https://doi.org/ 10.33472/AFJBS.6.Si2.2024.681-687

The Effect Of Administration Of Mangosteen Peel Extract On Reducing Blood Glucose Levels In Experimental Animals Induced Hyperglycemia

Novera Herdiani[1]*, Bambang Wirjatmadi[2], Kuntoro[3], Agus Aan Adriansyah[4]

[1]Doctoral Program of Public Health, Faculty of Publich Health, Universitas Airlangga, Surabaya, Indonesia
[2,3]Faculty of Public Health, Universitas Airlangga, Surabaya, Indonesia
[4]Department of Public Health, Faculty of Health, Universitas Nahdlatul Ulama Surabaya, Indonesia
**Corresponding author: novera.herdiani-2019@fkm.unair.ac.id*
Orchid ID : 0000-0002-4830-9037

Article History
Volume 6,Issue Si2, 2024
Received:10 Mar 2024
Accepted : 11 Apr 2024
doi: 10.33472/AFJBS.6.Si2.2024.681-687

Abstract
Diabetes Mellitus (DM) is a major health problem worldwide. DM with poor control of blood glucose levels can eventually cause pancreatic cell disorders, including a decrease in cell mass and function. Mangosteen rind contains xanthone compounds that can be used to protect and reduce cell damage, especially those caused by free radicals. This study aimed to analyze the effect of mangosteen peel on decreasing blood glucose in a streptozotocin-induced diabetes mellitus model.

The research carried out is experimental in the laboratory. The research design used was Randomized Post Test Only Control Group Design. Samples were 24 male Wistar rats. Rats were grouped into 6 groups, namely negative control group, positive control STZ, positive control STZ and metformin, mangosteen peel extract at a dose of 200 mg/kg body weight (P1), a dose of 400 mg/kg body weight (P2), and a dose of 600 mg/kg body weight (P3). Administration of therapy for 14 days orally.

The results of the treatment group with a dose of 600mg/kgbw mangosteen rind extract had the lowest fasting blood glucose level of 81 mg/dL, the P2 group at a dose of 400mg/kgbw had a higher fasting blood glucose level of 135 mg/dL, blood glucose levels 136 mg/dL at the P1 dose of treatment 200mg/kgbw. Based on the test using the general linear Manova model, a significance value was obtained, namely $p = 0.000$ ($p < 0.05$) there was a difference in the average fasting blood sugar level of each group after being treated with mangosteen peel extract.

The conclusion of the dose of mangosteen rind extract had an effect on decreasing blood glucose levels with an effective dose of 600 mg/kgbw. This research can provide information to the public about the benefits of mangosteen peel can be developed as an alternative treatment in humans caused by oxidative stress.

Keywords : Diabetes, Glucose, Mangosteen, Streptozotocin

1.Introduction

Diabetes Mellitus (DM) is a major health problem worldwide. DM is a group disease marked metabolic with hyperglycemia consequence of existence disturbance of insulin secretion, insulin activity, or both (Kangralkar et al., 2010). Related DM with inflammatory process occurs. Cytokines' proinflammatory damage could influence insulin sensitivity and the function of pancreatic beta cells. The pathogenesis of diabetes mellitus type 2 is marked by metabolic disturbance, that is, the drop response network peripheral in response to insulin (insulin resistance) (Kumawat et al., 2009). Damage to network peripheral suspected consequence from existing enhancement radical free in the body destroys insulin receptors or glucose transporters on the cell membrane. Radical free in excess amount will oxidize and attack membrane lipid components cell, so that occur lipid peroxidation. To dampen damage caused radical free antioxidants are needed (Jusman & Halim, 2010).

According to the International Diabetes Federation (IDF), it states: that on 2005 in, world There were 200 million (5.1%) people with diabetes (diabetes), and supposedly, in 20 years then, is 2025, it will increase to 333 million (6.3%) people (Atlas, 2015). So by 2030, Indonesia will have people with DM (diabetics) as many as 21.3 million people (Kusumawardani et al., 2018). Results Riskesdas 2018 in Indonesia shows an increased prevalence of DM from 6.9% in 2015 to 8.5% in 2018. DM with control rate glucose blood that doesn't look good on finally could cause pancreatic disturbance cells, among other things occur drop mass cell and its function (Ma et al., 2012).

Based on previous research (Widowati et al., 2018), herbal medicine from skin fruit mangosteen on patients with diabetes mellitus can control the rate of blood sugar. Other studies have been carried out in states that skin fruit mangosteen proved effective in lowering glucose blood (Chen et al., 2021). Mangosteen peel extract contains polyphenols, especially xanthones, which have natural abilities (Panda et al., 2013). Xanthones, phenols, and flavonoids in the mangosteen rind extract are thought to have the ability to work as anti-oxidation capable of reducing the negative impact of damage in the body due to free radical compounds or Reactive Oxygen Species (ROS). Xanthones bind unstable free oxygen, namely free radicals that destroy cells in the body, so that xanthones can inhibit the process of cell degradation or damage (Watanabe et al., 2018). Most studies examine blood glucose, but the problem is that it is not clear whether the mangosteen rind can lower blood glucose through mechanisms that occur simultaneously in the body (Xie et al., 2015). So required something compound active from extract ingredient nature that has through the separation process and purification that has been determined the dose through test pre-clinical (test) try to animal for knowing level security, so that still need to conduct a study on an animal toy mouse.

Related to the above problem, then need to search for something therapy support that can speed up recovery and reduce the number of complications in people with diabetes mellitus. Study this to see how it affects skin mangosteen to drop glucose blood. Study use skin mangosteen for Diabetes Mellitus therapy in man still very limited, so as Step beginning test for knowing the benefits gift skin fruit mangosteen to glucose blood will more formerly conduct development on animal try rat Wistar.

2. Materials and methods

This research is a *true experimental study* using a completely randomized design with a *randomized posttest-only control group design approach*. The research was conducted at the experimental animal laboratory, Universitas Airlangga Surabaya, with Ethical Approval No. 655/HRECC.FODM/VIII/2022. The research design used is Randomized Post Test Only Control Group Design. The research sample was taken randomly from an affordable population with inclusion criteria: white male rats, Wistar strain, aged ± three months, weighing between

175 -200 g, and in healthy condition (active and not disabled). Meanwhile, the exclusion criteria for the study sample were decreased body weight (less than 100 g), rats did not move actively, and rats dying during the study. Big B samples for each group were four rats, so the number of rats used in this research as much as 24 tails.

Rat grouped into six groups that is group control negative (KN), control STZ positive (K1), control positive for STZ and metformin (K2), extract skin mangosteen a dose of 200 mg/ kg body weight (P1), a dose of 400 mg/ kg body weight (P2), a dose of 600 mg/ kg body weight (P3). The dose of metformin in humans is 500 mg/per 50 kg body weight. Dose Streptozotocin (STZ) used is dose single 45 mg/kg body weight used for induce rat white male (Rattus norvegicus) intraperitoneally for get animal treatment on glucose blood already shows the Diabetes Mellitus model (Zafar & Naqvi, 2010).

The blood sugar of mice is to be checked using a digital glucometer. The blood of the rats to be examined was taken through a vein using the tail-cutting method-measurement of hyperglycemia four days after Streptozotocin (STZ) induction. In addition, measurement of fasting blood glucose at the time of therapy was carried out on the 7th and 14th days. Mice with a hyperglycemic state during fasting had fasting blood sugar levels >135 mg/dL (Paula et al., 2022).

The instrument used to measure white rats' blood glucose was an Easy Touch® GCU glucometer and an Easy Touch® glucose test strip. Equipment for weighing rats using a Camry digital scale in grams. The statistical analysis used to test the normality of the data is the *Kolmogorov Smirnov One Sample test*. To find out the difference in treatment of each dependent variable, an analysis with *Tukey HSD was conducted* using a 95% confidence level if there is a significant difference ($p < 0.05$) followed by a comparison test of the mean of each treatment group with the *Manova test.*

3. Results and discussion

The average fasting blood glucose levels after STZ induction in each group can be seen in table I. Based on table I, it can be seen that the average fasting blood glucose (GDP) levels of experimental animals after STZ induced increased beyond the normal limit (> 126 mg/dl). The highest average GDP levels were found in the CMC-Na (K1) solvent treatment group, 300 ± 102.32 mg/dL.

Table 1. Mean and Standard Deviation of Pre-Fasting Blood Glucose Level (GDP Pre) Control Group and Treatment Group

Group	n	Mean ± SD	Min	Max
K N	4	89^{a} ± 2.94 mg/dL	87	94
K1	4	300^{c} ± 102.32 mg/dL	222	440
K2	4	199^{b} ± 1 4.79 mg/dL	186	2 14
P1	4	187^{ab} ± 23.33 mg/dL	165	220
P2	4	209^{bc} ± 19.75 mg/dL	190	232
P3	4	204^{bc} ± 15.94mg/dL	188	220

The average fasting blood glucose levels after being treated with mangosteen peel extract in each group can be seen in table 2. Table 2 shows that the average fasting blood glucose (GDP) level of experimental animals after being treated with mangosteen peel extract with different doses showed that the average fasting blood sugar level decreased, and the lowest average fasting blood sugar level was in the group. P3 was given mangosteen peel extract at a dose of 600 mg/kg BW.

Table 2. Average and Standard Deviation Rate Glucose Fasting Blood Post (GDP Posts) Control Group and Treatment Group

Group	n	Mean ± SD	Min	Max
K N	4	86^{a} ± 2.00 mg/dL	86	90

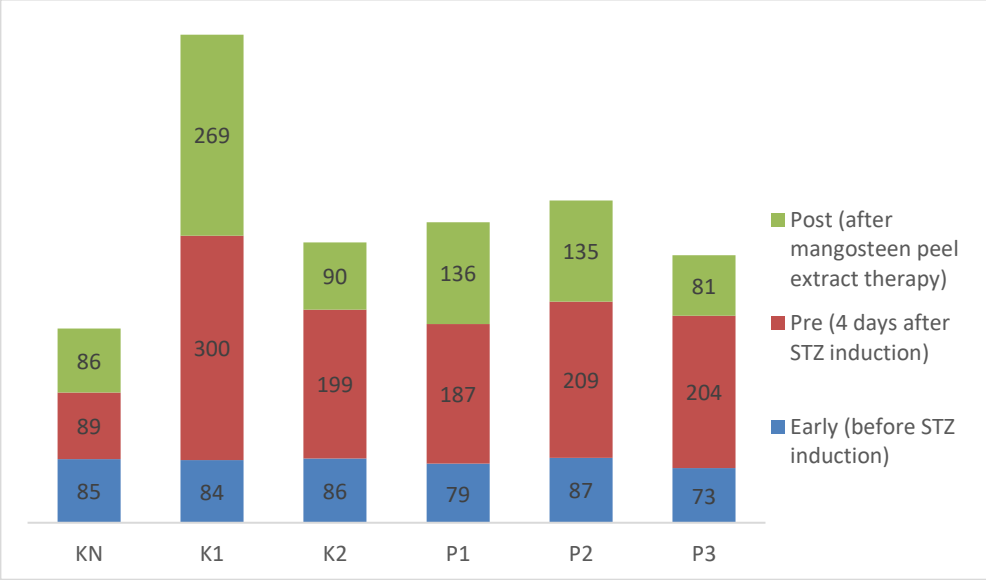
K1	4	269^{b} ± 97.79 mg/dL	196	402
K2	4	90^{a} ± 14.90 mg/dL	77	112
P1	4	136^{a} ± 32.99 mg/dL	85	172
P2	4	135^{a} ± 30.97 mg/dL	99	166
P3	4	81^{a} ± 3.20 mg/dL	79	85

Based on the test using the *general linear manova model*, which was analyzed with *Wilks' Lambda*, a significance value was obtained, namely $p = 0.000$ ($p < 0.05$), which means that there is a difference in the average fasting blood sugar level of each group after being treated with skin extract Mangosteen. To test the difference in fasting blood glucose levels after being given mangosteen peel extract between the control group and the treatment group, the *Tukey HSD test was carried out* with a 95% confidence level, the results of which can be seen in table 3 below.

Table 3. Score P Value Test Tukey HSD Rate Glucose Blood Post Each Group

Group	KN	K1	K2	P1	P2	P3
K N	-	-	-	-	-	-
K1	0.000	-	-	-	-	-
K2	1,000	0.000*	-	-	-	-
P1	0.635	0.006*	0.691	-	-	-
P2	0.658	0.006*	0.713	1,000	-	-
P3	1,000	0.000*	1,000	0.526	0.550	-

Table 3 shows significant differences in fasting blood glucose levels after treatment, with p < (0.05) being K1 different from K0, K2, P1, P2, and P3. Seeing the differences in the interaction of fasting blood glucose for each treatment given to each group can be seen in the following figure 1



Based on the picture above in figure 1, there are differences between initial fasting blood sugar, post- STZ fasting blood sugar, and mangosteen peel extract fasting blood sugar. The lowest fasting blood sugar levels in all control and treatment groups were initial fasting blood sugar, indicating that the experimental animals' blood sugar was still normal because they were not treated. However, there was a difference between the fasting blood sugar of experimental animals that had received STZ treatment and mangosteen peel extract. The

fasting sugar level of mangosteen peel extract was lower than post-STZ fasting blood sugar levels. This shows a decrease in sugar levels after administering mangosteen peel extract.

To see the difference in the interaction of mangosteen peel extract at each dose of P1 at a dose of 200mg/kg BW mangosteen peel extract, P2 at a dose of 400mg/kg BW, P3 at a dose of 600mg/kg BW can be seen in the graphic above figure 1. Based on the picture above in figure 1, there are differences in the dose of mangosteen peel extract that affects fasting blood glucose levels. For example, the P3 treatment group with a dose of 600mg/kg BW had the lowest fasting blood glucose level of 81 mg/dL. On the other hand, in the P2 group, mangosteen peel extract with a dose of 400mg/kg BW fasting blood glucose levels was higher at 135 mg/dL, and the highest blood glucose level was 136 g/dL in the treatment group P1 with a dose of mangosteen peel extract 200mg/kg BW.

This study examined blood glucose levels three times, namely, after acclimatization, STZ induction, and treatment. The initial fasting blood glucose level examination was carried out after acclimatization or before STZ induction to ensure that experimental animals did not experience hyperglycemia before STZ was induced. Furthermore, after STZ was induced, pre-treatment fasting blood glucose levels were checked to ensure that the experimental animals were hyperglycemic before being treated with mangosteen peel extract.

The results showed that the group that was given mangosteen peel extract P1 200mg/kg BW, P2 400mg/kg BW and P3 600mg/kg BW experienced a decrease in blood glucose levels. The highest decrease in blood glucose levels occurred in the group given mangosteen peel extract at a dose of 600mg/kg BW (P3), close to that of the metformin (K2) group. However, in the mangosteen rind extract group (P1 and P2), blood glucose levels decreased but were higher than the 600mg/kg BW (P3) dose group. Several things can cause this condition. Firstly, the biological conditions of the experimental animals in receiving treatment in the form of mangosteen peel extract are different, affecting the results given. Second, when consumed at high doses, the high antioxidant content of mangosteen peel extract is thought to trigger the formation of free radicals.

Based on the average fasting blood glucose level after being given treatment with mangosteen peel extract at various doses, the diagram shows that the lowest average fasting blood glucose (GDP) level after being given treatment is in the group given standard feed with the addition of mangosteen peel extract at a dose of 600mg/kg BW (P3) that is equal to 81 ± 3.20 mg/dL which is closest to the treatment group given metformin. However, based on the results of the analysis showed that there was an effect of giving mangosteen peel extract on blood sugar levels. Furthermore, based on the results of the comparison test showed that there was a significant difference in blood glucose levels between K1 and K2, P1, P2, and P3, meaning that the mangosteen rind extract was able to reduce blood glucose levels in the treatment group (P1, P2, and P3).

Flavonoids and their derivatives are a group of polyphenols widely found in plants. Bioactive compounds such as polyphenols in the extract can donate hydrogen atoms to free radicals and chelate metals so that they can break oxidative chain reactions and help overcome oxidative stress that occurs in pancreatic tissue. The contribution of the antioxidant activity of the extract also helps conserve the use of antioxidant enzymes to increase the capacity of intracellular antioxidant enzymes. Decreased oxidative stress will then inhibit the rate of beta cell damage (Ban et al., 2022). Inhibition of the rate of beta cell damage provides an opportunity for beta cells to secrete insulin so that glucose can be utilized by cells as an energy source. Utilization of glucose by cells can improve conditions of hyperglycemia and prevent the consequences of reactive oxygen species caused. Thus oxidative stress on pancreatic tissue can also be reduced, which helps prevent further damage to pancreatic beta cells. Utilization of glucose by cells can improve the condition of hyperglycemia and prevent the consequences

of reactive oxygen species caused. Based on research, increasing glucose levels are also influenced by oxidative stress (Aci & Keskin, 2023)

The increase in reactive oxygen species in cytosolic calcium concentrations causes rapid beta cell destruction (Simorangkir et al., 2022). States that hyperglycemia can exacerbate beta cell damage as a result of the formation of ROS through glucose metabolism pathways such as glucose autooxidation (Fonkoua et al., 2022). The measurement of the final fasting blood glucose level (GDP post) showed changes in rats' blood glucose levels, where there was a decrease in several treatment groups. This means that the treatment in the form of mangosteen peel extract for 14 days reduced glucose levels in rats with hyperglycemia after STZ induced.

The conclusion obtained from this discussion is that the content of natural antidiabetic and antioxidant compounds found in mangosteen rind extract is believed to reduce blood glucose levels so that they remain in normal condition by increasing the work of pancreatic beta cells.

4. Conclusion

The content of antidiabetic compounds and natural antioxidants found in mangosteen rind extract is believed to lower blood glucose levels so that they remain in normal condition by increasing the work of pancreatic beta cells. There is a difference in the dose of mangosteen rind extract affects decreasing blood glucose levels with an effective dose of 600 mg/kg BW.

Acknowledgment

Thank you to Universitas Nahdlatul Ulama Surabaya for research assistance and Universitas Airlangga Surabaya for permission to carry out the research.

Conflict of interest

The author declares there is no potential conflict of interest

References

Aci, R., & Keskin, A. (2023). Antioxidant Capacity of Melatonin against Oxidative Stress Caused by Exercise-Induced Weight Loss in Rats. *Indonesian Journal of Medical Laboratory Science and Technology*, *5*(2), 112–122.

Atlas, D. (2015). International diabetes federation. *IDF Diabetes Atlas, 7th Edn. Brussels, Belgium: International Diabetes Federation*, *33*(2).

Ban, C., Paengkoum, S., Yang, S., Tian, X., Thongpea, S., Purba, R. A. P., & Paengkoum, P. (2022). Feeding meat goats mangosteen (Garcinia mangostana L.) peel rich in condensed tannins, flavonoids, and cinnamic acid improves growth performance and plasma antioxidant activity under tropical conditions. *Journal of Applied Animal Research*, *50*(1), 307–315.

Chen, S.-P., Lin, S.-R., Chen, T.-H., Ng, H.-S., Yim, H.-S., Leong, M. K., & Weng, C.-F. (2021). Mangosteen xanthone γ-mangostin exerts lowering blood glucose effect with potentiating insulin sensitivity through the mediation of AMPK/PPARγ. *Biomedicine & Pharmacotherapy*, *144*, 112333.

Fonkoua, M., Ze, M. Z., Tazon, W. A., Youovop, J., Guemto, G. T., & Ngondi, J. L. (2022). Effect of aqueous extract of Scorodophloeuszenkeri bark on chronic hyperglycemia and its complications in a diabetic Wistar rat model induced by streptozotocin. *Metabolism Open*, 100203.

Jusman, S. A., & Halim, A. (2010). Oxidative stress in liver tissue of rat induced by chronic systemic hypoxia. *Makara Journal of Health Research*, 34–38.

Kangralkar, V. A., Patil, S. D., & Bandivadekar, R. M. (2010). Oxidative stress and diabetes:

a review. *Int J Pharm Appl*, *1*(1), 38–45.

Kumawat, M., Pahwa, M. B., Gahlaut, V. S., & Singh, N. (2009). Status of antioxidant enzymes and lipid peroxidation in type 2 diabetes mellitus with microvascular complications. *Open Endocrinol J*, *3*(1), 12–15.

Kusumawardani, N., Tarigan, I., Suparmi, et al, & Schlotheuber, A. (2018). Socio-economic, demographic and geographic correlates of cigarette smoking among Indonesian adolescents: results from the 2013 Indonesian Basic Health Research (RISKESDAS) survey. *Global Health Action*, *11*(sup1), 54–62.

Ma, Z. A., Zhao, Z., & Turk, J. (2012). Mitochondrial dysfunction and β-cell failure in type 2 diabetes mellitus. *Experimental Diabetes Research*, *2012*.

Panda, S. S., Chand, M., Sakhuja, R., & Jain, S. C. (2013). Xanthones as potential antioxidants. *Current Medicinal Chemistry*, *20*(36), 4481–4507.

Paula, V. G., Sinzato, Y. K., de Moraes-Souza, R. Q., Soares, T. S., Souza, F. Q. G., Karki, B., de Andrade Paes, A. M., Corrente, J. E., Damasceno, D. C., & Volpato, G. T. (2022). Metabolic changes in female rats exposed to intrauterine hyperglycemia and postweaning consumption of high-fat diet. *Biology of Reproduction*, *106*(1), 200–212.

Simorangkir, M., Sinaga, E., Pasaribu, R., & Silaban, S. (2022). Antidiabetic activity of leaf extract of Clerodenrum fragrans Vent Willd in Rattus novergicus induced by alloxan. *Jurnal Bioteknologi & Biosains Indonesia (JBBI)*, *9*(1), 119–125.

Watanabe, M., Gangitano, E., Francomano, D., Addessi, E., Toscano, R., Costantini, D., Tuccinardi, D., Mariani, S., Basciani, S., & Spera, G. (2018). Mangosteen extract shows a potent insulin sensitizing effect in obese female patients: A prospective randomized controlled pilot study. *Nutrients*, *10*(5), 586.

Widowati, W., Laksmitawati, D. R., Wargasetia, T. L., Afifah, E., Amalia, A., Arinta, Y., Rizal, R., & Suciati, T. (2018). Mangosteen peel extract (Garcinia mangostana L.) as protective agent in glucose-induced mesangial cell as in vitro model of diabetic glomerulosclerosis. *Iranian Journal of Basic Medical Sciences*, *21*(9), 972.

Xie, Z., Sintara, M., Chang, T., & Ou, B. (2015). Daily consumption of a mangosteen-based drink improves in vivo antioxidant and anti-inflammatory biomarkers in healthy adults: a randomized, double-blind, placebo-controlled clinical trial. *Food Science & Nutrition*, *3*(4), 342–348.

Zafar, M., & Naqvi, S. N.-H. (2010). Effects of STZ-induced diabetes on the relative weights of kidney, liver and pancreas in albino rats: a comparative study. *International Journal of Morphology*, *28*(1).