ANTIDIABETIC TEST OF BREADFUNNEL LEAVES (Artocarpus communis) ON REDUCING BLOOD SUGAR LEVELS IN MICE (Mus musculus)

Wa Ode Nur Asni [1], Sarni [2], Yayuk Sri Rahayu [3]*

[1,2,3]Politeknik Baubau, Baubau, Indonesia

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CORRESPONDING AUTHOR

Nama : Sarni
Address: Bau-Bau
E-mail : sarni02@gmail.com

A B S T R A C T

Breadfruit tree is one of the traditional medicinal plants that is believed to have antidiabetic activity, where breadfruit leaves contain flavonoids, have good benefits for health when consumed because they have the property of lowering blood sugar levels. This study aims to conduct an antidiabetic test of breadfruit leaves (Artocarpus communis) on reducing blood glucose in mice (Mus muculus). From the phytochemical research that has been done, several compounds of breadfruit leaves were obtained such as riboflavin, tannin, potassium, acetylcholine, hydrocyanic acid and so on. These compounds can treat infections, reduce cholesterol levels and liver disease, inflammation, heart, kidneys, blood vessels. Ethanol extract of breadfruit leaves has shown results that can regulate fasting blood glucose levels and glucose tolerance(Lee et al., 2012). Based on research (Mu'nisa et al., 2012) found that mice given ethanol extract with alloxan induction can reduce blood sugar levels. Breadfruit leaf extract has anti-free radical activity derived from the high antioxidant compounds it contains(Suryanto & Frenly, 2019). Breadfruit leaves can also improve the non-specific immune system in mice.(Yuswantina et al., 2013).

The type of research used was a laboratory experiment with a maceration method for in vivo extraction using mice (Mus musculus) as test animals. The treatment group was divided into 3 groups, including a positive control group (glibenclamide suspension), dose group I 500 mg/kg BW, and dose group II 1000 mg/kg BW which was tested for 10 days. Based on the results of this study, that breadfruit leaf extract (Artocarpus communis) has antidiabetic activity. A dose of 1000 mg/kg BW showed a decrease of 38.99%, greater than a dose of 500 mg/kg BW which showed a decrease of 33.58%.

INTRODUCTION

Based on ethnobotany records, it is known that there are approximately 800 plants that have properties as antidiabetics. WHO has recommended herbal plants as a cure for diabetes. Plant species found in ancient Ayurveda texts and Indian systems can be utilized towards better health services by implementing a modern approach.(Kitukale & Chandewar, 2014).

Indonesia is the second country in the world with the most biological wealth and has the potential to utilize various types of plants for treatment. Breadfruit (Artocarpus communis) is a plant that is easy to obtain and has long been believed and used for generations for traditional medicine. Almost all parts of this plant can be used as traditional medicine.(Riasari et al., 2018). Breadfruit leaf extract, whether from the stem, leaves, fruit or even the skin, contains many secondary metabolites that can be useful for various conditions such as cytotoxicity, tyrosinase inhibitors, anti-arthritis, anti-platelet, anti-fungal, anti-viral, anti-tubercular and anti-bacterial.(Jagtap & Bapat, 2010), as well as anti diabetes mellitus(Nasution et al., 2014).

Breadfruit (Artocarpus communis) belongs to the Moraceae family and grows wild. Empirically, this fruit is often used for several diseases such as high blood pressure, heart disease and cholesterol. The ability of breadfruit leaves is inseparable from the presence of bioactive compounds in breadfruit leaves.(Sumadji et al., 2022).

Breadfruit leaves as a plant that is often found are believed by the community as an antidiabetic drug, so many people use this plant as an antidiabetic drug (Merliana, 2017). This is thought to be because it contains flavonoids which also function to reduce blood glucose levels.(Munarsih & Anggun, 2018).

From the phytochemical research that has been done, several compounds of breadfruit leaves were obtained such as riboflavin, tannin, potassium, acetylcholine, hydrocyanic acid and so on. These

compounds can treat infections, reduce cholesterol levels and liver disease, inflammation, heart, kidneys, blood vessels. Ethanol extract of breadfruit leaves has shown results that can regulate fasting blood glucose levels and glucose tolerance(Lee et al., 2012). Based on research (Mu'nisa et al., 2012) found that mice given ethanol extract with alloxan induction can reduce blood sugar levels. Breadfruit leaf extract has anti-free radical activity derived from the high antioxidant compounds it contains(Suryanto & Frenly, 2019). Breadfruit leaves can also improve the non-specific immune system in mice.(Yuswantina et al., 2013).

Based on the background, we are interested in conducting research to determine the activity of breadfruit leaves (Artocarpus communis) in reducing blood sugar in mice (Mus musculus).

METHODOLOGY

Tool

The tools used in this study were a syringe for mice (One Med), a 0.1 ml syringe, a busen, a beaker glass, a stirring rod, an Erlenmeyer flask, a mortar, a pestle, a set of blood glucose measuring instruments (Nesco), and a rotavator.

Material

The sample materials used in this study were Aquadest, 96% Ethanol, Na.CMC (Sigma), breadfruit leaves (Artocarpus Communis), Alloxan, glibenclamide.

Sampling

Samples were taken in Baubau City. The breadfruit leaf samples to be used are old breadfruit leaves with fresh dark green characteristics and the front of the leaf looks shiny. A total of 1000 grams of smooth breadfruit leaves were taken without spots or holes.

Work procedures

Making Simple Drugs

The sample is washed clean in tap water to remove any contamination and dirt that sticks to the sample. After that, it is cut into small pieces to facilitate the drying process, until it is dried by airing it and then blended until smooth.

Preparation of test material extract

A 300 gram fine sample was mixed with 96% ethanol in a ratio of 1:10. Soaked in a tightly closed container for 3 days while occasionally stirring so that the sample and solvent blend. Furthermore, the mixture was concentrated using an evaporator at a temperature of 40◦C.

Making Alloxan Solution

Weigh Alloxan as much as 0.52 mg/20 g mouse body weight, 0.598 mg/23 g mouse body weight, 0.546 mg/21 g mouse body weight, 0.572 mg/22 g mouse body weight, 0.494 mg/19 g mouse body weight, 0.468 mg/18 g mouse body weight. Then each dose is dissolved in 0.5 ml of distilled water.

Making Na.CMC

1 gram of NaCMC is slowly dissolved in 50 mL of hot distilled water (temperature 70◦C) until it thickens, then the mixture is made up to 100 mL of distilled water in a measuring cup.

Preparation of Glibenclamide Solution

Weigh glibenclamide as much as 0.013 mg/20 g mouse body weight and 0.0143 mg/22 g mouse body weight then dissolve it in 1 mL of 0.5% Na CMC.

Extract Dosage Preparation

At a dose of 500 mg/kg BW, 9.5 mg, 11.5 mg, and 10.5 mg of breadfruit leaf extract were weighed. Then at a dose of 1000 mg, 18 mg, 21 mg, and 20 mg were weighed, after which each sample was dissolved in 1 ml of 0.5% Na CMC.

Antidiabetic Testing

The test animals were acclimatized and then not given any food except water for 16 hours, on the first day of the experiment, blood samples were taken from the mice and glucose measurements were carried out. After that, a glucose solution of 4.2 mg/20g of mouse body weight was given. Glucose stabilization was carried out for 3 days, after the mice tested positive for DM, the mice were then grouped and their blood was taken. All mice were grouped into 3 groups given the following treatments:

1. Glibenclamide suspension (positive control group),
2. Ethanol extract of breadfruit leaves with a dose of 500 mg/kg body weight of mice (Dose group I), orally every day in the morning.

3. Ethanol extract of breadfruit leaves at a dose of 1000 mg/kg body weight of mice (Dose group II), orally every day in the morning.

This treatment was carried out for 10 days. Blood glucose levels were measured on days 2, 5 and 10. Do not forget to check blood sugar levels after treatment. Blood samples from mice were taken from the tail of the mouse using a needle, the blood obtained was then measured using a glycometer until the glucose levels of the mice were seen.

Data Analysis

The blood glucose data of mice obtained before and after treatment were collected and the average was calculated. Then a comparison of blood sugar levels before and after treatment was conducted to see whether or not there was an effect of breadfruit leaves on the treatment of diabetes in mice test animals.

RESULTS & DISCUSSION

Research result

Extraction Results

Table 1. Maceration Extraction Results

No	Sample Name	Amount of Simple Ingredients (grams)	Extract Amount (grams)	Yield (%)
1	Breadfruit leaves (Artocarpus communis)	362	57	15.75

Antidiabetic Test

The antidiabetic activity test of breadfruit leaf extract (Artocarpus communis) on alloxan-induced diabetic mice was conducted for 10 days. During the 10 days, all mice received treatment according to their respective test groups. The following are the results of blood sugar level observation data on mice.

Positive Control Group

Mice in this group were given a suspension of glibenclamide in 0.5% Na CMC. The following are the results of testing the blood sugar levels of mice for 10 days and the decrease in blood sugar levels experienced by mice.

Table 2. Results of the decrease in blood sugar levels in mice in the positive control group (glibenclamide suspension)

No	KGP (mg/dl)	KGA (mg/dl)	KGR (mg/dl)	% Decrease in Blood Sugar Levels
1.	122	213	117	45.07%
2.	114	183	97	46.99%
3.	98	209	112	46.41%
Average % Decrease in Blood Sugar Levels in Mice				46.15%

Information :

KGP: Fasting Blood Sugar Levels Before Alloxan Induction

KGA: Blood Sugar Levels After Alloxan Induction

KGR: Blood Sugar Levels After Induction *Glibenclamide*

Dose group I (500 mg extract/kg BW)

Mice in this group were given breadfruit leaf extract (Artocarpus communis) at a dose of 500 mg/kg BW. The following are the results of testing the blood sugar levels of mice for 10 days and the decrease in blood sugar levels experienced by mice.

Table 3. Results of the decrease in blood sugar levels in mice in the Dose I group (500 mg extract/kg BW).

No	KGP (mg/dl)	KGA (mg/dl)	KGR (mg/dl)	% Decrease in Blood Sugar Levels
1	93	210	138	34.28%
2	107	193	125	35.23%
3	113	208	143	31.25%
Average % Decrease in Blood Sugar Levels in Mice				33.58%

Information :

KGP: Fasting Blood Sugar Levels Before Alloxan Induction

KGA: Blood Sugar Levels After Alloxan Induction
KGR: Blood Sugar Levels After Induction by Breadfruit Leaf Extract (*Artocarpus communis*) with a dose of 500 mg/kg BW

Dose group II (1000 mg extract/kg BW)

Mice in this group were given breadfruit leaf extract (Artocarpus communis) at a dose of 1000 mg/kg BW. The following are the results of testing the blood sugar levels of mice for 10 days and the decrease in blood sugar levels experienced by mice.

Table 4 Results of the decrease in blood sugar levels in mice in the II dose group (1000 mg extract/kg BB).

No	KGP (mg/dl)	KGA (mg/dl)	KGR (mg/dl)	% Decrease in Blood Sugar Levels
1.	74	172	99	42.44%
2.	117	203	128	36.94%
3.	133	218	136	37.61%
Average % Decrease in Blood Sugar Levels in Mice				38.99%

Information :
KGP: Fasting Blood Sugar Levels Before Alloxan Induction
KGA: Blood Sugar Levels After Alloxan Induction
KGR: Blood Sugar Levels After Induction by Breadfruit Leaf Extract (*Artocarpus communis*) with a dose of 1000 mg/kg BW

RESULTS & DISCUSSION

In this antidiabetic activity test study, breadfruit leaves (Artocarpus communis) obtained in the Baubau area were used. Breadfruit leaves were taken directly from the tree and made into simplicia, then ground for use in the extraction process. The milled breadfruit leaf simplicia was weighed 362 g then macerated with 96% ethanol solvent for 3 days. In this soaking process, the compounds contained in the breadfruit leaf simplicia that can dissolve in the solvent (96% ethanol) can be extracted out. Furthermore, the solvent was evaporated from the filtrate obtained during the soaking or maceration process using Rotavapor, so that an extract weighing 57 g with a yield of 15.72% was obtained.

The levels obtained from breadfruit leaves (Artocarpus communis) are influenced by the environment in which the plant grows. The influence of this environment is closely related to the metabolic processes of plants, including biochemical processes and the synthesis of secondary metabolite compounds. Environmental factors such as altitude with high environmental stress, such as temperature, high humidity and low sunlight intensity can affect the production of secondary metabolites including flavonoid and antioxidant levels in plant extracts (Sarni et al., 2020).

In this antidiabetic ability test, the test animals were 8-week-old male mice weighing 18-23 grams and still in good health (not diabetic). All mice were placed in cages at room temperature. Throughout the test, their food and drink needs were met with sufficient and equal levels, and their cleanliness was maintained.

To induce diabetes in all mice, intravenous injection of alloxan monohydrate was performed after the mice were deprived of food for 16 hours, but could be given drinking water. The alloxan solution was prepared immediately before use, because its stability only lasted 1.5 minutes in water at a temperature of 37°C. During the observation process, the blood sugar levels of the mice were measured three times. The measurement was carried out by slightly injuring the tip of the mouse's tail to obtain a drop of blood, which was then applied to the glucose strip in the glucometer. After a few seconds, the blood sugar level will be displayed on the glucometer.

In this study, there were 9 mice divided into 3 groups. The first group was a positive control group as a comparison, where mice induced by diabetes were given glibenclamide treatment. This group serves as a reference to evaluate the ability of breadfruit leaf extract (Artocarpus communis) in reducing blood sugar levels.

In addition, there were two test groups that received breadfruit leaf extract (Artocarpus communis) with varying doses. The first test group consisted of diabetic mice that were given breadfruit leaf extract with a dose of 500 mg/kg body weight. Meanwhile, the second test group included diabetic mice that received breadfruit leaf extract with a dose of 1000 mg/kg body weight.

Breadfruit leaf extract was administered orally using a cannula as an aid. Glucose observations were carried out three times during 10 days of observation: on day 2 (before alloxan induction and on

the same day as induction), day 5 (three days after alloxan induction, followed by administration of glibenclamide and breadfruit leaf extract), and day 10 (after five days of glibenclamide and breadfruit leaf extract, where the last measurement was carried out). Blood sugar levels on day 5 were considered as initial blood sugar levels (BG), while measurements on day 10 were as final blood sugar levels (FBS). The decrease in blood sugar levels was calculated from the difference between initial and final blood sugar levels.

The positive control group consisted of diabetic mice given glibenclamide suspension, an oral antidiabetic drug from the sulfonylurea class that works by stimulating insulin secretion from pancreatic beta cells, thereby lowering blood glucose levels. In this group, blood sugar levels in mice decreased by 46.15%.

In dose group I, consisting of diabetic mice that received breadfruit leaf extract (Artocarpus communis) at a dose of 500 mg/kg body weight, there was a fairly rapid reduction in blood sugar levels. The administration of this extract was stated to be able to reduce blood sugar levels in mice by 33.58% in a period of 5 days.

In dose group II, consisting of diabetic mice that received breadfruit leaf extract (Artocarpus communis) at a dose of 1000 mg/kg body weight, experienced a decrease in blood sugar levels of 38.99% in 5 days. This decrease was greater than that of dose group I in the same time period.

Based on the description, it can be stated that breadfruit leaf extract (Artocarpus communis) with a dose of 1000 mg/kg body weight produces a greater reduction in blood sugar levels in mice than a dose of 500 mg/kg. However, oral antidiabetic drugs such as glibenclamide are still better at reducing blood sugar levels, because this synthetic drug has been tested pharmacologically and clinically.

Although breadfruit leaf extract (Artocarpus communis) has the ability compared to synthetic drugs, however, breadfruit leaf extract (Artocarpus communis) is safer to use in the long term because it uses natural ingredients that have therapeutic or healing properties and do not have significant side effects, whereas synthetic drugs are a mixture of chemicals which, when viewed from the human physiological system, have side effects that are not good for long-term use.

Breadfruit leaves (Artocarpus communis) contain various beneficial chemical compounds, such as saponins, polyphenols, hydrocyanic acid, acetylcholine, tannins, riboflavin, phenols, and flavonoids. Flavonoid compounds contained in these leaves have the potential to reduce blood sugar levels in people with diabetes mellitus, because flavonoids function as inhibitors of the α-glucosidase enzyme. This enzyme plays a role in breaking down α-amylase products into glucose during the digestive process.(Lengkey, 2022).

In research(Sani et al., 2017), the percentage of decrease in blood sugar levels in mice for glibenclamide was 23.64%, Dose II 18.18%, and Dose I 5.12%. These figures are smaller than the results of this study, where the decrease in blood sugar in glibenclamide reached 46.15%, Dose II 38.99%, and Dose I 33.58%. This is because the doses used in the previous study were lower than those used in this study.

The results of this and previous studies prove that breadfruit leaf extract can be used as an antidiabetic drug because it has almost the same efficacy as synthetic drugs.

CONCLUSION

Based on the results of this study, it can be stated that breadfruit leaf extract (Artocarpus communis) has antidiabetic activity. A dose of 1000 mg/kg BW experienced a reduction of 38.99% greater than a dose of 500 mg/kg BW experienced a reduction of 33.58%.

Limitations in this study need to be considered, biological variability between mice can affect the response to treatment, so that the results of the study can vary. In addition, environmental factors such as temperature, humidity, and lighting can also affect the physiological condition of mice and affect the final results of the study.

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