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EFFECT OF ETHANOL EXTRACT OF BHEE FRUIT (MELASTOMA SP) ON CHOLESTEROL LEVELS IN DIABETIC MICE

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Abstract

Diabetes mellitus is a chronic disease that causes death. Diabetes is associated with increased total cholesterol levels. Insulin resistance causes glucose levels to increase in the blood and inhibits the circulation of food juice. The body will break down fat as an energy source due to glucose that cannot reach the body's cells, this causes an increase in cholesterol levels in the blood. Several studies have shown a correlation between increased blood glucose levels and increased cholesterol levels. Control of blood glucose levels in diabetics should be done so as not to cause an increase in blood cholesterol. Herbs are chosen as an alternative for antidiabetics. Bhee fruit (Melastoma Sp) has the potential to an antidiabetic because of its phytochemical content. In West Aceh, there has not been much research on diabetes herbal medicine and the use of Bhee Fruit as an herbal medicine. The purpose of this study was to determine the effect of ethanol extract of Bhee fruit on total cholesterol levels of alloxan-induced diabetic mice. Method: Laboratory experimental research with Complete Randomized Design (RAL) using 21 mice divided into 7 treatments namely KN, KP, KO, KD, P1, P2, and P3. Measurement of cholesterol levels using easy touch tools and Cholesterol strips. The dose of ethanol extract of Bhee fruit used is 100, 200, and 400 mg/kg body weight and given for 14 days. Data analysis was performed using One-way ANOVA and followed by the Duncan Analysis test. Results: Giving ethanol extract of Bhee fruit at doses of 100, 200, and 400 mg / dL was able to reduce total cholesterol levels in diabetic mice. Conclusion: Giving Bhee fruit extract affects reducing total cholesterol levels, with a dose of 400 mg/kg body weight which is most effective in reducing total cholesterol levels in diabetic mice. Suggestion: it is necessary to do further tests using different types of solvents and different doses.

Keywords: ***Bhee, Diabetes Mellitus, Total Cholesterol.***

1. INTRODUCTION

Diabetes mellitus is a chronic disease that can cause death. High blood glucose levels that exceed normal limits are a marker of someone having diabetes (Setyaji, 2023). The International Diabetes Federation (IDF) recorded that the number of diabetics aged >20 years reached 537 million people worldwide and there were 6.7 million cases of death or 1 case every 5 seconds (IDF, 2021). WHO (2023) recorded that death cases reached 1.5 million people in 2019, in addition to death cases caused by complications of diseases due to diabetes such as kidney and cardiovascular failure. Based on Riskesdas data (2018) in Indonesia, diabetes is the 3rd leading cause of death after stroke and heart disease. The prevalence of diabetes in Indonesia was 1.5% in 2013, while in 2018 it was 2.0% which indicates an increase of 0.5%. This can be seen by the increase in the percentage of blood measurement results carried out on residents aged >15 years, namely 6.9% to 8.5% in 2018, with the results of these data showing new cases found by 25% in diabetics (Riskesdas, 2018).

Diabetes cases also occur in Aceh province. The Aceh Health Office (2023) states that there is an increase in diabetes cases in 2021-2022. There were 184,527 cases in 2021 and a slight increase to 189,464 cases in 2022. The prevalence of diabetes was also recorded in the West Aceh

district. Diabetes cases in West Aceh district show an upward and downward trend from 2019-2023. In 2019, the West Aceh health office recorded 6,549 cases. Diabetes cases continued to increase by 7,350 cases in 2020 and 7,448 in 2021. Diabetes cases began to decline in 2022 by 4,125 cases but increased again in 2023 by 5,779 cases (West Aceh Health Office, 2023).

Diabetes is closely related to cholesterol levels in the blood. Susilo (2020) said that there are blood glucose levels with total cholesterol levels in diabetics. Cholesterol is a lipid component that is needed by other energy sources such as carbohydrates, proteins, vitamins, and minerals (Naim et al., 2019). Although cholesterol is needed as a source of energy by the body, if cholesterol levels are excessive it will cause cardiovascular disease. Cholesterol levels will continue to increase if there is inhibition of blood flow due to fat accumulation and plaque buildup so that blood vessels narrow (Suarsih, 2020).

Increased blood glucose levels occur due to insulin resistance which ultimately damages blood vessels. Insulin resistance will affect the circulation of food juice that is circulated through the blood. Glucose in the blood cannot enter the body's cells, this affects the source of energy. If such cases occur, the body will take energy reserves from the breakdown of fats and proteins. The fat distributed is in the form of cholesterol, so cholesterol increases because it continues to be used. Increased cholesterol will be able to inhibit the work of insulin to receive blood glucose in the body. This inhibition causes blood glucose levels to continue to rise (Haiti, 2023).

Blood glucose levels in diabetics should always be kept stable and do not cause complications of other diseases. Glucose levels that are too high (hyperglycemia) will affect the body's metabolic processes (Selly, 2023). Control of blood glucose levels can be done by taking synthetic chemical drugs or alloxane injection (Adriansyah, 2020). The use of synthetic drugs in the long term gives negative side effects such as hypoglycemia, weight gain, headaches, etc. (Jilao, 2017). Herbal plants can be used as an alternative treatment for diabetes. Herbal plants are considered safer because they come from natural ingredients aimed at recovering damaged organs, reducing side effects, and most importantly are easy to obtain (Wahyuningsih, 2023).

Indonesia has various types of plants with potential as herbal functional food. Plants that have the potential as an alternative treatment for diabetes one of them is Melastoma Sp better known in general as senggani or sensit. This plant is widely spread in the West Aceh Region as a shrub that has not been used as herbal medicine and is known as the "Bhee" plant. This plant is usually used as herbal medicine, but the fruit part has not been widely used and researched as herbal medicine. Bhee fruit contains phytochemicals that can lower blood glucose levels.

Not many references have been found for the use of Bhee fruit parts as antidiabetic herbal medicine. Novitalia (2022) states that Bhee fruit ethanol extract can reduce blood glucose levels in alloxan-induced zebrafish. Bhee fruit ethanol extract can also reduce glucose levels in alloxan-induced mice (Rinawati, 2023). The content of Bhee fruit contains several compounds that have high antioxidants, including flavonoid compounds (Wilsya, 2023). Flavonoids can act as anticholesterol by affecting the increase in fat cell catabolism in the process of energy formation to reduce cholesterol levels (Heliawati, 2018).

Based on this background, researchers were interested in looking at blood cholesterol levels in diabetic mice and the effect of giving ethanol extract of Bhee fruit on cholesterol levels.

2. IMPLEMENTATION METHOD

This study is a test of the antihypercholesterol activity of Bhee fruit ethanol extract (Melastoma Sp) in diabetic mice in a true experimental laboratory to determine the effects arising

from the administration of extracts with different doses. The study was conducted at the Veterinary Medicine laboratory of Syiah Kuala University for testing Bhee fruit extract (Melastoma sp) on test mice. The independent variable in this study was the dose of ethanol extract of Bhee fruit (Melastoma Sp) which was a dose of 100 mg/kg BB, 200 mg/kg BB, and 400 mg/kg BB and the dependent variable in this study was the percentage of reduced cholesterol levels in diabetic mice.

The study sample used 21 experimental mice, male sex with a body weight of 20-30 grams. Mice will be grouped using a Complete Random Design (RAL) design. In 21 mice, they were grouped into 7 groups with 3 repetitions. The group of normal mice (KN) was used as a comparison on changes in blood cholesterol levels of diabetic mice and mice given extract treatment. The drug control group (KO) aimed to compare the effectiveness of Bhee fruit extract and the drug. The treatment group (KP) aims to determine changes in blood cholesterol levels of normal mice given extract. The diabetes control group (KD) aims as a parameter to reduce blood cholesterol levels treated with Bhae fruit extract. Groups P1, P2, and P3 were included in mice that were extracted based on different doses to find out which dose was most appropriate. Administration of the extract is carried out for 14 days. Measurements are carried out every 7th day after being accrued first to adjust to the experimental environment. Cholesterol level examination is carried out with an easy touch tool in the form of blood taken from the peripheral blood vessels of the tail of mice as much as 0.05 ml using a small and sterile needle (Ardiani et al., 2020).

Experimental mice will be limited first for 7 days in a quiet room with enough feed and drink and enough air circulation, this aims to prevent mice from stress. After grouping, mice that will be used in diabetic conditions must be inducted alloxane intraperitoneally at a dose of 175 mg/kg BB. Within 48 hours, blood glucose levels will be checked. Mice that have blood glucose levels reaching >200 mg / dL are included in diabetic conditions (Susilawati, 2016).

Bhee fruit (Melastoma sp) is obtained from the West Aceh region. The fruit is separated from part of the stalk and petals. Then all samples are drained and dried in an oven at 40-50°C for 4-5 days until the moisture content remains. The dried sample is mashed with a blender and sifted with a sieve. After that, the obtained simplisia will be wrapped in plastic and stored for subsequent testing. The extraction manufacturing process is carried out by maceration. Bhee fruit simplisia powder (Melastoma Sp) that was previously stored will be put into an extractor as much as 500 grams and added with 96% ethanol solvent. Then it is packaged and allowed to stand for 3 days in a place protected from light, then the simplisia is filtered. The maceration results are evaporated using a Rotary Evaporator until the extract thickens (Wilsya, 2023).

Bhee fruit extract (Melastoma sp) is given in vivo using a sonde needle based on doses of 100 mg/kg BB, 200 mg/kg BB, and 400 mg/kg BB within a period of 14 days and every 7 days Checks are carried out on blood glucose levels, body weight, and blood cholesterol levels. Measurement before and after administration of the extract aims to determine the effect of ethanol extract of Bhee fruit on total cholesterol levels of diabetic mice.

Data analysis is carried out in a descriptive way in the form of tables and graphs. Data processing and analysis using computer aids. ANOVA analysis will be carried out which aims to measure blood cholesterol levels in each group, if there are differences between treatment groups then further analyzed with the DMRT test (Duncan multiple range test).

3. RESULTS AND DISCUSSION

Measurement of total cholesterol levels in diabetic mice aims to see the effect of alloxane induction and the effect of giving ethanol extract of Bhee fruit on changes in cholesterol levels.

3.1 Research Results

Aloxane can affect the total cholesterol of diabetic mice. The results of measuring total cholesterol levels after alloxane induction are shown in Table 1. Based on the data shown in Table 1, total cholesterol levels in diabetic mice have changed. Total cholesterol before alloxane induction did not differ markedly from treatment to treatment. This shows the uniformity of total cholesterol even though there is a slight difference in numerical values. This uniformity is indicated by the same superscript letters in each group.

Aloxane induction in the diabetic mice group (KD, KO, P1, P2, and P3) showed changes in total cholesterol levels compared to the KN and KP groups that were not alloxan-induced because it was intended for comparison. Nugroho (2022) total cholesterol is high in mice if the levels are higher than 130 mg/dL. Total cholesterol levels in Table 5 above show that the group of alloxan-induced mice (KO, KD, P1, P2, and P3) is higher than normal. Total cholesterol levels in the group of mice that were not induced by alloxane (KN and KP) were still at normal limits. Based on the results of ANOVA and Duncan's tests on measuring total cholesterol levels, it showed that there was a significant difference in alloxan-induced mice (KD, KO, P1, P2, and P3) with the non-alloxan-induced group (KN and KP) with a P-Value of 0.000 (P<0.05) and there was a real difference in the group.

Table 1. Average Cholesterol Levels Before and After Alloxane Induction in Diabetic Mice

Group	Before Alloxane Induction	After Alloxane Induction	*P Value*
KN	88.33±7,63[a]	90.33±1.52[a]	
KP	94.33±4,04[a]	96.66±5.77[a]	0.000
KD	94.33±6.02[a]	151.67±5.77[b]	
KO	85.00±5[a]	152.33±4.93[b]	
P1	94.67±5.50[a]	148.33±4.16[b]	
P2	87.67±2.51[a]	147.00±4.35[b]	
P3	91.00±3.60[a]	149.00.33±2.64[b]	

Description: Numbers followed by Superscript letters indicate a real difference

The increase in total cholesterol can be seen through the percentage value calculated using the following formula: % Increase in cholesterol = (average after average before) / (average after) x100% (Ningrum, 2019). The results of calculating the percentage increase in total cholesterol levels are displayed on the bar graph chart in Figure 1.

The data shown in the graph of Figure 1 shows that the KD, KO, P1, P2, and P3 groups have increased. The highest percentage increase in total cholesterol was shown in the knockout group at 44.2%. Total cholesterol in the KN and KP groups although increased, but the percentage was very small compared to the alloxan-induced mice group. When viewed from the percentage results above, alloxane induction can affect total cholesterol in mouse blood.

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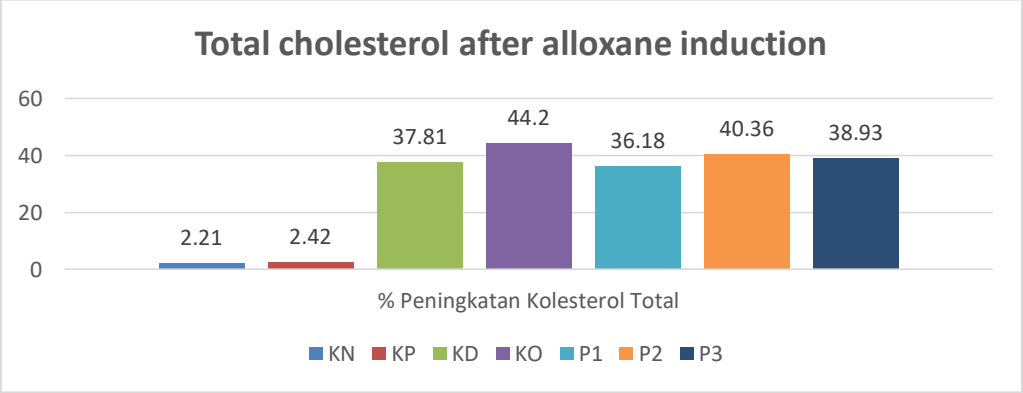

Description: Effect of alloxan induction on total cholesterol in mice

Figure 1. Percentage of total cholesterol after alloxan induction

The administration of the extract was carried out after the alloxan-induced group of mice experienced hyperglycemia. The extract aims to determine the effect of the extract on the total cholesterol of diabetic mice. Total cholesterol measurements are carried out on day 7 and day 14. The total cholesterol measurement results are shown in Table 2.

Giving ethanol extract of bhee fruit affects total cholesterol from the measurement results of day 7. Total cholesterol levels in the diabetic mice group (KD, KO, P1, P2, and P3) began to show differences. The KO and P3 groups showed no real difference. The P1 and P2 groups also showed no real difference. The KD group is a group of diabetic mice with the highest total cholesterol levels and is significantly different from other groups. The KN and KP groups are also not significantly different. This showed that the results of total cholesterol measurement on day 7 in the normal mice group given extract (KP) were no different from the group of mice that were not given any treatment.

The results of total cholesterol measurement on day 14 showed changes in total cholesterol levels. The value of total cholesterol levels in the KD group increased, while in the KO, P1, P2, and P3 groups decreased. Total cholesterol levels in the KO and P3 groups did not differ markedly. The P1 and P2 groups also showed no real difference between the two treatment groups. The KN and KP groups still did not differ markedly despite the decrease in total cholesterol levels.

Table 2. Total cholesterol levels in mice with the administration of ethanol extract of Bhee fruit

Group Treatment	After Alloxane Induction	H7	H14	*P Value*
KN	90.33±1.52[a]	93.00±7.00[a]	90.00±4.35[a]	
KP	96.66±5.77[a]	100.67±4.04[a]	93.33±5.77[a]	
KD	151.67±5.77[b]	154.33±5.13[d]	155.33±6.42[d]	
KO	152.33±4.93[b]	131.33±3.21[b]	118.67±1.52[b.]	
P1	148.33±4.16[b]	143.00±2.64[c]	137.00±6.55[c]	0.000
P2	147.00±4.35[b]	144.67±4.72[c]	130.67±4.72[c]	
P3	149.00.33±2.6[b]	133.67±5.50[b]	113.00±2.64[b]	

Description: **KN= Normal Control (without alloxane brooding and extract administration). KP=Treatment Control (normal mice + Extract). KD = Diabetes Control (without extract treatment). KO** = Drug Control (diabetic mice + Metformin hcl 500 mg), P1 = diabetic mice + extract dose 100 mg/kg BB. **P2 = Diabetic mice + extract dose 200 mg/kgBB,** P3 = **Diabetic mice + extract dose 400 mg/kgBB**

To find out how much influence ethanol extract has on the total cholesterol of diabetic mice, it can be seen through the percentage of total cholesterol reduction. The calculation of percentage decrease in total cholesterol can be calculated using the formula: % Cholesterol reduction = (average before average after)/(average before) x100% (Afriyeni, 2023). The percentage decrease in total cholesterol levels is shown in the graph in Figure 2.

Based on the graph in Figure 2, giving ethanol extract of Bhee fruit can affect the total cholesterol levels of mice. Administration of ethanol extract dose of 400 mg/kg BB in the P3 group showed the highest percentage reduction in total cholesterol levels of 24.16% compared to the P1 group (7.64%) with a dose of 100 mg/kg BB and P2 (11.11%) with a dose of 200 mg/kg BB. Based on Table 4.2, between the P3 and KO groups, there is no real difference. However, the percentage decrease in P3 is slightly greater than the knockout group with a percentage of 22.1%. The KN group that was not given any treatment experienced a slight decrease in cholesterol levels of 0.37%. The KP group, namely normal mice given extract treatment, also experienced a decrease in cholesterol by 3.46%. This suggests that Bhee fruit ethanol extract slightly affects normal mouse cholesterol. The KD group did not experience a decrease in total cholesterol levels by a percentage of -2.41%, this could be related to the state of mice that still have diabetes.

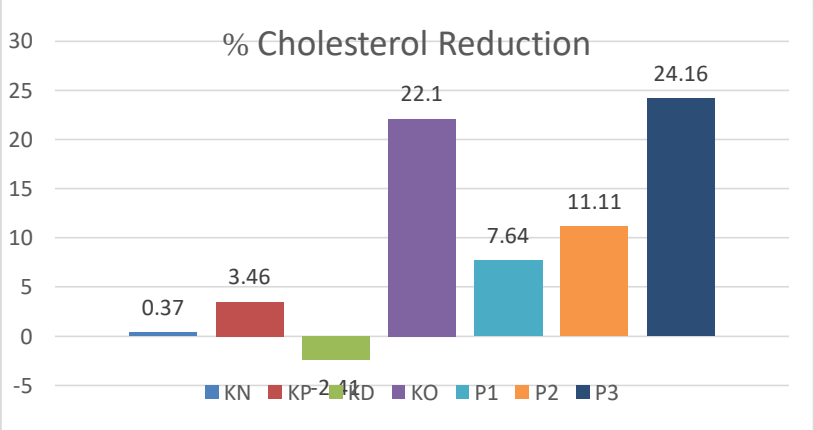

Figure 2. Percentage decrease in cholesterol levels

3.2 Discussion

The results of the study mentioned above show that alloxane induction can affect the value of total cholesterol levels in diabetic mice. Aloxane can trigger the formation of free radicals (Maharani, 2023) which is the main cause of damage to pancreatic β cells. The formation of free radicals starts from the induction of alloxan in mice that can reach the pancreas quickly. Aloxane that enters will damage pancreatic β cells and insulin receptors (Setiadi, 2020). Pancreatic damage due to alloxane can lead to necrosis (tissue death) and inflammation. This inflammation occurs due to the response of living tissue located next to necrosis tissue (Haerani, 2023). Damage to the pancreas and insulin receptors causes the body to be unable to absorb glucose optimally, as a result of which glucose levels in the blood increase and become the main cause of diabetes (Anisa, 2023).

According to Anggraini (2018), there is a strong correlation between blood glucose levels and cholesterol levels. Blood glucose levels increase, and the cholesterol levels in the blood will increase. Based on the results of the study above, the group of diabetic mice had high cholesterol levels as well. Induction of alloxin in mice causes glucose levels to increase and cholesterol levels to increase. This research is in line with the results of research conducted by Amalia (2022), namely blood glucose levels that increase directly proportional to the increase in cholesterol levels of experimental rats.

The determination of total cholesterol levels in humans and experimental animals was different. The Ministry of Health (2018) determined that normal levels of total cholesterol range from >200mg/dL, while according to Nugroho (2022), total cholesterol levels in mice range from 40-130mg/dL. This can be caused by the process of synthesizing cholesterol and bile acids in mice faster than in humans and serum LDL levels in mice are lower than in humans (Straienero, 2021).

Increased blood glucose levels caused by pancreatic damage will also affect cholesterol levels in the blood. The role of insulin in addition to being a blood glucose receptor also has a role in the lipase enzyme regulatory process, namely the LSH enzyme (Lipoprotein sensitive hormone) and LPL enzyme (Lipoprotein lipase). Low insulin secretion will increase the activity of LPL and LSH enzymes which disrupt the process of lipid metabolism, which causes total cholesterol levels to increase (Fransiska et al. 2020).

Free radicals formed due to pancreatic damage will form with cell receptors covalently, this can cause cell damage. In addition, free radicals will bind to LDL receptors in the liver, as a result of which many LDL cannot be bound by their receptors and cause an increase in total blood cholesterol levels to increase (Afriyeni, 2023).

Diabetes and cholesterol are interrelated between the two. The state of hyperglycemia in diabetics continuously will result in damage to blood vessels and inhibition of the process of energy formation as a source of energy to carry out various important activities of the body. Because glucose as an energy source cannot be absorbed, resulting in the breakdown of proteins and fats that the body stores as food reserves. This process causes cholesterol to accumulate in blood vessels. The buildup of cholesterol will form plaques that inhibit insulin receptors from capturing glucose, this is what can cause hyperglycemia. Hyperglycemia states cause LDL oxidation to take place faster (Haiti,2023).

Based on the results of data analysis using *One Way ANOVA* on the effect of ethanol extract of bhee fruit for 14 days, *a P-value of* 0.000 ($P<0.05$) was obtained. This value shows that there is an effect of giving ethanol extract of bhee fruit on total cholesterol in the blood of diabetic mice. The *Duncan* test was performed to determine the differences in each treatment group.

The administration of ethanol extract of bhee fruit consists of three different doses, namely 100 mg/kg BB at P1, dose 200 mg/kg BB at P2, and dose 400 mg/kg BB at P3. Nugroho (2022) said, normal levels of total mouse cholesterol range from 40-130 mg / dL. A dose of 100 mg/kg body weight can reduce total cholesterol to 137mg / dL, but these levels are still at the criteria of high cholesterol. Doses of 200 and 400 mg/kg body weight can reduce total cholesterol to reach normal criteria because the levels reach 130 mg/kg BB (P2) and 113 mg/kg BB (P3).

Based on *Duncan*'s test, it is known that the P1 and P2 groups are not significantly different. This means that the effect of dosing 100 and 200 mg/kg body weight is not much different. From the calculation of the percentage of total cholesterol reduction, the P2 group with a dose of 200 mg/kg BB was able to reduce total cholesterol levels by 11.11% and the P1 group with a dose of 100 mg/kg BB the percentage of decline was not too much different from P2 which was

7.64%. The P3 group with a dose of 400mg/kgBB has the highest ability to reduce total cholesterol levels compared to P1 and P2, which is 24.16%. This percentage indicates that the highest dose has the greatest ability to affect total cholesterol values in the blood of diabetic mice. The results of this study are in line with research conducted by Adhitama (2023), namely the higher the dose of extract, the greater the ability to lower cholesterol levels.

The ethanol extract ability of fruit bhee dose 400 mg/kg BB in the P3 group was not significantly different from the Drug Control (KO) group. The percentage of total cholesterol reduction in knockouts was slightly lower than in the P3 group at 22.1%. The drug used as a comparison in this study was metformin which aimed to lower blood glucose levels in diabetic mice. The role of metformin as an antidiabetic is to increase the sensitivity of insulin receptors so that the absorption of blood glucose levels can take place properly (Pangodian, 2023). The role of metformin in addition to lowering blood glucose levels can also help regenerate lipid profiles by inhibiting the synthesis of triglycerides and cholesterol. Metformin can also work to reduce lipid levels by lowering plasma triglyceride levels (Meliawati, 2023).

Ethanol extract from bhee fruit can reduce total cholesterol levels in diabetic mice because of its phytochemical content. Bhee fruit ethanol extract contains alkaloids, terpenoids, saponins, phenols, and tannins. The content of these phytochemicals affects blood glucose levels in diabetic mice. Tannins can delay glucose absorption after meals because they act as chelates that can constrict epithelial cell membranes in the small intestine. A delay in glucose absorption in the small intestine can control the rate of increase in blood glucose levels for the better. The hypoglycemic activity of tannins occurs because they can repair damage to pancreatic β cell tissue through increased muscle glycogenesis (Magfirah, 2022).

Terpenes act as antidiabetic because they have antioxidant activity and help increase insulin production through the process of inhibiting the signaling pathway of carbohydrate metabolism and effectively inhibiting the α-glucosidase process (Shehadeh, 2021). Saponins can play a role in minimizing damage to the liver due to insulin that cannot be produced so there is an increase in insulin signaling transduction (Feng, 2021). Flavonoids and alkaloids work as antidiabetic agents because they have antioxidant activity with intrapancreatic and extrapancreatic mechanisms. The intrapancreatic mechanism is a secondary metabolite mechanism that works to repair the pancreas by providing protection to pancreatic β cells, increasing insulin secretion, and helping repair damage to pancreatic β cells. The extrapancreatic mechanism is the ability of secondary metabolites that control blood glucose levels outside the pancreas by suppressing the ability to absorb blood glucose in the intestine and reducing glucogenesis activity (Suherman, 2022).

The phytochemicals mentioned above will act to lower blood glucose levels and will indirectly affect total cholesterol levels. The direct mechanism of alkaloids lowering cholesterol levels is by inhibiting the activity of pancreatic lipase enzymes. This inhibition can increase fat excretion so that cholesterol formation cannot occur because the fat that should be absorbed by the liver will be inhibited because the lipase enzyme activity does not run properly (Rindiany, 2022).

The ability of terpenoids to reduce cholesterol levels through the mechanism of inhibition of 3-hydroxy-3-methylglutaril (HMG-CoA) *reductase activity* which plays a role in cholesterol synthesis (Wardiatini, 2015). Saponins work to lower cholesterol through inhibition of cholesterol absorption in the intestine and inhibition of pancreatic lipase enzyme activity. Tannins act as inhibitors of the process of lipid absorption in the intestine through the reaction process to mucosal

and epithelial proteins in the intestine. This will cause the buildup of blood cholesterol to decrease (Hasanah, 2023).

Phenols have the potential to reduce cholesterol levels by reducing LDL levels, namely capturing free radicals. In addition, phenols can increase HDL levels through the work of macrophages by increasing the *Reverse Cholesterol Transport (*RCT) process and increasing the activity of *Lechitin cholesterol Acyl Transferase* (LACT) which functions as an enzyme to convert free cholesterol into new HDL-forming cholesterol esters so that HDL levels increase (Wardani, 2022).

4. CONCLUSION

Giving Bhee fruit extract (*Melastoma Sp*) in various doses can reduce total cholesterol levels in diabetes mellitus mice, where the dose of 400 mg/kg BB is the most effective in reducing total cholesterol levels in diabetic mice shown in the P3 group has the highest percentage of reduction in total cholesterol levels of 24.16% compared to the P1 group (7.64%) with a dose of 100 mg/kg BB and P2 (11.11%) with a dose of 200 mg/kg BB.

REFERENCES

Adhitama, S., Kuswanti, N., &; Khaleyla, F. (2023). The Effect of Kedondong Leaf Extract on Reducing Total Cholesterol Levels and Body Weight of Type II Diabetes Mellitus Mice. LenteraBio: Biological Scientific Periodical, 12(3), 354-362.

Adriansyah, I., Handito, D., &; Widyasari, R. (2020). EFEKTIVITAS BUBUK KOPI ROBUSTA FUNGSIONAL DIFORTIFIKASI BUBUK DAUN KERSEN TERHADAP PENURUNAN KADAR GULA DARAH MENCIT DIABETES: The Effectiveness of Functional Robusta Coffee Powder Fortified by Muntingia calabura L. Leaves Powder to Lower Blood Glucose Level in Diabetic Mice. Pro Food, 6(1), 581-590.

Afriyeni, H., Putri, N. I., &; Rizal, R. (2023). Effect of Dragon Scales Leaf Ethanol Extract (Pyrrosia Piloselloides L.) on Reducing Total Cholesterol Levels in Hypercholesterolemic Mice: Effect of Dragon Scales Leaf Ethanol Extract (Pyrrosia Piloselloides L.) on Reducing Total Cholesterol Levels in Hypercholesterolemic Mice. Journal of Science and Health, 5(4), 528-534.

AMALIA, I. (2022). ETHANOL EXTRACT ABILITY OF CHERRY LEAVES (Muntingia calabura L.) IN LOWERING GLUCOSE LEVELS AND TOTAL BLOOD CHOLESTEROL LEVELS IN MICE (Mus musculus L.) AFTER ALLOXAN-INDUCED.

Anggraini, R. (2018). Correlation of cholesterol levels with the incidence of type 2 diabetes mellitus in men. Medical and Health Science Journal, 2(2).

Anisa, S., Khumaidi, A., &; Khaerati, K. (2023). ACTIVITY OF EBONY LEAF EXTRACT (Diospyros celebica Bakh.) AGAINST ALLOXAN-INDUCED WHITE RAT DIABETIC WOUND HEALING: ACTIVITY OF EBONY LEAF EXTRACT (Diospyros celebica Bakh.) ON DIABETIC Wound Healing ALLOXAN-INDUCED WHITE RATS. Medical Science: Scientific Journal of Pharmacy, 8(2), 539-548.

Ardiani, R., Nasution, H. M., &; Tanjung, F. A. (2020, December). Activity Test of Binahong Leaf Extract (Anredera cordifolia (Ten.) Steenis) to the blood sugar levels of mice. In PROCEEDINGS OF THE NATIONAL SEMINAR ON RESEARCH RESULTS (Vol. 3, No. 1, pp. 484-490).

Aceh Health Office (2023). Aceh Health Profile 2022. https://dinkes.acehprov.go.id.

Feng, M., Liu, F., Xing, J., Zhong, Y., & Zhou, X. (2021). Anemarrhena saponins attenuate insulin resistance in rats with high-fat diet-induced obesity via the IRS-1/PI3K/AKT pathway. Journal of Ethnopharmacology, 277, 114251.

Fransiska, I., Indahyani, D. E., &; Handayani, A. T. W. (2020). Cholesterol Levels in Diabetic Mice (Mus-Musculus) After Consumption of Brown Seaweed Extract (Phaeophyta). Health Library, 8(1), 36-41.

Haerani, H., &; Zulkarnain, Z. (2023). The effect of palm vinegar on blood sugar levels and histopathology of male ICR mouse pancreas (Mus musculus). Technoscience: Science and Technology Information Media, 17(2), 210-219.

Haiti, M., & Christyawardani, L. S. (2023). Relationship of Glucose Levels in Blood with Cholesterol Levels. Journal of Silampary Nursing, 6(2), 1655-1663.

Hasanah, R., &; Purwanti, A. (2023). ACTIVITY TEST OF ETHYL ACETATE EXTRACT OF HORN BANANA PEEL (Musa acuminata x Musa balbisiana) AS ANTIBACTERIAL Propionibacterium acnes (Doctoral dissertation, dr. SOEBANDI University).

Heliawati, L. (2018). Organic chemistry of natural materials. Bogor: Pakuan University.

International Diabetes Federation (IDF).2021. International Diabetes Federation Diabetes Caces In The World.

Jilao, M. (2017). Adherence rate of oral antidiabetic drug use in diabetes mellitus patients at Koh-Libong Health Center Thailand (Doctoral dissertation, Maulana Malik Ibrahim State Islamic University).

Ministry of Health of the Republic of Indonesia. (2018). Normal Values of Total Cholesterol. P2PTM KEMKES.

Maghfirah, Y. S. (2022). EFFECT OF LIME PEEL EXTRACT (Citrus amblycarpa Hassk) ON SGOT AND SGPT LEVELS OF RATS (Rattus novergicus) FED A HIGH-FAT DIET.

Maharani, A. D. K., Santoso, P., &; Udayani, N. N. W. (2023). Effects of Dewandaru Fruit Ethanol Extract (Eugenia uniflora L) on Blood Glucose Lowering and Pancreatic Beta Cell Repair in Aloxane-Induced Mice. Usadha, 2(2), 39-44.

Meliawati, N. W. (2023). COST-EFFECTIVENESS ANALYSIS OF THE USE OF METFORMIN AND GLIMEPIRIDE IN PATIENTS WITH TYPE 2 DIABETES MELLITUS INPATIENT AT THE HOSPITAL. ROBERT WOLTER MONGISIDI MANADO CITY. Jurnal Farmasi Medica/Pharmacy Medical Journal (PMJ), 6(1), 68-76.

Naim, M. R., Sulastri, S., &; Hadi, S. (2019). Description of the results of cholesterol level examination in hypertensive patients at Syekh Yusuf Hospital, Gowa Regency. Journal of Media Laboran, 9(2), 33-38.

Novitalia, A., &; Miladiyah, I. (2022). Hypoglycemic activity of snedds ethanol extract of Harendong fruit (Melastoma affine D. Don) in alloxan-induced zebrafish (Danio rerio). Indonesian Journal of Medicinal Plants, 15(1), 48-56.

Nugroho, C. A., Sumadji, A. R., &; Ganjari, L. E. (2022). Cholesterol, HDL, and LDL Levels of Hypercholesterol Mice with Red Andong Leaf Extract Treatment. JIIP-Scientific Journal of Educational Sciences, 5(11), 4792-4796.

Pangondian, A., Rambe, R., Umaya, C., Athaillah, A., &; Jambak, K. (2023). The Potency of Striped Flower Extract (Clitorea ternatea L.) Against Antidiabetes in Male White Mice (Mus musculus). Forte Journal, 3(2), 150-157.

Rinawati, R., Muhsin, S. W., Sari, W., Hayuningtyas, A., Putri, S. E., Nursia, L. E., & Siregar, S. M. F. (2023). Phytochemical Screening and Blood Glucose Level Effects of Bhee Fruit Extract (Melastoma sp) on Diabetic Mice. J-Kesmas: Jurnal Fakultas Kesehatan Masyarakat (The Indonesian Journal of Public Health), 10(1), 15-19.

Rindiany, C. (2022). The. Effect. of. Giving. Noni. Fruit. Extract. Microcapsules (Morinda. Citrifolia L.) as. Feed Additive on Blood Cholesterol and Triglyceride Levels in Sentul Chicken. Jurnal Nutrisi Ternak Tropis dan Ilmu Pakan (Journal of Tropical Animal Nutrition and Feed Science), 4(4), 129-137.

Riskesdas. 2018. Key Results of Riskesdas 2018.

SELLY TRI, U. T. A. M. I. (2023). THE LEVEL OF SUITABILITY FOR THE USE OF ANTIDIABETIC DRUGS IN DIABETES MELLITUS PATIENTS WITH COMPLICATIONS OF CHRONIC KIDNEY FAILURE AT MAJENANG HOSPITAL FOR THE 2022 PERIOD (Doctoral dissertation, Al-Irsyad University Cilacap).

Setyaji, Y., Duri, I. D., Kuniasiwi, P., &; Putri, N. A. (2023). CONTROL DIABETES MELLITUS THROUGH EDUCATION AND CHECKING BLOOD SUGAR LEVELS WHILE AT ROTO KENONGO SEWON HOUSING. Borneo Community Health Service Journal, 3(2), 128-132.

Shehadeh, M. B., Suaifan, G. A., & Abu-Odeh, A. M. (2021). Plants secondary metabolites as blood glucose-lowering molecules. Molecules, 26(14), 4333.

Straniero, S., Laskar, A., Savva, C., Härdfeldt, J., Angelin, B., & Rudling, M. (2021). Murine bile acids explain species differences in the regulation of bile acid and cholesterol metabolism. Atherosclerosis, 331, e128.

Suarsih, C. (2020). The relationship between diet and the incidence of cholesterol in the elderly in the working area of the Tambaksari Health Center. Galuh Journal of Nursing, 2(1), 25-30.

Suherman, S., Hamzah, B., Pulukadang, S. H. V., Rahmawati, S., Hardani, M. F., Hardani, R., & Saifah, A. (2022). Antidiabetic Effect Test of Insulin Stem Extract (Tithonia diversifolia) Toward Streptozotocin-Induced Diabetic Rats (Rattus Norvegicus). Open Access Macedonian Journal of Medical Sciences, 10(A), 1006-1010.

Susilawati, Y., Muhtadi, A., Moektiwardoyo, M., &; Arifin, P. C. (2016). Antidiabetic Activity of Iler Leaf Ethanol Extract (Plectranthus scutellarioides (L.) R. Br.) in Wistar White Rats by Alloxan Induction Method. Farmaka, 14(2), 82-96.

Susilo, A. S., Zulfian, Z., &; Artini, I. (2020). Correlation of HbA1c Value with Total Cholesterol Levels in Type 2 Diabetes Mellitus Patients. Sandi Husada Health Scientific Journal, 9(2), 640-645.

Wahyuningsih, E. S., Sukmawati, I., Septiani, R. A., Winarti, S. A., &; Ikhtianingsih, W. (2023). THE EFFECTIVENESS OF THE TREATMENT OF DIABETES MELLITUS BY SYNTHETIC DRUGS AND NATURAL INGREDIENTS: LITERATURE REVIEW ARTICLE. Journal of Pharmacopolium, 6(1).

Wardani, S., Bogoriani, N. W., &; Rustini, N. L. (2022). ACTIVITY TEST OF COMBRANG FLOWER EXTRACT (Etlingera elatior Jack) AS HYPOLIPIDEMIA IN OBESE WISTAR RATS. Journal of Science and Applicative Technology, 6(2), 118-123.

Warditiani, N. K., Indrani, A. A. I. S., Sari, N. A. P. P., Swasti, I. A. S., Dewi, N. P. A. K., Widjaja, I. N. K., &; Wirasuta, I. M. A. G. (2015). Effect of administration of katuk leaf terpenoid fraction (Sauropus Androgynus (L.) Merr) on lipid profile of white rats (Rattus Novergicus, L.) male wistar strain induced fat-rich feed. Udayana Journal of Pharmacy, 4(2), 279791.

Wilsya, M., &; Agustin, Y. (2023). TEST OF ANTIDIARRHEAL EFFECT OF SENGGANI FRUIT EXTRACT (Melastoma malabathricum) AGAINST Shigella dysenteriae BACTERIA. Journal of Medical and Health Sciences, 10(1), 1388-1394.

World Health Organization (WHO). 2023. Global Report On Diabetes Mellitus.