Jurnal Kesehatan
Vol. 18, No. 2, September 2025, pp. 133~142
p-ISSN: 1979-7621, e-ISSN: 2620-7761, DOI: 10.23917/jk.v18i2.7244

The Effect of Mango Leaf Extract Administration on Fasting Blood Sugar Levels in Deksametason-Induced Mice

Aqilah Faizah Tola[1*], Syarifuddin Wahid[2], Indah Lestari Daeng Kanang[3], Prema Hapsari Hidayati[3], Andi Millaty Dirgahayu L[4]

[1]Medical Education Program, Faculty of Medicine, University of Muslim Indonesia
[2]Department of Anatomical Pathology, Faculty of Medicine, University of Muslim Indonesia, RSP Ibnu Sina YW- UMI
[3]Department of Pathology, Faculty of Medicine, University of Muslim Indonesia, RSP Ibnu Sina YW-UMI
[4]Department of Physiology, Faculty of Medicine, University of Muslim Indonesia, RSP Ibnu Sina YW-UMI

How to Cite: Tola, A. F., Wahid, S., Kanang, I. L. D., Hidayati, P. H., & Dirgahayu L, A. M. The Effect of Mango Leaf Extract Administration on Fasting Blood Sugar Levels in Deksametason-Induced Mice. Jurnal Kesehatan, 18(2), 133–142. https://doi.org/10.23917/jk.v18i2.7244

Article Information

Article History:
Submission: 23 November 2024
Revision: 26 May 2025
Reception: 25 June 2025

Keywords: Blood glucose, dexamethasone, mangiferin, plant extracts

ABSTRACT

Background: Mango leaves have anti-diabetic effects due to their high content of mangiferin. Mangiferin exerts its anti-diabetic effects by increasing the expression of GLUT4 and its translocation within muscle cells. The aim is to determine the effect of mango leaf extract *(Mangifera foetida)* on fasting blood glucose levels in mice previously induced with dexamethasone to elevate fasting blood glucose levels. **Method:** An experimental method with a *pre-test* and *post-test group control* design. The sample size was determined using the resource equation approach, with a total of 25 mice divided into five groups. Hyperglycemia was induced with dexamethasone at 1 mg/kg body weight per day for 7 days, followed by oral administration of mango leaf extract (150, 250, 350 mg/kg body weight per day) for 10 days. Fasting blood glucose levels were measured before and after induction, as well as on days 3, 7, and 10 of treatment. Statistical analysis was performed using multivariate methods. Data were analyzed using ANOVA, Post Hoc LSD, and Paired Sample T-Test. **Results:** There was a significant decrease in fasting blood glucose levels in mice before and after administration of mango leaf extract in group 2 (Mango leaf extract 150 mg/kg BW) with a p-value of 0.002, group 4 (Dexamethasone 1 mg/kg BW + Mango leaf extract 250 mg/kg BW) with a p-value of 0.001, and group 5 (Dexamethasone 1 mg/kg BW + Mango leaf extract 350 mg/kg BW) with a p-value of <0.001. **Conclusion:** Mango leaf extract (*Mangifera foetida)* can reduce fasting blood sugar levels in mice that have been induced.

Corresponding Authors: (*)
Medical Education Program, Faculty of Medicine, University of Muslim Indonesia, Jl. Urip Sumoharjo Km.05 Makassar, Makassar 90231

Email: aqilahtola@gmail.com

INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by hyperglycemia due to impaired insulin secretion, insulin action, or both (Banday, Sameer, and Nissar, 2020). DM is one of the major health problems in Indonesia. According to the *International Diabetes Federation* (IDF) Atlas 2017, Indonesia ranks sixth worldwide in the number of DM patients aged 20–79 years, with approximately 10.3 million people (Ministry of Health of the Republic of Indonesia, 2018).

DM management requires a long-term approach, including diet management, physical activity, self-monitoring of blood glucose, and the use of pharmacological therapies such as oral hypoglycemic agents or lifelong insulin (Banday, Sameer, and Nissar, 2020). However, long-term side effects and limited access to modern medications have driven the search for safer, more affordable, and effective natural-based alternatives.

One of the local plants with potential as an antidiabetic agent is the mango tree (*Mangifera indica*), which grows abundantly in Indonesia. In addition to its fruit, mango leaves are known to contain active compounds such as mangiferin, which has antihyperglycemic effects. Mangiferin works by increasing the expression and translocation of GLUT4 in muscle cells, thereby aiding in the absorption of blood glucose (Permatasari *et al.,* 2018). Young leaves contain the highest concentration of mangiferin, approximately 172 g/kg (Dacilia and Musfiroh, 2020).

Although several studies have revealed the antidiabetic potential of mangiferin, research on the efficacy of mango leaf extract against hyperglycemia specifically induced by insulin resistance, such as through dexamethasone exposure, remains limited. Dexamethasone is known to induce insulin resistance and hyperglycemia in experimental animals, making it a relevant model for evaluating diabetes mellitus (DM) therapy candidates (Gundala, Naidu, and Das, 2018).

This study aims to investigate the effect of mango leaf extract *(Mangifera foetida)* on fasting blood glucose levels in mice previously induced with dexamethasone to increase fasting blood glucose levels.

LITERATURE REVIEW

Diabetes Mellitus

Diabetes mellitus (DM) is a chronic disease characterized by hyperglycemia due to impaired insulin secretion, insulin action, or both. Diabetes mellitus (DM) has several categories, including type 1 DM, type 2 DM, and other types of DM. Type 1 diabetes mellitus typically develops in children or adolescents. Type 2 diabetes mellitus typically develops in adults due to prolonged hyperglycemia caused by an unhealthy lifestyle. Other types of diabetes mellitus include maturity-onset diabetes of the young (MODY), gestational diabetes, neonatal diabetes, and others (Sapra and Bhandari, 2023).

Mango Leaves as an Antidiabetic Agent

Mango leaves contain numerous beneficial compounds, one of which is polyphenols. Polyphenols are found in many plants, but mango fruits and leaves have higher concentrations. Long-term consumption of a diet rich in polyphenols protects against certain types of cancer, cardiovascular disease, type 2 diabetes, osteoporosis, pancreatitis, digestive issues, lung damage, and neurodegenerative diseases (Cory *et al.*, 2018). Mango leaves may have anti-diabetic effects, possibly due to the presence of phytochemicals such as phenolic compounds and flavonoids (Samanta, 2022). Among flavonoids, mangiferin has a unique structure compared to other flavonoids. Mangiferin belongs to the xanthone C-glycoside category, found in high quantities in higher plants and various parts of the mango fruit, such as the skin, stem, leaves, bark, and seeds. Mangiferin exerts its antidiabetic effects by increasing the expression of GLUT4 and its translocation into muscle cells. The highest mangiferin content in mango trees is found in young leaves (172 g/kg) (Girón *et al.*, 2009). In a study of mangiferin on STZ-induced high-fat diet mice, mangiferin was found to restore impaired glucose homeostasis and improve insulin sensitivity, as indicated by HOMA-IR and β-cell function, suggesting that it can reverse insulin resistance (Saleh *et al.*, 2014).

Mice (Mus musculus)

Mice are commonly used laboratory animals in research due to their low cost, ease of handling, short lifespan, adaptability, and rapid reproduction, which allow for the study of all stages of the life cycle. Additionally, mice share similarities with humans, such as DNA, genes, reproductive systems, nervous systems, diseases, and even fear responses. This is why mice are frequently used as experimental animals in research. Male mice are considered more stable hormonally than females, who experience hormonal changes during certain periods such as pregnancy and lactation. Male mice are also believed to have lower stress levels than females, making them less disruptive during experiments (Junaid *et al.*, 2024).

Dexamethasone-Induced Insulin Resistance

Dexamethasone is a synthetic glucocorticoid with an affinity approximately 50 times stronger than cortisol for glucocorticoid receptors. Clinically, dexamethasone is widely used due to its anti-inflammatory, anti-allergic, and immunosuppressive effects. However, long-term use or high doses can cause side effects such as muscle catabolism, increased appetite, fat accumulation, and insulin resistance (Gounarides *et al.*, 2008; Batista *et al.*, 2024). Insulin resistance caused by dexamethasone occurs through several mechanisms, including increased glucagon levels that trigger gluconeogenesis in the liver and muscles, and reduced expression of IRS-1 and PKB, which inhibit the translocation of GLUT4 to the cell membrane, thereby reducing glucose uptake by cells (Rachmansyah, Junaidi, and Efendi, 2020).

Various studies have demonstrated that dexamethasone induction is effective in creating hyperglycemic conditions resembling type 2 diabetes mellitus (Rachmansyah, Junaidi, and Efendi, 2020). indicates that mice injected with 10 mg/kg body weight of dexamethasone subcutaneously for 10 days exhibited increased blood glucose levels. Tayate et al (2012) reported that mice induced with dexamethasone 1 mg/kg intramuscularly for 7 days experienced increased glucose and triglyceride levels, as well as weight loss. Similar findings were reported by Md. Shalam, M.S Harish, and S.A Farhana, (2006) in Wistar rats induced with dexamethasone 10 mg/kg body weight subcutaneously per day for 10 days, showing significant increases in glucose and triglyceride levels, as well as weight loss. These findings support the use of dexamethasone as a model for inducing insulin resistance in experimental studies related to diabetes.

METHOD

The study is an experimental study using a *pre-test and post-test group control* design. The study will be conducted at the Faculty of Medicine, University of Muslim Indonesia, and the Faculty of Pharmacy, University of Muslim Indonesia, in August-September 2024.

This study used male mice (*Mus musculus*) as research subjects because they are more hormonally stable than female mice. The number of test animals in this study was determined using the *resource equation* approach for preliminary studies. This method considers *the degrees of freedom of error* in analysis of variance (ANOVA), with a recommended range of 10 to 20 to ensure adequate statistical validity. In this study, there are 5 treatment groups, each containing 5 mice, resulting in a total of 25 mice used. The degrees of freedom are calculated using the formula:

$$E = N - G$$

$$E = 25 - 5 = 20$$

Where E is the degrees of freedom for error, N is the total number of animals (25), and G is the number of groups (5). E = 20 is within the upper limit of the recommended range, so this design is considered adequate according to the resource equation approach. This approach also aligns with the 3R principles (Replacement, Reduction, Refinement) in animal research ethics, which aim to minimize the number of animals used without compromising data quality.

The inclusion criteria for this study were mice that were not defective, adult males, with a body weight of 20–40 grams. Meanwhile, the exclusion criteria were mice that experienced weight loss during adaptation, while the *dropout* criteria included mice that died during the study and mice that did not show an increase in blood glucose levels after dexamethasone induction for seven days.

The equipment used in this study included animal cages with accessories, a glucometer, restrainer, syringe, scissors, analytical scale, oral probe, gloves, filter paper, oven, beaker, stirrer, mortar, and rotary evaporator. The materials used included mango leaves (*Mangifera foetida),* 95% ethanol, male mice, dexamethasone, and mouse pellets. Mango leaf extract was prepared using the maceration technique with 95% ethanol.

Mango leaf extract was obtained through a maceration process, in which dried and ground leaves were soaked in ethanol for one week with periodic stirring. The solution is then filtered and evaporated using a rotary evaporator until a concentrated extract is obtained. Before treatment, male mice were acclimatized for one week, then induced with dexamethasone 1 mg/kg body weight (BW) per day via intramuscular injection for seven days to induce insulin resistance. Fasting blood glucose levels (FBG) were measured before and after induction to confirm an increase in glucose levels. The mice were then divided into five groups: control, 150 mg/kg body weight extract, combination of dexamethasone and 150 mg/kg body weight extract, combination of dexamethasone and 250 mg/kg body weight extract, and combination of dexamethasone and 350 mg/kg body weight extract. The treatment was administered orally for ten days, and GDP measurements were taken on days 3, 7, and 10 after a 5–6-hour fast to evaluate the glucose-lowering effects of mango leaf extract.

The research data were analyzed using SPSS 17.0. The analysis began with a normality and homogeneity test of the data to determine the appropriate statistical method. If the data were normally distributed and homogeneous, analysis was performed using a One-Way ANOVA test to compare the mean fasting blood glucose levels (FBG) between groups, followed by a Post Hoc Least Significant Difference (LSD) test to identify specific differences between groups. If the data were not normally distributed, a non-parametric Kruskal-Wallis test was used. Additionally, the Paired Sample T-Test is used to assess the effectiveness of the treatment within each group by comparing FBG levels before and after the administration of mango leaf extract.

This research has obtained ethical approval from the Research Ethics Committee of the University of Muslim Indonesia with registration number: UMI012406360.

RESULTS AND DISCUSSION

In this study, a comparative analysis of the percentage decrease in fasting blood glucose levels in mice was conducted using the One-Way ANOVA method. Prior to the analysis, assumption tests were performed. The results of the Shapiro-Wilk normality test showed a p-value >0.05, indicating that the data were normally distributed. Additionally, the Levene Test for homogeneity of variances also yielded a p-value >0.05, indicating that the data had homogenous variation ( ). With both assumptions met, the data were deemed suitable for statistical analysis using One-Way ANOVA.

Table 1. One-Way ANOVA Test.

Group	Intervention	n	Mean± SD	p
1	Control, no mango leaf extract administered	5	152.60 ± 17.785	<0.001
2	Extract dose 150 mg/kg BW/day	5	92.80 ± 10.257	
3	Extract dose 150 mg/kg BW/day and dexamethasone 1 mg/kg BW/day	5	150.80 ± 11.883	
4	Extract dose 250 mg/kg BW/day and dexamethasone 1 mg/kg BW/day	5	103.60 ± 9.990	
5	Extract dose 350 mg/kg BW/day and dexamethasone 1 mg/kg BW/day	5	81.20 ± 14.890	
Total		25	116.20 ± 32.790	

Based on Table 1, it can be seen that Group 2 (92.80 ± 10.257), Group 4 (103.60 ± 9.990), and Group 5 (81.20 ± 14.890) have lower average GDP levels compared to Group 1 (152.60 ± 17.785) and Group 3 (150.80 ± 11.883), which have higher average GDP levels. Significant differences were also observed between groups with p-values <0.001, indicating that mango leaf extract has an effect on GDP levels in mice across groups.

Next, a comparison of the average fasting blood sugar levels of mice in each group was conducted using the Post Hoc Test Least Significant Difference (LSD) to determine which groups differed specifically. The results of the Post Hoc Test LSD with an asterisk (*) on *the mean difference* or average difference indicate significant differences between groups with $p < 0.05$.

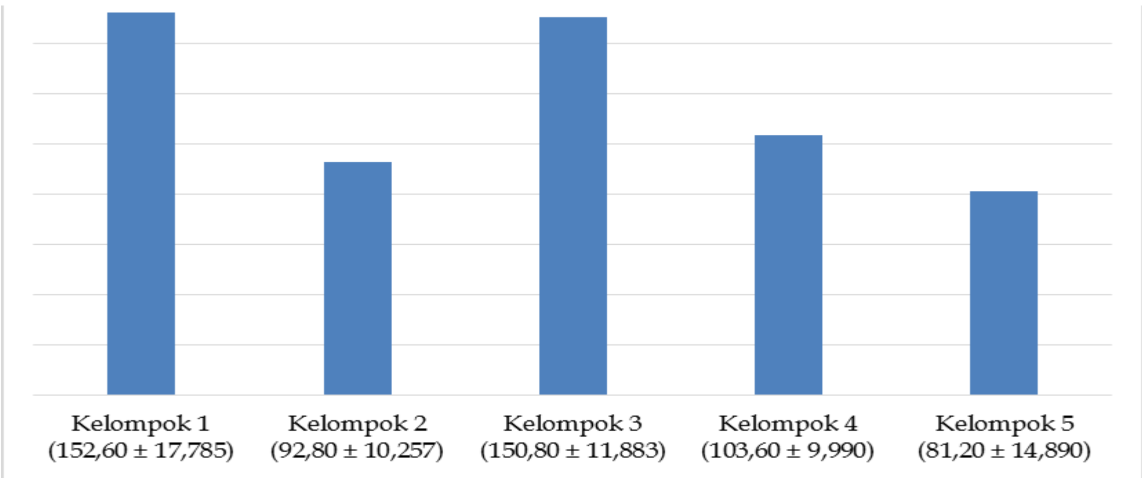

Figure 1. Average GDP levels per group

Based on the Post Hoc LSD test, group 1 had the highest average GDP levels, significantly different from group 2 (p < 0.001), group 4 (p < 0.001), and group 5 (p < 0.001), but not from group 3 (p = 0.833) due to similar averages. Group 2 showed significantly lower GDP than group 1 (p < 0.001) and group 3 (p < 0.001), with no significant difference from group 4 (p = 0.214) or group 5 (p = 0.183). Group 3 had significantly higher GDP than group 2 (p < 0.001), group 4 (p < 0.001), and group 5 (p < 0.001), but did not differ from group 1 (p = 0.833). Group 4 showed significantly lower GDP than group 1 (p < 0.001) and group 3 (p < 0.001), but significantly higher than group 5 (p = 0.015) and not different from group 2 (p = 0.214). Finally, group 5 had the lowest GDP, significantly lower than group 1 (p < 0.001), group 3 (p < 0.001), and group 4 (p = 0.015), with no significant difference from group 2 (p = 0.183). Following the Post Hoc LSD analysis, a Paired Sample T-Test was conducted to compare fasting blood sugar levels in mice before (post-dexamethasone administration) and after (day 10) treatment (Picture 1).

Table 2. Paired Sample T-Test.

		N	Mean ± SD	Percentage of Decrease (%)	p
Pair 1	**Pre-Post Group 1** Not given mango leaf extract	5	-6,000±6,633	-	0
Pair 2	**Pre-Post Group 2** Mango leaf extract 150 mg/kg BW	5	55.200±16.208	37	0
Pair 3	**Pre-Post Group 3** Dexamethasone 1 mg/kg body weight + Mango leaf extract 150 mg/kg body weight	5	0.200±11.819	0.13	0
Pair 4	**Pre-Post Group 4** Dexamethasone 1 mg/kg BW + Mango leaf extract 250 mg/kg BW	5	46,000±12,689	30.7	0
Pair 5	**Pre-Post Group 5** Dexamethasone 1 mg/kg body weight + Mango leaf extract 350 mg/kg body weight	5	64,800±10,640	44.3	<0.001

Based on Table 2, a p-value of <0.05 was obtained in the *pre-post test* results for Groups 2, 4, and 5, indicating a significant difference in fasting blood glucose levels ( ) between the *pre-test* and *post-test* data. Additionally, the pre-post test results for Groups 1 and 3 showed no significant difference, as the p-value was >0.05. Based on the results obtained in Table 5, it can be concluded that the administration of mango leaf extract has an effect on reducing fasting blood sugar levels in mice in group 2 (mango leaf extract 150 mg/kg BW), group 4 (Dexamethasone 1 mg/kg BW + mango leaf extract 250 mg/kg BW), and group 5 (Dexamethasone 1 mg/kg BW + Mango Leaf Extract 350 mg/kg BW).

DISCUSSION

The Effect of Dexamethasone Administration on Fasting Blood Glucose Levels in Mice

Dexamethasone is a synthetic non-selective glucocorticoid drug commonly administered due to its anti-inflammatory, anti-allergic, and immunosuppressive properties. Long-term administration of dexamethasone can lead to the formation of free radicals such as superoxide, hydrogen peroxide, and hydroxyl radicals, which contribute to oxidative stress activation and impair insulin function and secretion. This can result in the onset of type 2 diabetes mellitus (Batista *et al.*, 2024) .In a study by Tayade PM using mice as experimental animals, mice were administered dexamethasone at 1 mg/kg intramuscularly daily for 7 days. After 7 days of induction, the mice were divided into several groups. For some groups, dexamethasone administration was continued until the end of the study. The results showed that dexamethasone administration in mice caused an increase *in plasma glucose levels, serum triglyceride levels,* and a decrease in body weight.(Tayade *et al.*, 2012) Based on the results obtained, it was proven that dexamethasone can increase fasting blood sugar levels with a p-value <0.001, indicating a significant difference in fasting blood sugar levels before and after dexamethasone induction. This was also supported by the increase in average fasting blood sugar levels after dexamethasone administration. The average fasting blood sugar level of mice before dexamethasone administration was 132.24 ± 23.349, and the average fasting blood sugar level after administration was 148.24 ± 16.576, with a percentage increase of 12.09% in the average level before and after dexamethasone administration.

Stopping dexamethasone administration after induction for 7 days, as in groups 1 and 2, can cause reversible effects, meaning that elevated blood glucose levels can return to normal after dexamethasone induction is discontinued. However, the body requires time to restore insulin sensitivity and glucose levels to normal. In the study results (Rafacho *et al.*, 2010), adverse morphophysiological changes caused by dexamethasone, such as insulin resistance in the endocrine pancreas, were reversible after 5 days of dexamethasone induction followed by discontinuation for 10 days. In this study, the duration of dexamethasone induction was longer, at 7 days, which may require a longer recovery time.

The Effect of Mango Leaf Extract Administration on Fasting Blood Glucose Levels

This blood sugar-lowering effect is consistent with previous studies reporting that mango leaves contain active compounds that can lower blood sugar levels, such as phenolics and flavonoids. Mango leaves can lower blood sugar levels in several ways, such as by inhibiting α-glucosidase and α-amylase, key enzymes responsible for the digestion of dietary carbohydrates into glucose. Phenolic acids can also regulate postprandial glycemia and inhibit the development of glucose intolerance through insulin-facilitated responses and weakened secretion of insulin-tropic polypeptide and GLP-1-dependent insulin (Vinayagam, Jayachandran, and Xu, 2016).

In a study (Permatasari *et al.*, 2018), mango leaves, particularly the young leaves, contain mangiferin, a flavonoid compound that can lower blood sugar levels. Mangiferin exerts its antidiabetic effects by increasing the expression and translocation of GLUT4 in muscle cells. The highest mangiferin content in mango trees is found in young leaves (172 g/kg). (Dacilia and Musfiroh, 2020)

Based on the results obtained, there was a decrease in fasting blood sugar levels in the group treated with mango leaves compared to the control group, which was only induced with dexamethasone without mango leaf treatment. This can be proven by the Post Hoc LSD test results, which show significant changes in groups 2, 4, and 5. Meanwhile, in group 3, there were no significant changes compared to the control group.

Group 5, which was given dexamethasone and mango leaf extract at a dose of 350 mg/kg BW, had the lowest average fasting blood sugar level at 81.20 ± 14.890. Group 2, which received only mango leaf extract at a dose of 150 mg/kg BW, had an average fasting blood sugar level of 92.80 ± 10.257. Group 4, which was given dexamethasone and mango leaf extract at a dose of 250 mg/kg BW, had the third-lowest average blood sugar level, which was 103.60 ± 9.990. Finally, Group 1, which was not given mango leaf extract

(*Mangifera foetida)* and Group 3, which received dexamethasone and mango leaf extract at a dose of 150 mg/kg BW, had fasting blood glucose levels that were not significantly different, at 152.60 ± 17.785 (Group 1) and 150.80 ± 11.883 (Group 3).

In the Post-Hoc LSD test comparing group 2 (mango leaf extract 150 mg/kg BW) with group 3 (dexamethasone induction 1 mg/kg BW + mango leaf extract 150 mg/kg BW), there was a significant difference. The average GDP levels in group 2 were significantly lower than those in group 3, indicating that dexamethasone induction further exacerbated insulin sensitivity, rendering the administration of mango leaf extract at a dose of 150 mg/kg BW ineffective in reducing GDP levels in mice. Higher doses are required to reduce GDP levels in mice, specifically 250 mg/kg BW and 350 mg/kg BW.

In addition, it can also be proven that mango leaf extract has been shown to reduce fasting blood sugar levels in mice that have been previously induced with dexamethasone. This can be demonstrated by the results of the Paired Sample T-Test in Table 2, which show significant changes between pre-test and post-test in Group 2 (Mango leaf extract 150 mg/kg BW), Group 4 (Dexamethasone 1 mg/kg BW + Mango leaf extract 250 mg/kg BW), and group 5 (Dexamethasone 1 mg/kg BW + Mango Leaf Extract 350 mg/kg BW) with a p-value <0.05. Therefore, it can be concluded that Hypothesis 1, which states that mango leaf extract affects the reduction of fasting blood glucose levels in mice, is proven true, with the optimal dose for reducing fasting blood glucose levels being 350 mg/kg BW.

However, it should also be noted that the reduction in fasting blood glucose levels observed in this study may have been influenced by other factors such as the dose of the extract, the effects of stress, *the rebound effect* of dexamethasone causing blood glucose levels to rise after discontinuation before eventually decreasing, and other factors**.**

Limitations of the Study and Recommendations

This study has several limitations, including the absence of insulin level measurements or the HOMA-IR index, which could provide more detailed information about insulin resistance levels. Additionally, animal stress factors, the potential rebound effect after dexamethasone discontinuation, and individual variations in mice's response to treatment may also influence the results. The duration of post-dexamethasone induction observation may also be insufficient to fully evaluate the blood glucose recovery process.

For further research, it is recommended to measure additional parameters such as insulin levels, GLUT4 expression, and oxidative stress biomarkers to support the proposed mechanism. Toxicity testing of mango leaf extract should also be conducted to ensure its long-term safety. Additionally, further studies with longer treatment durations and more varied doses will help optimize the therapeutic potential of mango leaves as a natural antidiabetic agent.

CONCLUSION

Based on the results of the study titled "The Effect of Mango Leaf Extract Administration on Fasting Blood Glucose Levels in Dexamethasone-Induced Mice," it was concluded that the average fasting blood glucose level of mice before dexamethasone administration was 132.24 mg/dl and after dexamethasone administration was 148.24 mg/dl, therefore, it can be concluded that dexamethasone induction at a dose of 1 mg/kg body weight in mice can increase fasting blood sugar levels in mice. Discontinuing dexamethasone induction and administering low-dose mango leaf extract (150 mg/kg BW) can reduce fasting blood sugar levels in mice, whereas continuous dexamethasone induction with the same dose of mango leaf extract cannot reduce fasting blood sugar levels. If dexamethasone induction is performed continuously, a high dose of mango leaf extract (350 mg/kg BW) is required to reduce fasting blood glucose levels in mice.

This study indicates that mango leaf extract has potential as a natural antidiabetic agent, particularly in conditions of hyperglycemia caused by glucocorticoids. However, to support clinical application, further studies are needed, including toxicity testing, identification of the optimal dose, and additional testing on other animal models and clinical trials in humans to assess its efficacy, safety, and bioavailability more comprehensively.

ACKNOWLEDGEMENT

The authors would like to express their sincere gratitude to the Faculty of Medicine, University of Muslim Indonesia, for the facilities and academic support provided during the completion of this study. Special thanks are also extended to all laboratory staff for their technical assistance and to colleagues in the Medical Education Program for their valuable input throughout the research process.

REFERENCES

Banday, M.Z., Sameer, A.S. and Nissar, S. (2020). Pathophysiology of diabetes: An overview. *Avicenna Journal of Medicine*, 10(04), pp. 174–188. Available at: https://doi.org/10.4103/ajm.ajm_53_20.

Batista, E.K. *et al.* (2024) Dexamethasone-Induced Insulin Resistance Attenuation by Oral Sulfur–Oxidovanadium (IV) Complex Treatment in Mice. *Pharmaceuticals*, 17(6), p. 760. Available at: https://doi.org/10.3390/ph17060760.

Kementrian Kesehatan RI (2018) Cegah, Cegah, dan Cegah: Suara Dunia Perangi Diabetes. in. Available at: https://www.kemkes.go.id/article/view/18121200001/prevent-prevent-and-prevent-the-voice-of-the-world-fight-diabetes.html (Accessed: 11 June 2023).

Cory, H. *et al.* (2018). The Role of Polyphenols in Human Health and Food Systems: A Mini-Review. *Frontiers in Nutrition*. Frontiers Media S.A. Available at: https://doi.org/10.3389/fnut.2018.00087.

Dacilia H, B. and Musfiroh, I. (2020). *Review Artikel: Pemanfaatan Daun Mangga (Mangifera Indica L.) Sebagai Obat Herbal Untuk Diabetes Mellitus*.

Girón, M.D. *et al.* (2009). Salacia oblonga extract increases glucose transporter 4-mediated glucose uptake in L6 rat myotubes: Role of mangiferin. *Clinical Nutrition*, 28(5), pp. 565–574. Available at: https://doi.org/10.1016/j.clnu.2009.04.018.

Gounarides, J.S. *et al.* (2008). Effect of dexamethasone on glucose tolerance and fat metabolism in a diet-induced obesity mouse model. *Endocrinology*, 149(2), pp. 758–766. Available at: https://doi.org/10.1210/en.2007-1214.

Gundala, N.K.V., Naidu, V.G.M. and Das, U.N. (2018). Amelioration of streptozotocin-induced type 2 diabetes mellitus in Wistar rats by arachidonic acid. *Biochemical and Biophysical Research Communications*, 496(1), pp. 105–113. Available at: https://doi.org/10.1016/j.bbrc.2018.01.007.

Junaid, N.M. *et al.* (2024). Pengaruh Puasa 12 Jam Terhadap Kadar Glukosa Darah Puasa dan Berat Badan Pada Mencit (Mus Musculus) Hiperglikemia Induksi Aloksan. *MAHESA : Malahayati Health Student Journal*, 4(7), pp. 2986–2998. Available at: https://doi.org/10.33024/mahesa.v4i7.14787.

Md. Shalam, M.S Harish and S.A Farhana (2006). Prevention of dexamethasone- and fructose-induced insulin resistance in rats by SH-01D, a herbal preparation. *Indian*

J Pharmacol, 38(6), pp. 419–422. Available at: https://doi.org/https://doi.org/10.4103/0253-7613.28209.

Permatasari, S. *et al.* (2018). Pucuk Daun Mangga (Mangifera indica L.) Kultivar Cengkir Sebagai Penurun Kadar Glukosa Darah. *Jurnal Biologi dan Pembelajaran Biologi*, 3(2). Available at: http://jurnal.unmuhjember.ac.id/index.php/BIOMA.

Rachmansyah, M.S., Junaidi, E. and Efendi, E. (2020). Penurunan Kadar Glukosa Darah oleh Cuka Apel pada Mencit yang diinduksi Deksametason, Journal of Agromedicine and Medical Sciences. *Journal of Agromedicine and Medical Sciences*, 6(3). Available at: : https://doi.org/10.33024/jams.v7i8.15419

Rafacho, A. *et al.* (2010). The adaptive compensations in endocrine pancreas from glucocorticoid-treated rats are reversible after the interruption of treatment. *Acta Physiologica*, 200(3), pp. 223–235. Available at: https://doi.org/10.1111/j.1748-1716.2010.02146.x.

Saleh, S. *et al.* (2014). Modulation of diabetes and dyslipidemia in diabetic insulin-resistant rats by mangiferin: Role of adiponectin and TNF-α. *Anais da Academia Brasileira de Ciencias*, 86(4), pp. 1935–1947. Available at: https://doi.org/10.1590/0001-3765201420140212.

Samanta, S. (2022). Anti-diabetic activity of mango (Mangifera indica): a review. Available at: https://doi.org/10.15406/mojbb.2019.06.00131.

Tayade, P.M. *et al.* (2012). Effect of Psoralea corylifolia on dexamethasone-induced insulin resistance in mice. *Journal of King Saud University - Science*, 24(3), pp. 251–255. Available at: https://doi.org/10.1016/j.jksus.2011.03.007.

Vinayagam, R., Jayachandran, M. and Xu, B. (2016). Antidiabetic Effects of Simple Phenolic Acids: A Comprehensive Review. *Phytotherapy Research*. John Wiley and Sons Ltd, pp. 184–199. Available at: https://doi.org/10.1002/ptr.5528.