

Antidiabetic Effectiveness of Ethanol Extract from Sweet Mango Leaves (*Mangifera indica* L. var. Arum Manis) on Blood Glucose Levels in Streptozotocin-Induced Male Mice (*Mus musculus* L.)Rara Widiya Marisha¹, Astriani Natalia Br Ginting^{2,3*}, Daimah Wirdatus Sanaun Harahap^{2,3}¹Bachelor of Clinical Pharmacy, Faculty of Health Sciences, Universitas Prima Indonesia, Medan, 20118, Indonesia²Dapertemen of Clinical Pharmacy, Faculty of Health Sciences, Universitas Prima Indonesia, Medan, 20118, Indonesia³PUI Phyto Degenerative & Lifestyle Medicine**Article History**

Received : January 02, 2026

Accepted : January 11, 2026

Published : January 13, 2026

Available Online:

January 13, 2026

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Marisha, R. W., Astriani Natalia Br Ginting, & Daimah Wirdatus Sanaun Harahap. (2025). Antidiabetic Effectiveness of Ethanol Extract from Sweet Mango Leaves (*Mangifera indica* L. var. Arum Manis) on Blood Glucose Levels in Streptozotocin-Induced Male Mice (*Mus musculus* L.). *Jurnal Kesehatan Dan Kedokteran*, 5(1), 143–156.

DOI:<https://doi.org/10.56127/jukeke.v5i1.2467>

Abstract: Diabetes mellitus (DM) is a growing public health concern worldwide, particularly in Indonesia, where its prevalence continues to rise, causing significant health and economic burdens. The need for effective, accessible, and safe therapies is critical, as current treatments often come with side effects and limitations. Alternative natural treatments, such as herbal remedies, are being explored for their potential to offer safer and more sustainable options for managing DM. **Objective:** This study aims to evaluate the antidiabetic effectiveness of ethanol extract of sweet mango leaves (*Mangifera indica* L. var. sweet mango) on reducing blood glucose levels in streptozotocin (STZ)-induced diabetic mice. **Methodology:** A true experimental post-test only control group design was employed using mice (*Mus musculus*) divided into six groups: normal control, negative control (STZ), positive control (glibenclamide), and three treatment groups of mango leaf extract with doses of 50, 100, and 150 mg/kgBW. The extraction was carried out using the maceration method with 70% ethanol, and the antidiabetic activity was tested over a 15-day period. **Results:** The results showed that administration of ethanol extract of sweet mango leaves significantly reduced blood glucose levels ($p < 0.001$) compared to the negative control. A dose-response pattern was observed, with a dose of 150 mg/kgBW providing the most significant blood glucose lowering effect, closely approaching the effectiveness of glibenclamide. **Discussion:** The antidiabetic activity of the extract is thought to be related to its bioactive compounds, such as flavonoids, phenolics, and mangiferin, which are believed to enhance insulin sensitivity, inhibit gluconeogenesis, and protect pancreatic β cells from oxidative stress. **Originality and Contribution:** This study provides new insights into the antidiabetic potential of the ethanol extract of sweet mango leaves (*Mangifera indica* var. Arum Manis), a variety not extensively studied for its effects on diabetes. The research contributes to the growing body of knowledge on natural-based therapies for DM, offering an alternative to conventional treatments with potentially fewer side effects and wider accessibility. The findings support the further development of mango leaf extract as a natural candidate for diabetes management.

Keywords: Diabetes mellitus; Ethanol extract of sweet mango leaves; *Mangifera indica* L.; Antidiabetic; Streptozotocin; Blood glucose levels.

INTRODUCTION

Diabetes Mellitus (DM) is a chronic disease whose prevalence continues to increase in both Indonesia and the world. According to the IDF Diabetes Atlas 10th edition (IDF, 2021). Indonesia ranks fifth in the world, with approximately 19.47 million people suffering from diabetes in 2021, and this number is expected to rise to 28.6 million by 2050. In 2024, the prevalence of diabetes in Indonesia is estimated to reach 20.4 million adults (aged 20–79 years) with a prevalence of approximately 11.3%, adjusted for age. This phenomenon shows that more than 1 in 9 adults in Indonesia live with diabetes, which has significant social and economic impacts, including increased healthcare costs and a decline in quality of life (Ginting, et al., 2025). Furthermore, approximately 3 out of 4 people with diabetes are unaware of their condition because many have not been diagnosed (Kemenkes, 2021). Therefore, it is important to find more efficient treatment solutions, including through the use of natural ingredients such as Arum Manis mango leaves, which have great potential in helping address this issue.

Moreover, although conventional treatments such as chemical drugs are often used to control blood sugar levels, many patients experience side effects or difficulties in undergoing long-term therapy. This phenomenon encourages the search for safer and more natural treatment alternatives. Herbal plants, such as *Mangifera indica*, which contains active compounds such as mangiferin, flavonoids, and polyphenols, have been known to have potential as antidiabetic agents

(Aderibigbe & Saleem, 2001; Ginting, Kaban, et al., 2025). Research into the antidiabetic potential of Arum Manis mango leaves (*Mangifera indica* var. Arum Manis) shows great promise in developing natural-based therapies that could be used as an alternative or complement to conventional treatments, with fewer side effects and easier access for the public (Harefa et al., 2025).

Research on *Mangifera indica*, particularly the extracts from its leaves and seeds, has shown significant potential in the treatment of diabetes mellitus. Ethanol extracts from *Mangifera indica* leaves have been proven to have significant hypoglycemic effects in rats with diabetes induced by alloxan and streptozotocin

(Kemasari et al., 2011; Ramesh Petchi et al., 2011). Some of the mechanisms found include increased insulin secretion from pancreatic β -cells, inhibition of carbohydrate-digesting enzymes such as α -glucosidase and α -amylase, and a reduction in glucose absorption in the intestine (Bhowmik et al., 2009; Kulkarni & Rathod, 2018). Active

compounds in the leaf extract such as mangiferin, flavonoids, and tannins are known to play an important role in this antidiabetic activity, which is also accompanied by antioxidant effects that reduce oxidative stress in diabetic patients ([Hossain et al., 2010](#); [Patarakijavanich et al., 2019](#)). However, a key limitation of this research is the limited testing on local varieties of *Mangifera indica* such as Arum Manis, and the need to compare the effectiveness of different extracts (water, ethanol, and nanoherbal) as well as their combination with standard antidiabetic drugs to optimize plant-based treatments.

Research on *Mangifera indica*, especially its leaf extract and bioactive content such as mangiferin, has shown significant potential in treating diabetes mellitus ([Ningsih et al., 2025](#)). Mangiferin, a flavonoid compound found in *Mangifera indica* leaves, has been shown to effectively lower blood glucose levels ([Ginting, Ginting, et al., 2025](#)), improve insulin sensitivity, and enhance glucose uptake by tissues ([Du et al., 2018](#); [Muruganandan et al., 2005](#)). Several studies also indicate that *Mangifera indica* leaf extract can inhibit enzymes involved in glucose metabolism, such as α -amylase and α -glucosidase, which contribute to the reduction of post-meal blood glucose levels ([Suryawanshi et al., 2025](#)). Additionally, *Mangifera indica* contains flavonoids and other phenolic compounds with antioxidant activity, which is beneficial in addressing oxidative stress in diabetic patients ([Hossain et al., 2010](#); [Quintana et al., 2021](#)). The use of herbal medicine, including *Mangifera indica* leaf extract, is becoming increasingly popular because it has fewer side effects compared to conventional antidiabetic drugs and offers a more natural and accessible treatment alternative ([Li et al., 2013](#)). Nevertheless, there are still gaps in this research, such as the limited testing on local varieties of *Mangifera indica* and the need for a comparison of the effectiveness of ethanol, water, and nanoherbal extracts to further assess their therapeutic potential.

Diabetes Mellitus (DM) has become one of the chronic diseases with increasing prevalence worldwide, including in Indonesia. Recent findings indicate that the use of *Mus musculus* (mouse) models induced by streptozotocin (STZ) to replicate diabetes in humans plays a significant role in developing new therapies ([Hasanah et al., 2024](#)). Recent research shows that *Mangifera indica*, particularly leaf extract, which is rich in flavonoids such as mangiferin, has significant antidiabetic potential ([Desita, 2025](#); [Harefa et al., 2025](#)). *Mangifera indica* leaf extract has been shown to reduce blood glucose levels, improve glucose tolerance, and enhance lipid profiles in the STZ-induced diabetic mouse model ([Irondi et al., 2016](#); [Khan et al., 2024](#)). This potential is driven by bioactive compounds in

Mangifera indica, such as mangiferin and other flavonoids, which function as antioxidants and antidiabetic agents. While herbal treatments based on *Mangifera indica* are gaining attention as a safer diabetes treatment with minimal side effects (Li et al., 2013), gaps still exist in research regarding the effectiveness and mechanisms of leaf extracts from different local varieties, such as Arum Manis, as well as the need for further testing on combinations of extracts with conventional therapies.

This study aims to evaluate the effectiveness of ethanol extract from Arum Manis mango leaves (*Mangifera indica* var. Arum Manis) as an antidiabetic therapy in a streptozotocin (STZ)-induced diabetes model in mice (*Mus musculus* L.) (Firmanto et al., 2023). The main objective of this study is to address gaps in previous research that were limited to testing specific *Mangifera indica* varieties, especially local varieties such as Arum Manis. Previous research has not compared the effectiveness of various mango leaf extracts, such as ethanol, water, and nanoherbal extracts, as well as their combination with conventional antidiabetic drugs to optimize plant-based therapies.

Based on previous studies by (Safitri et al., 2022) streptozotocin (STZ) is used to create a diabetes model in animals, particularly mice, by damaging pancreatic beta cells, resulting in insulin deficiency and hyperglycemia. The hypothesis in this study is that ethanol extract from Arum Manis mango leaves (*Mangifera indica* L. var. Arum Manis) can improve the pathological condition of diabetes induced by STZ in mice, through mechanisms such as increasing insulin secretion, inhibiting carbohydrate-digesting enzymes (such as α -glucosidase and α -amylase), and reducing glucose absorption in the intestine. It is expected that the Arum Manis mango leaf extract will reduce blood glucose levels in STZ-induced mice, with an additional effect of reducing oxidative stress commonly associated with pancreatic beta cell damage. This study aims to test the effectiveness of ethanol extract from Arum Manis mango leaves in providing glycemic control in the diabetes model and evaluate its potential as a safer alternative therapy compared to conventional drugs like metformin.

RESEARCH METHOD

This research employs a laboratory experimental design using a true experimental post-test only control group design. The study utilizes male *Mus musculus* (mice) as the research subjects to evaluate the antidiabetic effects of *Mangifera indica* (Mangga Arum Manis) leaf extract.

The research will be conducted at the Faculty of Medicine, Dentistry, and Health Sciences of Universitas Prima Indonesia and Universitas Sumatera Utara from February to March 2025. The necessary laboratory equipment includes glassware, cages, water bottles, animal containers, cotton, tissue, 3 mL injection syringes (Terumo), oral probes, rotary evaporators, analytical scales, mouse weighing scales, triple balances, maceration containers, Erlenmeyer flasks, porcelain crucibles, spray bottles, gloves, stir rods, glass bottles, syringes, digital blood glucose meters, and glucose strips.

Sampling Method

The samples used in this study are fresh leaves of *Mangifera indica* var. *Arum Manis* (approximately 3 kg) collected from Jln. Dr. Mansyur, Medan Baru District, Padang Bulan, North Sumatra Province. The identification of the sample was performed at the FMIPA laboratory of Universitas Sumatera Utara.

Extraction of *Mangifera indica* (Mangga Arum Manis) Leaf Sample

Fresh *Mangifera indica* leaves (approximately 3 kg) were cleaned thoroughly with running water to remove any dirt or contaminants. After cleaning, the leaves were chopped and placed in a maceration bottle, with 70% ethanol added until the leaves were submerged. The maceration process was carried out in a dark place for 5 days, with occasional stirring. The macerate was filtered using cotton, and the process was repeated up to three times until the solvent became clear. The combined extracts were then evaporated using a rotary evaporator to obtain a concentrated extract.

Experimental Procedure

Male *Mus musculus* mice were randomly divided into several groups, including a normal control group (K1), a negative control group (K2), a positive control group receiving glibenclamide (K3), and experimental groups receiving varying doses of *Mangifera indica* leaf extract (50 mg/kg, 100 mg/kg, and 150 mg/kg body weight). The mice were induced with diabetes using streptozotocin (STZ) to mimic the diabetic condition. The experiment was conducted over a period of 15 days, with blood glucose levels measured on specified days before induction and at regular intervals thereafter.

Data Collection and Analysis

Blood glucose levels were measured using a digital blood glucose meter and glucose strips. The blood samples were collected at baseline (before induction) and on days 3, 6, 9, 12, and 15 post-treatment. The results were analyzed using One-Way ANOVA to assess the statistical significance of the changes in blood glucose levels across different groups. A Tukey LSD post-hoc test was performed to compare between groups and determine which treatments yielded the most significant reduction in blood glucose levels.

The data collected from this study will be used to evaluate the effectiveness of *Mangifera indica* leaf extract in controlling blood glucose in *Mus musculus* mice and compare its effects with that of the conventional antidiabetic drug glibenclamide.

RESULT AND DISCUSSION

Relationship between Phytochemical Content and Antidiabetic Activity

This section discusses the connection between the phytochemical components (such as flavonoids, phenolics, and mangiferin) in *Mangifera indica* and their potential antidiabetic effects. The data shows how these bioactive compounds contribute to blood glucose reduction, highlighting the mechanisms involved.

The data shows the glucose levels from different groups after induction and various doses of treatment with *Mangifera indica*. Based on Table 1, we can observe the glucose levels before induction and throughout the experiment period (days 0, 3, 6, 9, 12, and 15).

Table 1. Average ± SD Blood Glucose Levels (mg/dL)

Time	K1 Normal	K2 Negative	K3 Glibenclamide	K4 (50 mg/kgBW)	K5 100 mg/kgBW	K6 150 mg/kgBW
Before Induction	98.00 ± 3.16	100.40 ± 2.70	98.00 ± 2.55	100.00 ± 2.74	100.80 ± 2.59	98.20 ± 2.17
Day 0	100.60 ± 2.88	491.00 ± 8.28	525.00 ± 15.70	473.80 ± 16.68	477.20 ± 9.37	476.60 ± 17.18
Day 3	98.80 ± 3.70	514.40 ± 4.62	228.80 ± 14.06	435.40 ± 12.60	414.20 ± 10.62	413.20 ± 9.20
Day 6	99.20 ± 3.27	532.40 ± 9.61	155.40 ± 12.30	412.80 ± 1.92	403.60 ± 5.86	392.40 ± 6.69
Day 9	99.20 ± 3.11	553.40 ± 5.23	155.40 ± 12.30	394.00 ± 2.92	374.60 ± 3.78	360.00 ± 4.30
Day 12	100.00 ± 3.54	568.00 ± 4.74	120.40 ± 8.33	278.40 ± 5.03	267.80 ± 33.95	218.60 ± 15.85
Day 15	100.80 ± 3.19	580.40 ± 3.65	104.80 ± 5.98	161.20 ± 9.99	143.20 ± 8.70	130.60 ± 3.65

These results suggest that *Mangifera indica* leaf extract, especially at higher doses (100 and 150 mg/kgBW), has a significant potential to reduce blood glucose levels in diabetic

mice induced by STZ. The extract showed a clear dose-response relationship, with higher doses leading to more significant glucose reductions. While the *Mangifera indica* extract was not as effective as glibenclamide, the results indicate its potential as a natural alternative or adjunct to conventional diabetes treatments. This finding highlights the importance of exploring natural plant-based therapies for managing diabetes, offering a promising option with fewer side effects than traditional pharmaceutical drugs.

Dose-Response Effect of *Mangifera indica* Extract on Blood Glucose Levels

This section covers the dose-response relationship between the varying doses of *Mangifera indica* leaf extract and its impact on blood glucose levels in diabetic mice. The data shows a significant reduction in glucose levels at higher doses, confirming a dose-dependent effect. The percentage of reduction in blood glucose levels across different groups at various time points is presented in Table 2.

Table 2. Persentase Penurunan KGD

Time	K1 (Normal)	K2 (Negative)	K3 (Glibenclamide)	K4 (50 mg/kgBW)	K5 (100 mg/kgBW)	K6 (150 mg/kgBW)
Day 3	1.79 % ↓	-4.76 % ↑	56.42 % ↓	8.10 % ↓	13.20 % ↓	13.31 % ↓
Day 6	1.39 % ↓	-8.43 % ↑	70.40 % ↓	12.89 % ↓	15.41 % ↓	17.67 % ↓
Day 9	1.39 % ↓	-12.71 % ↑	70.40 % ↓	16.82 % ↓	21.51 % ↓	24.45 % ↓
Day 12	0.60 % ↓	-15.68 % ↑	77.07 % ↓	41.25 % ↓	43.87 % ↓	54.15 % ↓
Day 15	-0.20 % ↑	-18.21 % ↑	80.04 % ↓	65.97 % ↓	69.99 % ↓	72.60 % ↓

Table 2 provides the percentage reduction in glucose levels across all groups. The control group (K2) shows an increase in blood glucose levels over time, consistent with the disease progression. The treatment groups, especially the high doses of *Mangifera indica* extract (K5, K6), show a steady decrease in glucose levels over time.

The data presented in Table 2 reinforces the observation that higher doses of *Mangifera indica* extract significantly reduce blood glucose. This suggests a dose-dependent relationship, where higher doses yield greater reductions in glucose levels. The results also suggest that the effectiveness of *Mangifera indica* extracts is comparable to that of glibenclamide, although not as rapid or extensive.

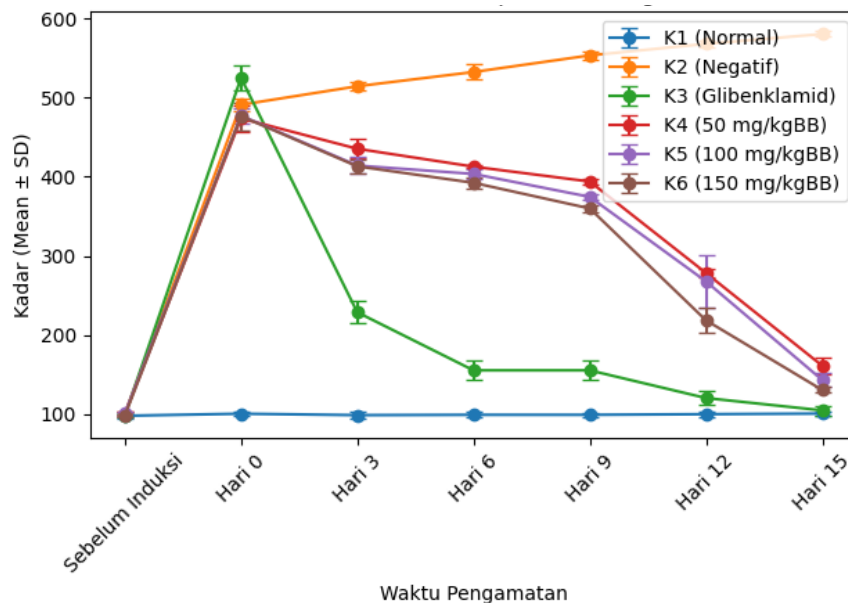


Figure 1. Graph Showing the Changes in Blood Glucose Levels

The results of the study show that in the negative control group (K2) induced with streptozotocin without treatment, blood glucose levels progressively increased up to day 15, reflecting persistent hyperglycemia due to β -cell pancreatic damage caused by STZ. This pattern is consistent with the pathological mechanism of the STZ-induced type 1 diabetes model, where this nitrosourea agonist triggers oxidative stress and apoptosis of β -cells, leading to a drastic decrease in insulin secretion and sustained high blood glucose without therapeutic intervention.

In contrast, the group receiving glibenclamide (K3) exhibited the fastest and most significant reduction in blood glucose levels starting from day 3, with a decrease of more than 50% from the initial day of treatment. This aligns with the pharmacological characteristics of glibenclamide as a sulfonylurea, which quickly enhances insulin secretion by closing ATP-sensitive potassium channels on β -pancreatic cells, thus significantly improving glycemic control in a short period.

The treatment groups with ethanol extract of *Mangifera indica* var. Arum Manis leaves (K4–K6) also showed a statistically significant reduction in blood glucose levels ($p < 0.001$), with a dose-response pattern; the higher the dose of the extract, the greater the percentage of glucose reduction. This reduction indicates the gradual antidiabetic potential of *Mangifera indica* leaf extract, likely related to bioactive compounds such as flavonoids and polyphenols, which contribute to improved insulin sensitivity, inhibition of

carbohydrate-digesting enzymes, and antioxidant effects that protect β -cells from oxidative damage (Singh et al., 2023). The glucose reduction effect at a dose of 150 mg/kgBW (K6), approaching the reduction values of glibenclamide, demonstrates that the mango leaf extract has the potential to provide competitive glycemic control compared to standard antidiabetic agents in animal models.

Meanwhile, the normal group (K1) maintained relatively stable blood glucose levels throughout the observation period, reinforcing the validity of the experimental model and the role of the normal control in this study. This pattern suggests that the significant changes observed in groups K2–K6 were primarily due to STZ induction and therapeutic effects, rather than other biological factors unrelated to the treatment or induction

Comparison of Extract Effectiveness with Glibenclamide

Glibenclamide works by stimulating insulin secretion from the remaining functional β pancreatic cells. The observed decrease in blood glucose levels in the positive control group indicates that the diabetes model still has residual β cells (Ghasemi et al., 2021). The *Mangifera indica* leaf extract showed a glucose reduction pattern similar to that of the glibenclamide group, suggesting that the extract holds potential as a natural-based alternative antidiabetic therapy.

The group treated with glibenclamide (K3) exhibited the most rapid and significant reduction in blood glucose levels, approaching normoglycemia. This is consistent with the pharmacological mechanism of glibenclamide, which stimulates insulin secretion from the remaining β cells in the pancreas after streptozotocin (STZ) induction.

Although the effectiveness of the *Mangifera indica* leaf extract is still below that of glibenclamide, the significant reduction observed with the extract, especially at the 150 mg/kgBW dose, indicates the potential of mango leaves as a natural antidiabetic candidate.

Tukey LSD Test Results

A Tukey LSD test was performed to analyze the blood glucose levels before induction and on days 0, 3, 6, 9, 12, and 15. The results of this analysis are shown in Table 2. The significant differences in blood glucose levels were determined for each time point, indicating the influence of the treatment and induction.

Table 3. Tukey LSD Test Results for Blood Glucose Levels (mg/dL)

Time	K1 (Normal)	K2 (Negative)	K3 (Glibenclamide)	K4 (50 mg/kgBW)	K5 (100 mg/kgBW)	K6 (150 mg/kgBW)	p- value
Before Induction	98.00 ± 3.16	100.40 ± 2.70	98.00 ± 2.55	100.00 ± 2.74	100.80 ± 2.59	98.20 ± 2.17	0.824
Day 0	100.60 ± 2.88 *b,c,d,e,f,g	491.00 ± 8.28 *b,c,d,e,f,g	525.00 ± 15.70 *b,c,d,e,f,g	473.80 ± 16.68 *b,c,d,e,f,g	477.20 ± 9.37 *b,c,d,e,f,g	476.60 ± 17.18 *b,c,d,e,f,g	<0.001
Day 3	98.80 ± 3.70 *a,b,d,e,f,g	514.40 ± 4.62 *a,b,d,e,f,g	228.80 ± 14.06 *a,b,d,e,f,g	435.40 ± 12.60 *a,b,d,e,f,g	414.20 ± 10.62 *a,b,d,e,f,g	413.20 ± 9.20 *a,b,d,e,f,g	<0.001
Day 6	99.20 ± 3.27 *a,b,c,e,f,g	532.40 ± 9.61 *a,b,c,e,f,g	155.40 ± 12.30 *a,b,c,e,f,g	412.80 ± 1.92 *a,b,c,e,f,g	403.60 ± 5.86 *a,b,c,e,f,g	392.40 ± 6.69 *a,b,c,e,f,g	<0.001
Day 9	99.20 ± 3.11 *a,b,c,d,f,g	553.40 ± 5.23 *a,b,c,d,f,g	155.40 ± 12.30 *a,b,c,d,f,g	394.00 ± 2.92 *a,b,c,d,f,g	374.60 ± 3.78 *a,b,c,d,f,g	360.00 ± 4.30 *a,b,c,d,f,g	<0.001
Day 12	100.00 ± 3.54 *a,b,c,d,e,g	568.00 ± 4.74 *a,b,c,d,e,g	120.40 ± 8.33 *a,b,c,d,e,g	278.40 ± 5.03 *a,b,c,d,e,g	267.80 ± 33.95 *a,b,c,d,e,g	218.60 ± 15.85 *a,b,c,d,e,g	<0.001
Day 15	100.80 ± 3.19 *a,b,c,d,e,f	580.40 ± 3.65 *a,b,c,d,e,f	104.80 ± 5.98 *a,b,c,d,e,f	161.20 ± 9.99 *a,b,c,d,e,f	143.20 ± 8.70 *a,b,c,d,e,f	130.60 ± 3.65 *a,b,c,d,e,f	<0.001

From Table 3, the Tukey LSD test results show that there were significant differences in the blood glucose levels across the time points for the treated groups (K2-K6). For the normal group (K1), no significant changes were observed across time points ($p > 0.05$). However, the treated groups (K2–K6) exhibited significant changes in blood glucose levels ($p < 0.001$), indicating the effectiveness of the treatments. The changes in blood glucose levels were more pronounced in the glibenclamide group (K3) and the groups treated with higher doses of the *Mangifera indica* leaf extract (K4-K6).

The Tukey LSD test results support the conclusion that the ethanol extract of *Mangifera indica* leaves has a significant impact on lowering blood glucose levels in a dose-dependent manner. The 150 mg/kgBW dose (K6) showed a response similar to glibenclamide (K3), suggesting that *Mangifera indica* extract could be a competitive alternative to conventional antidiabetic medications. The significant reduction in blood glucose levels, especially at the higher doses of *Mangifera indica* extract, highlights its potential as a natural and effective therapy for managing diabetes.

DISCUSSION

This study evaluated the antidiabetic effect of *Mangifera indica* leaf ethanol extract in STZ-induced diabetic mice and found a clear dose–response pattern: higher doses produced greater reductions in blood glucose. At 150 mg/kgBW, the glucose-lowering effect

approached that of glibenclamide, suggesting the extract could serve as a natural complementary or alternative option for diabetes management. The effect is likely linked to bioactive constituents such as flavonoids, phenolics, and mangiferin, which may improve insulin sensitivity, protect pancreatic β -cells from oxidative stress, inhibit gluconeogenesis, and enhance peripheral glucose uptake mechanisms consistent with the observed dose-dependent response.

The findings of this study align with previous research on *Mangifera indica*, which has demonstrated the plant's potential as an antidiabetic agent. (Khan et al., 2024) and (Zarasvand et al., 2023) also reported significant reductions in blood glucose levels in diabetes models following treatment with *Mangifera indica* extract, specifically in high doses. Additionally, the dose-response relationship observed in our study supports the findings of (Ramesh Petchi et al., 2011), who also found that higher doses of plant extracts lead to more significant effects in diabetic models. However, our study extends the existing knowledge by comparing the efficacy of *Mangifera indica* leaf extract with that of glibenclamide, demonstrating that the leaf extract has comparable effects in controlling blood glucose levels at higher doses, thus providing a new insight into the potential of *Mangifera indica* as a viable alternative to synthetic drugs.

The results of this study have important implications for developing alternative diabetes therapies. As diabetes continues to rise globally including in Indonesia where access to conventional medicines can be limited plant-based remedies such as *Mangifera indica* offer a promising, affordable, and accessible option. The observed reduction in blood glucose levels in STZ-induced diabetic mice suggests that this leaf extract may serve as a cost-effective complementary approach for managing type 2 diabetes, particularly in communities that face barriers to expensive pharmaceutical treatments. More broadly, these findings support ongoing efforts in natural product-based therapy development and encourage further exploration of plant-derived compounds with antidiabetic potential.

At the same time, the implications are both encouraging and cautious. On the positive side, *Mangifera indica* may provide a safer long-term alternative because it is associated with fewer side effects than synthetic drugs such as glibenclamide. However, additional research is needed to determine the most effective formulation (e.g., ethanol-based, water-based, or nanoherbal preparations) and to evaluate long-term safety and efficacy, especially in humans. Although the animal results are promising, clinical trials are essential to confirm effectiveness and safety in real-world populations. From a policy perspective, the findings

support increased funding for research on locally available plant-based therapies, consideration of validated natural remedies as complementary options in diabetes management guidelines for low-access regions, and stronger regulation and quality control if *Mangifera indica* is integrated into traditional medicine practices.

CONCLUSION

This study found that ethanol extract of *Mangifera indica* (Arum Manis mango leaf) can lower blood glucose levels in streptozotocin-induced male mice. Phytochemical screening identified bioactive compounds alkaloids, flavonoids, tannins, phenols, and steroids/triterpenoids that likely contribute to its antidiabetic effect. The extract reduced glucose significantly compared with the negative control in a dose-dependent manner, with 150 mg/kgBW showing the strongest effect. Although it was less effective than glibenclamide, the results indicate that *M. indica* leaf extract is a promising natural antidiabetic candidate.

This study contributes to the growing body of knowledge on plant-based therapies, providing insight into the antidiabetic potential of *Mangifera indica*, especially in its local variety, Arum Manis. It adds valuable data on the bioactive compounds in the leaf extract and their role in managing diabetes, offering a promising alternative to conventional treatments.

However, the study does have limitations. The research was conducted on an animal model, and the findings need to be verified in human clinical trials. Additionally, the long-term effects and optimal formulation of the extract (e.g., ethanol, water, or nanoherbal extracts) were not explored. Future studies should focus on clinical trials in humans and a deeper investigation into the mechanism of action and safety profile of *Mangifera indica* leaf extract.

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