Negative control group of mice, will be given a diet in the form of standard feed without alloxan and dragon tail leaf extract for 23 days.

K+ : Positive control group, will be induced with alloxan 100 mg/kgBW for 72 hours.

Kmet : Comparison group, induced by alloxan 100 mg/kgBW and metformin 250 mg/kgBW for 23 days.

P1 : Treatment group of mice, induced with alloxan 100 mg/kgBW and dragon tail leaf extract 125 mg/kgBW for 23 days.

P2 : Treatment group of mice, induced with alloxan 100 mg/kgBW and dragon tail leaf extract 250 mg/kgBW for 23 days.

P3 : Treatment group of mice, induced with alloxan 100 mg/kgBW and dragon tail leaf extract 375 mg/kgBW for 23 days.

Prior to treatment, all mice underwent a baseline blood glucose measurement (pretest). Next, diabetes was induced by administering alloxan intraperitoneally at a dose of 100 mg/kg body weight. Mice were considered hyperglycemic if their blood glucose levels were >200 mg/dL after 72 hours of induction.

After hyperglycemia was achieved, blood glucose levels were measured again as the initial value for the treatment. The treatment group was then given dragon's tail leaf extract orally using a tube for 23 days, while the control group was given distilled water. At the end of the treatment period, a posttest was performed *to* assess changes in blood glucose levels in each group.

Measurement of Blood Glucose Levels

Blood glucose level examination was carried out using the point of care testing (POCT) method using the Accu-Chek device. Point of care testing (POCT) is a tool used to measure total blood glucose levels based on electrochemical detection by coating the glucose oxidase enzyme on a membrane strip (Endiyasa et al., 2019). Blood was taken through a 1mm incision in the tail using sterilized scissors. Blood glucose level examination in mice was carried out at the initial screening before alloxan administration, after alloxan administration and final screening of the effect of dragon's tail leaf extract administration in mice.

Data analysis

Analysis of differences between treatment groups was performed using Two-Way Repeated Measures Analysis of Variance (ANOVA) to evaluate the effect of time (pretest and posttest), treatment group, and the interaction between time and group on blood glucose levels, as there were two factors analyzed repeatedly. Post hoc tests were performed if there were significant differences. The significance value was set at $p<0.05$.

RESULTS AND DISCUSSION

In the research group, blood glucose levels were measured in mice, measured at the initial conditions, namely the 8th day after acclimatization (before alloxan induction), on the 12th day (after alloxan induction) and on the 36th day after administration of dragon tail leaf extract for 23 days. The results showed a highly significant change in blood glucose levels during the study period ($p = 0.001$). Initial and post-alloxan-induced blood glucose levels demonstrated that alloxan can induce diabetes mellitus in rat models, as shown in Table 1.

Table 1. Results of Blood Glucose Level Measurements After Alloxan Induction

Blood Glucose Level (mg/dL)	($\bar{x}$ ± SEM)	n	p
Initial blood glucose levels	73.83±2,21	36	0.001
Post-alloxan-induced blood glucose levels	246.66±38,63	36	

The results of measuring blood glucose levels can be seen in Figure 1 and Figure 2 as follows.

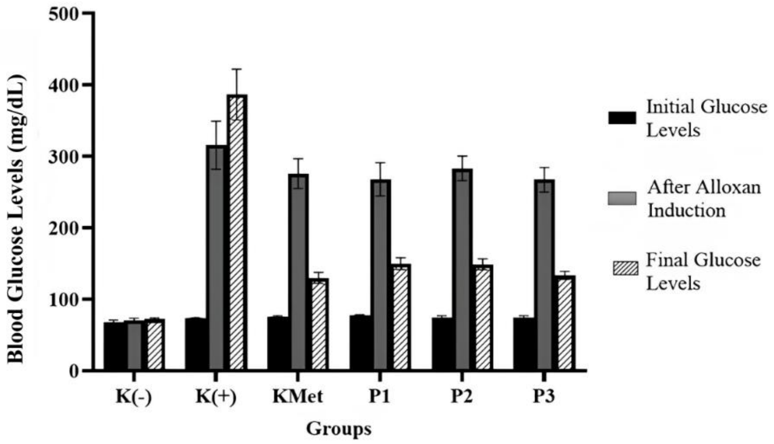

Figure 1. Blood Glucose Levels in Rats (Mean±SEM; mg/dL)

K-= negative group; K+= positive group (induced by alloxan); Kmet= group given metformin; P1= group given dragon's tail leaf extract at a dose of 125 mg/kgBW; P2= group given dragon's tail leaf extract at a dose of 250 mg/kgBW; P3= group given dragon's tail leaf extract at a dose of 375 mg/kgBW; (Two-Way Repeated Measures ANOVA) (Source: Personal Document).

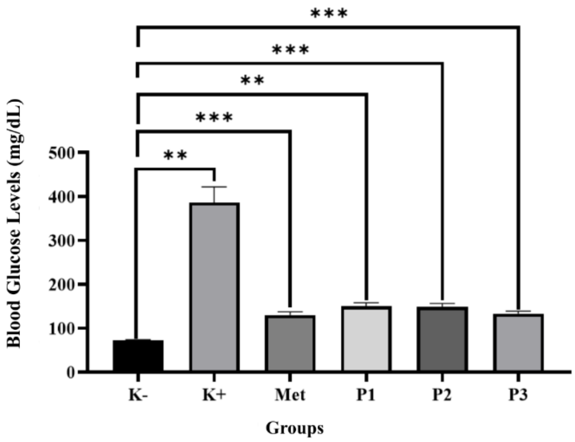

Figure 2. Final Blood Glucose Levels of Each Group (Mean±SEM; mg/dL).

K-= negative group; K+= positive group (induced by alloxan); Kmet= group given metformin; P1= group given dragon's tail leaf extract at a dose of 125 mg/kgBW; P2= group given dragon's tail leaf extract at a dose of 250 mg/kgBW; P3= group given dragon's tail leaf extract at a dose of 375 mg/kgBW; *p ≤ 0.05 **p< 0.02; *** p< 0.001 (Two-Way Repeated Measures ANOVA, Post-hoc Games-Howell) (Source: Personal Document). Analysis of blood glucose levels in alloxan-induced rats was performed using Two-Way Repeated Measures ANOVA to evaluate the dynamics of changes in glucose levels longitudinally at three measurement points, namely before induction (baseline), after alloxan induction and after treatment. This analysis design was considered the most appropriate because it was able to describe the physiological changes that occurred in the same subject over time. Initial descriptive results showed that alloxan induction successfully created a diabetes mellitus model in experimental animals, which was characterized by a significant increase in blood glucose levels in the positive control and treatment groups. This finding is in line with research reports stating that alloxan is an effective diabetogenic agent in inducing stable hyperglycemic conditions through selective destruction of pancreatic (Kim, 2024).

Statistical prerequisite tests showed that the data were normally distributed based on the Shapiro–Wilk test (p > 0.05), although the assumption of homogeneity of variance was not met in the post-induction measurement with a p value = 0.003 (p > 0.05) and the final with a p value = 0.001 (p > 0.05). Therefore, the analysis was continued using the Games–Howell post hoc test which is more appropriate for conditions of inhomogeneous variance. The results of the main test showed a significant time effect with a p value = 0.001 (p < 0.05), indicating a significant change in blood glucose levels during the study period. The interaction effect between time and group was also significant (p < 0.001), indicating that changes in blood glucose levels differed significantly between treatment groups. The initial blood glucose levels of the mice (73.83 ± 2.21 mg/dL) were within the normal range, indicating a stable metabolic condition before treatment. After alloxan induction at a dose of 100 mg/kgBW, there was a sharp increase in blood glucose levels to 246.66 ± 38.63 mg/dL. This proves the successful induction of diabetes in the experimental animal model. This increase is consistent with the mechanism of action of alloxan as a selective cytotoxic agent that damages pancreatic β cells , resulting in decreased insulin secretion and acute hyperglycemia (Rita et al., 2023). The significant increase in blood glucose (p < 0.001) after induction strengthens the validity of the model used and demonstrates the consistency of the biological response to diabetogenic agents.

After the treatment phase, blood glucose levels decreased significantly in all treatment groups compared to the positive control. This pattern of decrease indicates the effectiveness of the intervention in improving blood glucose status. Post-hoc analysis results showed that the metformin group and the three dragon's tail leaf extract groups (P1, P2, and P3) were significantly different from the positive control with a p value <0.001 (p <0.05), but there was no significant difference between the metformin group and the three extract doses (p > 0.05). This indicates that dragon's tail leaf extract has comparable effectiveness to metformin in lowering blood glucose levels. These results are in line with research reporting that Tribulus terrestris extract has an antihyperglycemic effect comparable to metformin in a diabetic rat model, thus demonstrating the potential of herbal extracts as an alternative antidiabetic therapy (Al-Eisa et al., 2022).

The negative control group (K–) maintained blood glucose levels within normal limits throughout the study, indicating intact pancreatic function and metabolic stability. This condition supports that with the implementation of appropriate acclimatization protocols and sampling procedures that have been shown to minimize stress responses and maintain stability, the negative control group maintained consistent basal glucose levels throughout the study (Marin et al., 2023; Moro & Magnan, 2025). The positive control group (K+) showed the highest blood glucose levels and did not improve until the end of the study. This indicates permanent damage to pancreatic β cells without regeneration or endogenous compensation, as explained by previous studies that alloxan-induced Wistar rats showed persistent hyperglycemia without therapeutic intervention (Kim, 2024).

The metformin (KMet) group showed a significant decrease in blood glucose levels compared to the positive control group (K+). This hypoglycemic effect is related to the mechanism of action of metformin which increases insulin sensitivity through activation of the AMPK pathway and suppresses gluconeogenesis in the liver (Herman et al., 2022; Lamoia & Shulman, 2021). Experimental studies also reported that metformin effectively reduces blood glucose levels in alloxan-induced diabetic rats, demonstrating the consistency of its antidiabetic effect (Yasin et al., 2022). A similar decrease was also observed in the group receiving dragon's tail leaf extract. Group P1 (low dose) showed a significant decrease in glucose levels, indicating a pharmacological response from the initial dose. This effect likely originates from the flavonoid and phenolic content that plays a role in protecting pancreatic β cells from oxidative damage (Ménégaut et al., 2023).

In group P2 (medium dose), the reduction in blood glucose levels was stronger than in group P1, indicating a dose-response relationship. This is likely mediated by increased activity of compounds that mimic the action of insulin and stimulation of glucose uptake in peripheral tissues through activation of the AMPK pathway and GLUT4 translocation, as reported for Phyllanthus emblica and Cyperus rotundus extracts (Li et al., 2024; Pichetkun et al., 2024). The more pronounced antihyperglycemic effect at medium doses compared to low doses is also consistent with the ability of polyphenols and flavonoids to increase insulin sensitivity and *glucose uptake* (Ansari et al., 2024; Sarker et al., 2024). Group P3 (high dose) showed the most significant reduction in blood glucose levels, approaching the values of the metformin group. This indicates that increasing the extract dose is directly proportional to the ability to normalize blood glucose levels. This mechanism is likely related to increased insulin sensitivity and activation of the GLUT-4 transporter in muscle tissue due to the role of active compounds such as flavonoids, terpenoids, and alkaloids (Neuhauser et al., 2024).

The final measurement results showed an average blood glucose level of 169.97 ± 44.01 mg/dL with a significant variation in response between treatment groups. The significant decrease in blood glucose levels in the extract and metformin groups indicates that both treatments have a therapeutic effect on alloxan-induced hyperglycemia. A significant interaction between time and group indicates that changes in blood glucose levels are highly dependent on the type of treatment given. These findings are consistent with research reports that emphasize the importance of longitudinal measurement of blood glucose levels in assessing the effectiveness of antidiabetic therapy, given the adaptive variation and complex dynamics of glucose fluctuations in experimental diabetes models (Alkhatieb et al., 2023). The results of this study strengthen the evidence that dragon's tail leaf extract has the potential to be an effective antidiabetic agent and is able to reduce blood glucose levels significantly, comparable to standard metformin therapy, as also reported for active plant compounds with high antioxidant activity (Tanjung RM, 2024).

CONCLUSION AND SUGGESTIONS

It can be concluded that administration of dragon's tail leaf extract (*Epipremnum pinnatum* (L.) Engl) at doses of 125 mg/kgBW, 250 mg/kgBW, and 375 mg/kgBW can significantly reduce blood glucose levels in alloxan-induced rats ($p<0.05$). Alloxan induction was proven effective in increasing blood glucose levels to hyperglycemic conditions, so that a diabetes mellitus model was successfully formed. After administration of the extract for 23 days, there was a significant decrease in blood glucose levels in all treatment groups compared to the positive control group. The effect of lowering blood glucose showed a tendency for a dose-response relationship, where the highest dose provided a more optimal effect and approached the effectiveness of metformin as a comparative control. Thus, dragon's tail leaf extract has the potential as a natural antihyperglycemic agent that can be developed as an additional therapy in the management of diabetes mellitus. This study only measure level glucose blood without examine other biomarkers that play a role in pathogenesis of diabetes mellitus, such as insulin levels, stress oxidative, and cytokines inflammation. Furthermore, it needs to measure other biomarkers related to diabetes and toxicity parameter.

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