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EFFECT OF BREWING BHEE FRUIT POWDER (*Melastoma sp*) AGAINST THE WEIGHT OF DIABETIC MICE

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Abstract

Diabetes is a metabolic syndrome that causes hyperglycemia. Diabetes can lead to weight loss. Glucose level control can indirectly restore weight. Glucose levels can be controlled using synthetic drugs and herbal drugs. Bhee fruit (*Melastoma sp*) is an herbaceous plant with antidiabetic effects. This study aims to determine the effect of Bhee fruit (*Melastoma sp*) infusion on weight changes in diabetic mice. The research method was a laboratory experiment using 24 mice which were divided into 6 treatment groups and four replicates, namely normal control, drug control, diabetes control, Treatment 1 (dose 100 mg/kgBB), Treatment 2 (dose 200 mg/kgBB) and treatment 3 (dose 400 mg/kgBB). The results showed that the weight in normal control increased slowly. The diabetes control group experienced weight loss until the last week of observation. The drug control group experienced a weight gain of 31.25%. Weight gain in the treatment group reached 6% (P1), 14.87% (P2), and 25% (P3). Conclusion: The higher the dose, the higher the ability to help restore body weight.

Keywords: ***Hyperglycemia, alloxan, secondary metabolites.***

INTRODUCTION

Diabetes is a chronic metabolic disease that is increasingly prevalent among the global population. Instant food and unhealthy lifestyles are among the factors contributing to the onset of diabetes. The global prevalence of diabetes, particularly type 2 diabetes, has increased by 30% (Busui, 2022). It is estimated that the global prevalence of diabetes will reach 10.5% (537 million cases) in 2023, with projections rising to 12.2% (783 million) by 2045 (Saedi, 2019). National prevalence data on diabetes collected by Riskesdas in 2023 indicate a rise in cases from 6.2% (2018) to 10.6% (2023), equivalent to 28.7 million adult individuals. Serious measures related to diabetes management need to be implemented to prevent further increases in its prevalence.

Diabetes Mellitus is one of the non-communicable diseases caused by damage to the pancreas, which prevents it from synthesizing the insulin needed for glucose breakdown. Disrupted insulin production will affect blood glucose levels, continually increasing and becoming uncontrolled. Usually, when blood glucose levels rise, the pancreas releases the hormone insulin. The mechanism of insulin action involves binding to insulin receptors on the cell surface, which triggers intracellular signaling and the translocation of GLUT4 to the membranes of muscle and fat cells. This process facilitates the absorption of blood glucose into the cells. Insulin is also involved in inhibiting glucose production in the liver through the inhibition of gluconeogenesis and glycogenolysis.

People with Diabetes must consistently monitor their blood glucose levels by taking medication, maintaining a proper diet, or adopting a healthy lifestyle (Widiastuti, 2024). The control of glucose levels using medication is considered more practical and has quicker effects. However, the use of chemical drugs is thought to have greater side effects when used long-term, leading the public to explore plants with potential as diabetes remedies as an alternative (Widiastuti, 2022). The Bhee fruit (*Melastoma sp*) is derived from a shrub widely distributed in various regions, including West Aceh. The Bhee fruit shows potential as a herbal anti-diabetic remedy (Rinawati, 2023).

Diabetes can affect weight. When the body experiences insulin deficiency, there will be an increase in lipolysis and proteolysis due to glucose that cannot enter the body's cells. The catabolic process can reduce the mass of adipose tissue and muscle (Sinanta, 2016). Increased lipolysis activity in adipose tissue results in excess free fatty acid (FFA), while muscle proteolysis releases amino acids into the circulation. Both substrates are metabolized in

the liver through gluconeogenesis, further exacerbating hyperglycemia. Hyperglycemia conditions will cause polyuria and polydipsia, which will impact the loss of excess fluid so that weight decreases (Mubarok, 2024). Research conducted using mice as an animal model of diabetes shows that there is a relationship between hyperglycemia and weight loss. When mice are induced with diabetogenic agents, glucose metabolism is disrupted due to insulin deficiency. The body responds by breaking down protein and fat reserves, which will decrease visceral fat mass and skeletal muscle atrophy (Ukratalo, 2024). According to Munoz (2023), insulin resistance will cause hyperglycemia in mice, with a decrease in fat mass of 42% and lean mass of 15% in 12 weeks. Controlling glucose levels using herbal plant extracts reduces glucose levels by up to 40%, accompanied by increased body weight through increased insulin receptor sensitivity (Karampatsi, 2021). Improving insulin receptors will improve α-glucosidase inhibition so that it helps glucose absorption in body cells and helps restore weight gain in mice (Pratiwi, 2023). Therefore, this study aims to prove the effectiveness of Bhee fruit powder (*Melastoma sp*) on the body weight of diabetic mice.

METHOD

Place of Research

The research was conducted at the Laboratory Animal Management Unit (UPHL) of IPB.

Tools and Materials

Tools: Sonde needle, cage, and weight scales to measure the development of body weight of experimental animals before, during, and after treatment.

Materials: Bhee fruit (Melastoma sp) distilled water, male mice with an average weight of 20-30 gr, mice food, and alloxan to condition the mice to become diabetic.

ResearchStages

Simplicia extraction:

Bhee fruit (Melastoma sp) is taken from the West Aceh area. The fruit is separated from the stalk and petals, so no dirt sticks. Then, it is dried in the oven at 60-80°C for 4 days until the moisture content remains. The dry sample is then mashed with a blender and sifted with a sieve. The obtained simplicia is wrapped in a dark container and stored for further testing.

Diabetic test animal manufacturing:

Mice are acclimatized first for 7 days in a quiet room. Mice are given enough water and feed and adequate air circulation. This is to avoid stressing mice. After grouping, mice conditioned with diabetes must be induced by alloxan intraperitoneally with a dose of 120 mg/kgBB; after 48 hours, blood glucose levels are checked. Mice are already in a diabetes condition if the glucose level reaches >200 mg/dL (Susilawati, 2016). The number of mice used was obtained through the calculation of Federer's formula [(t-1) (n-1) ≥15], where t is the number of treatments to be given, and n is the number of samples per group to be sought.

Extract testing on experimental animals.

Bhee fruit powder (Melastoma sp) was given to test animals in vivo using a sonde needle at a dose of 100 mg/KgBB, 200 mg/KgBB 400 mg/KgBB for 28 days, and blood glucose levels and body weight were checked every 7 days.

Dosage of Metformin as a comparison drug

Metformin is a comparison drug to reduce glucose levels in diabetic mice. The dose of metformin used was 500 mg/KgBB of human body weight, with a body weight of 70 Kg. The results of dose conversion from humans to mice amounted to 1.3 mg/20 gBB. Dosing is adjusted to the body weight of the mice. The metformin results obtained are dissolved in distilled water until the volume reaches 10 ml (Hasma, 2020).

Research Design

Mice were grouped using a completely randomized design (CRD). 24 mice were grouped into six groups with four replicates as follows:

Normal Control (KN) = Group of mice (only given feed and distilled water)
Drug Control (KO) = Group of mice given Metformin hcl as a 1.3 mg / kgBB comparison dose.

Diabetes Control (KD) = Group of mice conditioned to diabetes without administering *Melastoma sp* fruit powder.
Treatment 1 (P1) = Group of diabetic mice given a dose of 100 mg/kgBB of *Melastoma sp* fruit powder.
Treatment 2 (P2) = Group of diabetic mice given a dose of 200 mg/kgBB *Melastoma sp* fruit powder brew
Treatment 3 (P3 = Group of diabetic mice given a 400 mg/kgBB *Melastoma sp* fruit powder.

The Normal group compares changes in blood glucose levels in diabetic-conditioned mice and mice treated with the drug Control group to compare the effectiveness of *Melastoma sp* fruit powder compared to drugs. Diabetic control is a group of diabetic mice that act as a parameter in reducing blood glucose levels given *Melastoma sp* fruit powder. P1, P2, and P3 groups are mice given *Melastoma sp* fruit powder with different doses to determine the most appropriate dose. The treatment of extract administration was carried out for 28 days. Measurements were taken every 7 days

RESULTS AND DISCUSSION

Body weight measurements were taken to determine the effect of alloxan induction on body weight changes and the effect of extracts on changes in body weight of diabetic mice. Changes in body weight caused by alloxan induction are shown in table 1 below:

Table 1. Weight Measurement Results of Mice Before and After Alloxan Induction

Groups	Average Body Weight	
	Before Induction of Alloxan	After Induction of Alloxan
KN	20.00±1[a]	21.00±0.50[b]
KO	20.00±0.50 [a]	16.00±1.29[a]
KD	20.67±0.57 [a]	15.67±0.57 [a]
P1	20.00±0.00 [a]	16.67±0.95[a]
P2	20.33±0.50 [a]	15.67±0.57 [a]
P3	20.00±0.50 [a]	16.00±0.95[a]

Table 1 above shows that the average body weight of mice is ± 20g. There is no difference in mice body weight in each treatment. This shows the uniformity of the body weight of the mice used in the research process. Changes in body weight occur after mice are induced by alloxan as a diabetogenic agent. A significant difference exists between the normal control group (KN) and the alloxan-induced mice group (KO, KD, P1, P2, and P3). Based on the table above, the normal control group had an increase in body weight, and the minute group induced by alloxan had a decrease in body weight. The percentage change is shown in the following graph:

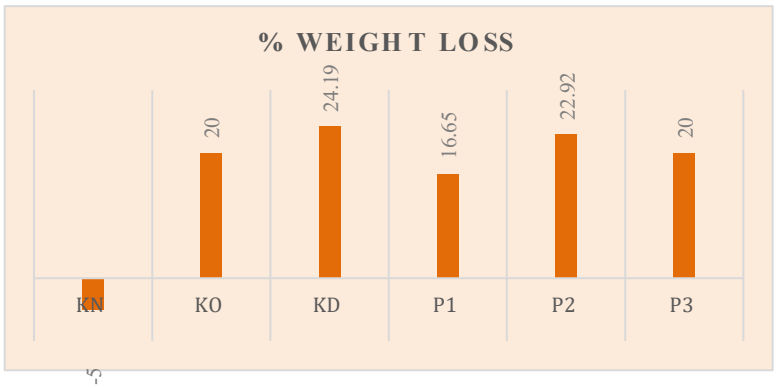

Figure 1. Graph of changes in body weight of mice after alloxan induction.

Based on the graph above, the normal control group experienced an increase in body weight, while the alloxan-induced mice group (KO, KD, P1, P2, and P3) experienced a decrease in body weight, with a percentage that was not so different. The highest percentage of weight loss was shown in the drug control group (KD), at 24.19%. These data show that alloxan can affect the body weight of mice. Alloxan is a diabetogenic agent composed of 5,5 hydroxyl pyrimidine-2,4,6-trion derived from urea derivatives (Wulandari, 2024). Alloxan contains radicals that damage pancreatic β-cells. A damaged DNA structure and blocking of the thiol group in the enzyme glucokinase cause the destruction process. Damaged β-cell DNA causes necrosis in pancreatic β-cells. The blocking of thiol groups in the glucokinase process will inhibit the process of ATP production; if this happens, it will cause insulin secretion to decrease (Marzuki, 2022). Insulin deficiency will affect blood glucose levels to increase, due to the inability of glucose to enter body cells (Fatimah, 2015). Glucose is used by the body as a source of energy and stored as a reserve. When the body needs glucose, but the cells do not get enough, the body will break down fat and protein. If this continues, food reserves will be reduced. This condition causes weight loss (Ferrannini, 2016). The condition of diabetes, followed by glycogenolysis, lipolysis, and gluconeogenesis, results in a reduction in muscle and protein so that body weight decreases (Aleydaputri, 2022).

Controlling blood glucose levels can be done using insulin therapy or drug consumption. Insulin therapy can redifferentiate pancreatic β-cells, and restore insulin content and drug responsiveness (Wang, 2014). Antidiabetic drugs act as glucose controllers and protect pancreatic β-cells. Glucagon-like peptide- 1 receptor agonists stimulate insulin secretion, reduce glucose production, and improve β-cell function (Yang, 2023). Pancreas regeneration and stable glucose levels indirectly play a role in restoring the weight of diabetic mice. According to Datu (2023), the administration of herbal plant extracts can improve the body weight of experimental animals until their body weight stabilizes. The results of the study of the effect of Bhee powder on the body weight of diabetic mice are shown in the table below:

Table 2. Mean Body Weight of Mice Before and After Giving the Extract for Four Weeks

Groups	Average Body Weight				
	After Induction of Alloxan	Week 1	Week 2	Week 3	Week 4
KN	21.00±0.50^{b}	22.00±1.63^{c}	22.00±1.91^{c}	22.67±1.29^{d}	23.33±0.95^{e}
KO	16.00±1.29^{a}	19.00±0.95^{b}	19.33±1.25^{b}	20.00±0.81^{c}	21.00±0.95^{d}
KD	15.67±0.57 ^{a}	14.67±0.50^{a}	15.33±1.29^{a}	15.00±1.50^{a}	14.33±2.21^{a}
P1	16.67±0.95^{a}	17.67±1.41^{b}	17.67±1.25^{ab}	17.33±1.25^{b}	17.67±1.29^{b}
P2	15.67±0.57 ^{a}	17.67±1 ^{b}	17.67±0.50^{b}	18.33±0.57^{b}	17.67±0.50^{bc}
P3	16.00±0.95^{a}	18.00±1.29^{b}	17.67±1.41^{b}	18.00±1.73^{bc}	20.67±0.81^{cd}

The Shapiro-Wilk test results show that the data is normally distributed (P>0.05). In inhomogeneity testing, the data obtained is homogeneous (P>0.05). The ANOVA test results showed a significant difference between the treatment groups, with p<0.05 at 0.05. Based on Duncan's test, there was a significant difference in each treatment group. The data above shows a change in body weight in each experimental group. The normal control group tended to continue to increase body weight every week. The diabetic control group tends to continue to experience weight loss; this is because alloxan still affects insulin sensitivity in mice. The KO, P1, P2, and P3 groups experienced fluctuations in average body weight changes every week, indicating that the fruit powder brew can restore the body weight of diabetic mice (P1, P2, and P3). The percentage change in mice's body weight is depicted in the following graph:

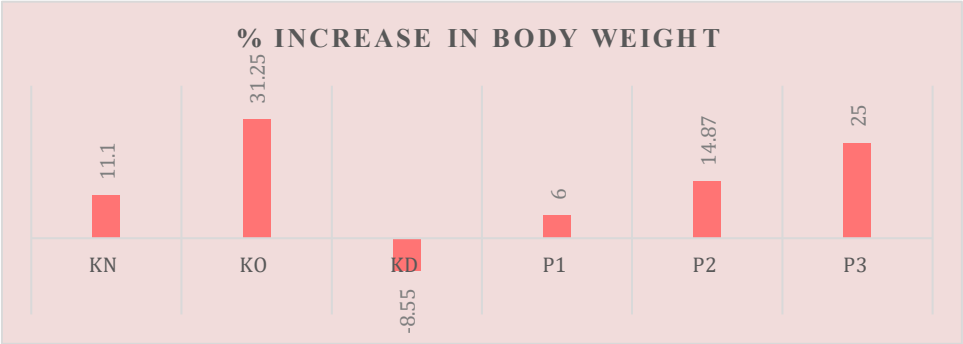

Figure 2. Graph of percentage change in body weight of mice after administration of Bhee fruit powder brew.

The graph above shows that the normal control group experienced an increase in body weight of 11.1%. Although the percentage is not high, this condition is considered reasonable because mice in the normal control group were not given any treatment. The increase in body weight is caused by food consumption every day. The diabetic control group (KD) continued to experience weight loss, reaching 8.55%; this is thought to be alloxan damaging the pancreas so that insulin cannot be produced so that continuous hyperglycemia occurs and results in weight loss. The weight gain percentage occurred in the drug control group (KO). The drug used in this study is metformin. The role of metformin as a protector of MIN6 β-cells against palmitic acid-induced apoptosis has the potential to suppress proliferation under normal conditions (Jiang, 2014). In addition, metformin can prevent glucotoxicity-induced dysfunction and ultrastructure and maintain glucose-stimulated insulin secretion and ATP/ADP ratio (Masini, 2014., Kaneto, 2021).

In the treatment group, the highest percentage increase was shown in the P3 group by 25%, followed by the P2 group (14.87%) and P3 (6%). This percentage shows that the higher the dose, the more effective it is to help restore the body weight of diabetic mice. Although the P3 group showed the highest percentage increase in body weight, it still did not match the drug control group. Bhee fruit powder's ability to help restore mice's body weight is thought to be due to the content of secondary metabolites. Bhee fruit contains alkaloids, terpenoids, saponins, flavonoids, and tannins (Rinawati, 2023). The content of these secondary metabolites, in general, can help control blood glucose levels to stabilize and repair damage to pancreatic β cells and help insulin sensitivity (Mohan, 2013).

The role of saponins in helping to restore the body weight of diabetic mice is by increasing the absorption of nutrients such as fat and protein. Increased intake of nutrients and calories plays a role in increasing body weight (Ukratalo, 2024). Diabetic conditions usually cause a decrease in appetite; alkaloids have a bitter taste that can increase appetite, so they also contribute to increasing body weight (Siregar, 2015). Alkaloids also play a role in improving the metabolic process of glucose so that it can be absorbed by body cells that need it. This process also helps restore mice's body weight that was initially lost due to alloxan induction (Solikhah, 2021). Tannins play a role in the process of stimulating the metabolic process of glucose and fat; this also causes maintaining blood glucose stability, which ultimately affects changes in body weight (Gholamin, 2024).

CONCLUSION

Hyperglycemia conditions in mice induced by alloxan affect changes in mice's body weight. The body weight of mice after alloxan induction decreased. Giving Bhee fruit powder can restore the body weight of diabetic mice. The dose of 400 mg / kbB (P3 group) is the greatest to increase the body weight of mice, reaching 25%. The higher the dose, the greater the ability to increase body weight. Bhee fruit powder can help restore mice's body weight due to its content of secondary metabolites

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