Antidiabetic Activity of Ethanol Extract of Robusta Coffee (Coffea canephora) Leaves in Alloxan-Induced Mice (Mus musculus)

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ABSTRACT
Robusta coffee leaves are widely used by the community as a drink to lower blood glucose levels. According to several studies, robusta coffee leaves have a hypoglycemic effect because they contain bioactive compounds that are useful for lowering blood glucose levels. The purpose of this study was to determine the antidiabetic activity of the ethanol extract of robusta coffee leaves in alloxan-induced mice. In this study, mice were divided into 6 groups each consisting of 5 mice. Group I normal control, group II negative control was given 0.5% Na CMC, group III positive control was given acarbose 1%, group IV, V, and VI were treated with ethanol extract of robusta coffee leaves in successive doses of 50, 100, and 200 mg/kg body weight. Mice group II, III, IV, V, and VI were made hyperglycemic by inducing alloxan 200 mg/kgBW intraperitoneally. Mice blood was taken through a lateral vein and blood glucose levels were measured using a glucometer. The research data were analyzed using statistical analysis. The results of the study showed a decrease in blood glucose levels in group IV 25.1%, group V 40.9% and group VI 56.7%. Based on the results of this study, it can be concluded that the ethanol extract of robusta coffee leaves has antidiabetic activity which can reduce blood glucose levels in mice induced by alloxan and the optimal dose to reduce blood glucose levels is 200 mg/kgBW. The research data were analyzed using statistical analysis. The results of the study showed a decrease in blood glucose levels in group IV 25.1%, group V 40.9% and group VI 56.7%. Based on the results of this study, it can be concluded that the ethanolic extract of robusta coffee leaves has antidiabetic activity which can reduce blood glucose levels in mice induced by alloxan and the optimal dose to reduce blood glucose levels is 200 mg/kgBW. The research data were analyzed using statistical analysis. The results of the study showed a decrease in blood glucose levels in group IV 25.1%, group V 40.9% and group VI 56.7%. Based on the results of this study, it can be concluded that the ethanolic extract of robusta coffee leaves has antidiabetic activity which can reduce blood glucose levels in mice induced by alloxan and the optimal dose to reduce blood glucose levels is 200 mg/kgBW.

Keywords: Diabetes mellitus, *Coffea canephora*, alloxan.

INTRODUCTION

A. Background

According to the 2018 Basic Health Research Report (RISKESDAS) by the Ministry of Health, there was an increase in the prevalence of diabetes mellitus to 8.5% (Perkeni, 2019). In 2017, Indonesia was ranked sixth in the world with the highest prevalence of diabetes mellitus in the world along with China, India, the United States, Brazil and Mexico (ADA, 2006). Diabetes Mellitus is a disease with relatively expensive treatment costs for both individuals and families. In many countries, the cost of insulin injections and monitoring can cost half of the average family income, and access to drugs is difficult, therefore alternatives are needed to make it easier for the community in terms of treatment and care for diabetes mellitus.

Diabetes mellitus can be treated in various ways, one of which is by lowering blood glucose levels after eating, namely by preventing the absorption of carbohydrates, therefore inhibitors of carbohydrate hydrolyzing enzymes (such *as α glucosidase and α amylase*) can be useful as oral drugs to control increased blood glucose (Oboh G, et al, 2015).

Synthetic drugs used to inhibit the absorption of carbohydrates after eating in patients with diabetes mellitus are acarbose and other alpha glucosidase inhibitors (Oboh G, et al, 2015). An alternative that is often found in the community is to use traditional plants which are empirically and for generations believed to be used to lower blood glucose levels. Traditional plants that are often used by the community to reduce blood glucose levels are coffee plants, both robusta coffee and arabica coffee (Ristiana D, 2017). Robusta coffee plants grow a lot in areas outside Java such as North Sumatra, Lampung, Aceh, Sulawesi and other areas. Basically, Robusta coffee leaves are different from Arabica coffee leaves. Robusta coffee leaves are larger than Arabica, wavy on the sides, slightly light green and tapered at the ends (Kuit et al, 2004). Based on the age, coffee leaves consist of young leaves and old leaves. Young leaves are leaves that have a glossy appearance and are about 10-30 days old, while old leaves are dark green leaves with varying ages of about 6-12 months (Cahyani N, 2015).

The use of coffee leaves for health is related to the abundant bioactive components in coffee leaves (Xiumin C, 2018). Robusta coffee leaves have several bioactive compounds including antioxidant compounds, alkaloids, flavonoids, saponins, tannins, steroids, triterpenoids and coumarins (Shiyan S et al, 2017). According to research conducted by Pristiana, coffee leaves are a good source of phenolic compounds, and the type of robusta coffee leaf has a higher phenol content than the type of Arabica coffee leaf (Ristiana D, 2017). One of the phenolic compounds found in coffee leaves is chlorogenic acid which has beneficial effects on health such as antioxidant, anti-mutagenic, anti-carcinogenic and anti-inflammatory (Hudacova, 2016) (Cahyani, 2015).

The content of chlorogenic acid in coffee leaves also has benefits for lowering blood glucose levels because the chlorogenic acid it contains can regulate fat and glucose metabolism by reducing glucose production in the liver and fat synthesis (Farhaty, 2014). Chlorogenic acid contained in coffee leaves also has the effect of inhibiting the enzymes -amylase and -glucosidase which play a role in the breakdown of carbohydrates in the digestive tract so that it is relevant to control the increase in blood glucose after eating in patients with diabetes mellitus (Oboh G, 2015)). The content of bioactive compounds such as chlorogenic acid in each coffee leaf is influenced by several factors such as soil type, genetic factors, planting method, climate, temperature, and the surrounding environment (Farah, 2006).

The content of compounds in coffee leaves other than chlorogenic acid is flavonoid compounds that can stimulate insulin release signals by increasing the release of Ca2+ ions so as to improve insulin receptor sensitivity, in addition, flavonoids also have benefits as antioxidants that can reduce oxidative stress and can reduce reactive oxygen species. ROS) so that it can have a protective effect on pancreatic beta cells (H Kaneto, 1999).

Knowing the presence of abundant and beneficial bioactive compounds for health from coffee leaves, the researchers wished to conduct research to determine whether robusta coffee

leaves
has antidiabetic activity in mice (Mus musculus) induced by alloxan

METHODS

A. Ethics Review Protocol

The ethical review was conducted at the Health Research Ethics Commission (KEPK) of the National Development University (UPN) "Veterans" Jakarta.

B. Determination of Robusta Coffee Leaf Plants (Coffea canephora)

Determination of Robusta coffee (Coffea Canephora) was carried out in the Biota Collection Room, Faculty of Mathematics and Natural Sciences, University of Indonesia, Depok, West Java.

C. Robusta Coffee (*Coffea canephora*) Leaf Extract Production

The dried robusta coffee leaves are blended until they become a fine powder. Robusta coffee leaf fine powder was weighed as much as 500 grams then extracted by kinetic maceration using 70% ethanol solvent and then filtered. Remaceration was carried out 3 times from dark colored to colorless maserate. The obtained filtrate is then collected and concentrated by means of a rotary evaporator

D. Phytochemical Screening

Phytochemical screening was carried out on robusta coffee leaf simplicia powder based on "Phytochemical screening" Farnsworth

1. Identification of alkaloid compounds

A total of 2 grams of simplicia powder of robusta coffee leaves was weighed and moistened with 5 ml of 30% ammonium, ground in a mortar, then added 20 ml of chloroform and crushed again vigorously, the mixture was filtered with filter paper, the filtrate in the form of an organic solution was taken (as solution A) , a portion of solution A (10 ml) was extracted with 1:10 HCl solution with shaking in a test tube, taking the top solution (solution B). Solution A was dripped with a few drops on filter paper and sprayed or dripped with Dragendorff's reagent, a red/orange color was formed on the filter paper indicating the presence of alkaloid compounds. Solution B was divided into 2 test tubes, added Dragendorff's reagent and Mayer's reagent, respectively.

2. Identification of Flavonoid compounds

A total of 2 grams of simplicia powder was weighed, added with 100 ml of hot water, boiled for 5 minutes, filtered with filter paper, the filtrate was obtained which would be used as an experimental solution. Into 5 ml of the experimental solution (in a test tube) added magnesium powder or plate to taste and 1 ml of concentrated HCl, add 5 ml of amyl alcohol, shaken vigorously and allow to separate, a color is formed in the amylalcohol color solution indicating the presence of flavonoid compounds.

3. Identification of saponins

As much as 10 ml of the experimental solution obtained from experiment no. 2 was put into a test tube and shaken vertically for 10 minutes, a stable foam was formed in the test tube indicating the presence of saponin group compounds. When 1 drop of 1% HCl is added (dilute) the foam remains stable.

4. Identification of Tannin Compounds

A total of 2 grams of coffee leaf simplicia powder was added to 100 ml of water, boiled for 15 minutes, cooled and filtered with filter paper and the filtrate was divided into two parts. To the first filtrate, 1% Ferrri (III) chloride was added to form a blackish green or blue-black color indicating the presence of tannins. Into the second filtrate added 15 ml of static reagent (30% formaldehyde: 2:1 concentrated HCl), heated on a water bath to form a pink color indicating the presence of catechol tannins. Furthermore, the precipitate was filtered, the filtrate was saturated with sodium acetate, a few drops of 1% ferric (III) chloride solution were added to form a blue ink color indicating the presence of faulty tannins.

5. Identification of quinone compouds

Take 5 ml of experimental solution no.2, then put it in a test tube, add a few drops of 1% NaOH, a red color is formed indicating the presence of quinone group compounds

6. Identification of steroids and trterpenoid

Weighed as much as 2 grams of coffee leaf simplicia powder, macerated with 20 ml of ether for 2 hours (in a container with a tight lid) filtered and the filtrate was taken, 5 ml of the filtrate was evaporated in a vaporizer cup until residue was obtained, 2 drops of acid were added to the residue. acetic anhydride and 1 drop of concentrated sulfuric acid (Libermann-Burchard reagent), a green or red color is formed indicating the presence of steroid and triterpenoid compounds.

7. Identification of essential oil compounds

A total of 2 grams of robusta coffee leaf simplicia powder was weighed and put into a test tube, added 10 mml of petroleum ether solvent and put a funnel (which was given a layer of cotton that had been moistened with water) in the mouth of the tube, heated for 10 minutes on a water bath and cooled, filtered with using filter paper, the filtrate obtained was evaporated in a vaporizer cup, the residue with an aromatic/pleasant smell indicated the presence of volatile oil group compounds.

8. Identification of coumarin compounds

A total of 2 grams of robusta coffee leaf simplicia powder was weighed and put into a test tube, added 10 ml of chloroform solvent and put a funnel (which was given a layer of cotton that has been moistened with water) at the mouth of the tube, heated for 20 minutes on a water bath, cooled, filtered with filter paper, the filtrate is evaporated in an evaporating dish to dry, the remainder is added 10 ml of hot water, cooled, the solution is put into a test tube, add 0.5 ml of ammonia (NH4OH), observed under ultraviolet light at a wavelength of 365 nm, fluorescence occurs Blue or green color indicates the presence of coumarin group compounds.

E. Preparation of Test Material

1. Preparation of 0.5% CMC Sodium Suspension

   A suspension of CMC-Na was made by weighing 0.5 g of sodium CMC suspended in hot water with a volume of 100 ml, then allowed to stand for approximately 30 minutes until the Sodium CMC swelled.

2. Preparation of 1% Acarbose Suspension

   Take a 100 mg acarbose tablet, grind it finely, add 0.5% sodium CMC suspension to taste, grind until homogeneous, put in a 10 ml volumetric flask then mix until homogeneous and the volume is made up to the mark.

3. Preparation of 1% Alloxan solution

   A solution of alloxan was made by weighing 100 mg of alloxan powder, put it in a 100 ml volumetric flask, added a physiological solution of 0.9% NaCl, shaken until dissolved and then made up to volume.

4. Make a diabetic mouse model

   Each mouse was weighed, then the dose and volume of injection of 1% alloxan solution were calculated. Alloxan injection was done intraperitoneally and only once. Measurement of blood glucose levels is done after 48 hours

F. Anti-diabetic Activity Test

1. Grouping of test animals

Experimental animals were divided into 6 groups, each group consisting of 5 experimental animals. Tests were carried out with each group as follows:

a) Normal control group: group of male mice given standard feed

b) Negative control group: group of mice that were given standard feed and induced with alloxan and given 0.5% Na CMC

c) Positive control group: group of mice that were induced with alloxan and given 1% acarbose suspension for 14 days
d) Test Group I: group of mice that were induced with alloxan and given ethanol extract of robusta coffee leaves at a dose of 50 mg/kgBW for 14 days
e) Test Group II: group of mice that were induced with alloxan and given ethanol extract of robusta coffee leaves with dose of 100 mg/KgBW for 14 days
f) Test Group III: group of mice that were induced with alloxan and given ethanol extract of robusta coffee leaves at a dose of 200 mg/KgBW for 14 days

2. Blood Glucose Level Measurement

a) The glucometer is calibrated by inserting the code strip into the instrument until the code number appears
b) The measured mice blood was taken from the lateral vein in the tail of the mice. The tip of the tail is pierced using a blood lancet and then the mouse tail is pressed to release a drop of blood
c) Drops of blood are placed on the glucometer strip and observed until a number appears which is the blood sugar level of the mice
d) Examination of the blood glucose levels of mice was carried out on all mice and carried out on day 0, day 3, day 7 and day 14.
e) Records are made for every inspection carried out

I. Data analysis

The data obtained from the calculation of blood glucose levels in each test group were processed by statistical analysis using SPSS (Statistic Package The Social Sciences) version 24.0. The data obtained were tested for normality (Kolmogrov-Smirnov test) and homogeneity (Levene test). If the data is normally distributed and homogeneous, a statistical statistical test is performed using the one-way analysis of variance (ANOVA) method, and if the results show a significant difference, then proceed with the Post Hoc LSD (Least Significant Difference) test to see if there is a difference in each treatment group, if any If one ANOVA condition is not met, a non-parametric Kruskal-Walls analysis is performed, and if the results show a significant difference, then Mann-Whitney is tested to see if there is a difference in each treatment group.

RESULTS AND DISCUSSION

A. Plant Determination

From the results of plant determinations carried out at Herbarium Depokensis (DEP), Biota Collection Room, University of Indonesia, it shows that the plant part (leaf) used in this study is true robusta coffee leaf (Coffea canephora).

B. Results of Making Ethanol Extract of Robusta Coffee Leaves (Coffea canephora)

Making the test sample, namely the ethanol extract of robusta coffee leaves using coffee leaves from one of the people's gardens in Bittuang District, Tana Toraja Regency with the maceration method. Extraction is carried out to attract polar compounds so that 70% ethanol is used as a solvent. Extraction by maceration method is a cold extraction, this method is not carried out by heating in the extraction process which is expected to damage the chemical compounds contained in the sample. Maceration is also carried out in a closed room to avoid the influence of sunlight on the stability of the compounds to be taken. From the weight of 150 grams of coffee leaf powder, 75 grams of robusta coffee leaf ethanol extract was obtained so that the yield produced was 15%.

C. Results of Phytochemical Screening Simplicia powder of robusta coffee (Coffea canephora) leaves

Phytochemical screening was carried out with the aim of knowing the components of the

compounds contained in the simplicia of robusta coffee leaves. The tests carried out included checking the content of alkaloids, saponins, flavonoids, tannins, steroids/triterpenoids, coumarins, and essential oils. From the results of phytochemical screening carried out on the simplicia powder of robusta coffee leaves, it shows that the simplicia powder contains alkaloids, flavonoids, saponins, tannins, quinones and steroids/triterpenoids.

D. Results of Examination of Total Phenol Levels in Robusta Coffee Leaves (Coffea canephora)

Examination of the total phenol content of robusta coffee leaves was carried out at the Testing and Research Services Laboratory of the Faculty of Pharmacy, Pancasila University. In the examination of total phenol levels, the total phenol content of the ethanol extract of robusta coffee leaves from Tana Toraja was 13.09% while robusta coffee leaves from the Research Institute for Spices and Medicinal Plants (Balitro) Bogor obtained total phenol levels of 13.86%. The difference in total phenol levels in the two coffee leaf extracts is thought to occur due to differences in the place or growing environment between the two types of plants. One of the phenolic compounds in coffee leaves is chlorogenic acid which has an effect on lowering blood glucose levels and is useful as an antioxidant (6).

E. Results of Measurement of Blood Glucose Levels in Mice After Alloxan Induction

To obtain a hyperglycemic mouse model, induction was performed with alloxan at a dose of 200 mg/kgBW. The diabetogenic agent used in this study was alloxan monohydrate. Alloxan is a diabetogenic agent that is commonly used to assess the antidiabetic or hypoglycemic potential of pure compounds and plant extracts. This compound is most widely used to induce diabetes in experimental studies in animals because it is more affordable and available. Giving alloxan causes an increase in blood glucose levels in mice caused by the formation of free radicals through redox reactions and damage to cell membrane permeability resulting in damage to pancreatic beta cells that produce insulin (Stevani H, 2016).

Table 1. Results of measuring blood glucose levels after alloxan induction

Klp Treatment	Initial Blood Glucose Level	Blood glucose level after alloxan induction
II	102.0	249.8
III	87.6	304.2
IV	99.2	159.2
V	101.4	206.4
VI	99.6	245.8

The data for measuring blood glucose levels of mice in hyperglycemic conditions was carried out to see the effect of giving alloxan to mice in groups II, III, IV, V and VI, whether it could make mice in that group hyperglycemic by using group I (normal control group) as a comparison. The data in the table shows an increase in blood glucose levels of mice in groups II, III, IV, V and VI after alloxan was induced. Based on the results of the Kruskal-Wallis analysis, a significance value of 0.003 (p 0.05) was obtained, meaning that there was a significant difference in the blood glucose levels of mice in groups I, II, III, IV, V and VI. Data analysis of blood glucose levels in mice was followed by the Mann-Whitney test. Based on the test results with the Mann-Whitney statistical test, it showed that there were significant

differences in blood glucose levels in group I (normal control) with groups II, III, IV, V, and VI. This shows that alloxan induction is able to make mice with hyperglycemic conditions.

F. The difference in blood glucose levels of mice on day 0 with day 14

The difference in blood glucose levels in mice before and after treatment was calculated the difference between glucose levels on day 0 and day 14 to see if there was a decrease in blood glucose levels in mice after each group was given treatment. Data on the difference in blood glucose levels of mice can be seen in table 2

Table 2. Differences in blood glucose levels of mice on day 0 with day 14

Mice	Blood glucose levels in mice on day 14 (mg/dl)				
	II	**III**	**IV**	**V**	**VI**
1	-7	74	24	110	137
2	18	234	16	81	372
3	20	156	53	64	90
4	-3	45	90	69	80
5	15	66	30	100	83
X	8.6	115	42.6	84.8	152.4

From the results of the Kruskal-Wallis analysis, a significance value of 0.003 ($p < 0.05$) was obtained, this indicated that there was a significant difference in the difference in blood glucose levels of mice between the treatment groups, so the analysis continued with the Mann-Whitney analysis. The results of the Mann-Whitney analysis can be seen in table 3.

Table 3. Significance value (Asymp.sig.2-tailed) difference in blood glucose levels of mice on day 0 with day 14

Group	II	III	IV	V	VI
II					
III	0.009*				
IV	0.009*	0.076			
V	0.009*	0.917	0.047*		
VI	0.009*	0.347	0.036*	0.251	

*there is a significant difference ($p<0.05$)

Information:

I : Normal control
II : Negative control
III : Positive Control
IV : Robusta coffee leaf extract dose 50mg/kgBB
V : Robusta coffee leaf extract dose of 100mg/kgBB
VI : Robusta coffee leaf extract dose of 200mg/kgBB

From the results of the Mann-Whitney analysis showed that the difference in blood glucose levels of mice before and after treatment in group II had a significant difference with groups III, IV, V and VI, this indicates that the blood glucose levels of mice that were given treatment decreased compared to the group that received treatment. not given treatment (group II). The results of the Mann-Whitney analysis showed that there was no significant difference between the difference in the decrease in blood glucose levels of mice given the extract and those given acarbose. Robusta coffee leaves contain flavonoid and phenolic compounds such as chlorogenic acid which can reduce blood glucose levels by one of the mechanisms, namely inhibiting the alpha glucosidase enzyme in the intestine such as the mechanism of reducing blood glucose levels by acarbose (Oboh, 2015).

G. Measurement of blood glucose levels after treatment (day -14)

Measurement of blood glucose in mice on day 14 was carried out to see the decrease in blood glucose levels of mice given the test preparation, namely ethanol extract of robusta coffee leaves. Data on the blood glucose levels of mice after receiving treatment (day 14) can be seen in table 4

Table 4. Data on blood glucose levels after treatment (day 14)

Mice	Blood glucose levels in mice on day 14 (mg/dl)					
	I	II	III	IV	V	VI
1	104	479	141	117	110	74
2	94	367	346	127	99	103
3	91	210	157	103	128	103
4	119	201	140	125	142	83
5	89	356	162	111	129	104

Based on the data in the table above, it can be seen that the mice that had experienced hyperglycemic conditions due to alloxan induction, then experienced a decrease in blood glucose levels on day 14 except in the negative control group. From the results of the Kruskal-Wallis test from data on blood glucose levels on the 14th day, a significance value of 0.001 ($p < 0.05$) was obtained, this indicates that there is a significant difference in the blood glucose levels of mice on the 14th day between group II, III, IV, V, and VI. The data were then analyzed using the Mann-Whitney test to determine differences in blood glucose levels in each treatment group.

Table 5. Significance values (Asymp.sig.2-tailed) glucose levels of mice in each treatment group after treatment (14th day)

Group	I	II	III	IV	V	VI
I						
II	0.009*					
III	0.009*	0.028*				
IV	0.076	0.009*	0.009*			
V	0.057	0.009*	0.028*	0.347		
VI	0.528	0.009*	0.028*	0.032*	0.026	

On the 14th day there was a decrease in blood glucose levels in group III, IV, V and VI mice. In group III it was still classified as hyperglycemic with an average blood glucose level of 189.2 mg/mice, but the administration of acarbose was able to reduce blood glucose levels of mice. In the treatment groups IV, V and VI who were given ethanol extract of robusta coffee leaves 50 mg/kgBW, 100 mg/kgBW and 200 mg/kgBW there was a decrease in blood glucose levels, where the average was 116.6 mg/dL; 121.6 mg/dL; and 93.4 mg/dL. On day 14, there was an insignificant decrease in blood glucose levels in group II, this could be due to the unstable duration of hyperglycemic alloxan (Ighodaro, 2017).

G. PERCENT REDUCTION OF BLOOD GLUCOSE LEVELS AFTER TREATMENT (Day 14)

To see the difference in the decrease in blood glucose levels in mice, data on blood glucose levels in mice were used when they were hyperglycemic (day 0) and blood glucose levels in mice on day 14 after treatment, the formula used to calculate the decrease in blood glucose levels (Pratiwi, 2018).

% PKGD = (ab)/ax 100%

Information:

a = blood glucose levels of mice after alloxan induction

b = blood glucose levels of mice at the time of observation on day t

PKGD = Decrease in blood glucose levels

The value of decreasing blood glucose levels in mice for 14 days receiving treatment can be seen in table 6.

Table 6. Percent decrease in blood glucose levels on day 14

Treatment Group	% PKGD		
	Day 3	Day 7	Day 14
1	-	-	-
II	-	-	-
III	13.4	17.7	35.6
IV	-	8,612	25,064
V	12.4	25.3	40.9
VI	2.6	19.3	56.7

Based on the data obtained, it can be seen that the ethanolic extract of robusta coffee leaves has the effect of reducing blood glucose levels, especially at a dose of 200 mg/kgBW for 14 days which is able to reduce blood glucose levels in mice to normal levels, with a percent decrease in blood glucose levels of 56 0.7 %, followed by a dose of 100 mg/kgBW of 40.9% and a dose of 50 mg/kgBW of 25.1%, this is also evidenced by statistical analysis, namely on the 14th day after treatment there was a significant difference in levels. blood glucose of mice in each group against the negative control that was not given any treatment.In the data on the difference in blood glucose levels of mice before and after being given treatment (difference in glucose levels from day 0 to day 14) it is known that there is a significant difference between the negative control and the treatment group which indicates that there is a decrease in blood glucose levels in the group given treatment for 14 days. compared with negative control that was not given treatment

In the research conducted, the decrease in blood glucose levels in the extract group at doses of 100 mg/kgBW and 200 mg/kgBW was better than the positive group, namely acarbose, this is presumably because Robusta coffee leaves are natural ingredients that have a lot of

bioactive content and in this study no isolation of certain bioactive compounds was carried out, so that the mechanism of lowering blood glucose levels could be better than the positive control. The decrease in blood glucose levels in the group given ethanol extract of robusta coffee leaves is thought to be due to the presence of bioactive compounds in robusta coffee leaves which have the effect of lowering blood glucose levels. Robusta coffee leaves are known to contain compounds that have pharmacological effects as antidiabetic agents, one of which is flavonoids and phenolic compounds, namely chlorogenic acid. Chlorogenic acid has been shown to be a specific competitive inhibitor of glucose-phosphate transfer in the rat intestine (Higdon, 2006). According to research by Shaum Shiyan et al, coffee leaves contain flavonoid and mangiferin compounds that are useful as antioxidants and have been shown to reduce oxidative stress and have the potential to treat diabetes mellitus (Shiyan, 2017).

CONCLUSION

Ethanol extract of robusta coffee leaves (Coffea canephora) has antidiabetic activity that can reduce blood glucose levels of mice (Mus musculus) induced by alloxan

The most optimal dose of robusta coffee leaf ethanol extract (Coffea canephora) in reducing blood glucose levels in mice induced by alloxan is 200 mg/kgBW.

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