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The Effect of Infusion Breadfruit Leaves (*Artocarpus altilis* (Parkinson) Fosberg) On Blood Glucose Levels in Male Mice (*Mus musculus*) Diabetes Mellitus Type 2

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ABSTRACT

Objective: The purpose of this study was to determine the content of secondary metabolite compounds contained in breadfruit leaf infusions which affect blood glucose levels and to determine the effective concentration of breadfruit leaf infusions which play a role in lowering blood glucose levels.

Methods: The research method was carried out experimentally with the stages of making simplicia, making infusion, phytochemical screening and testing the breadfruit leaf infusion using the alloxan induction method. Antidiabetic testing was carried out in vivo on animal testing with 5 treatment groups (Na-CMC 1% w/v, Glibenclamide 0.65 mg / kg BW, breadfruit leaf infusion 300 mg/kg BW, 400mg/kg BW, 500 mg/kg BW).

Results: The results of phytochemical screening on breadfruit leaf infusion showed flavonoids, saponins and tannins. The results of the antidiabetic test with the alloxan induction method showed a decrease in blood glucose levels at the concentration of breadfruit leaf infusion 300 mg / kg BW, 400 mg / kg BW, 500 mg / kg BW.

Conclusion: Breadfruit leaf infusion has an effect on reducing blood glucose levels in male type 2 diabetes mellitus mice.

Keywords: Infusion, breadfruit leaves, *Artocarpus altilis*, BGL.

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INTRODUCTION

Diabetes mellitus is a disease caused by a disruption in glucose, lipid and protein metabolism characterized by hyperglycemia which results in a decreased insulin secretion from pancreatic beta cells causing abnormally high blood glucose levels^{1,2}.

Several synthetic drugs in diabetes therapy such as glibenclamide, metformin, glimepiride have been widely used to treat diabetes mellitus, but have side effects such as vomiting, nausea, hypoglycemia, abnormal weight gain, and kidney disorders³. So we need alternatives in diabetes therapy using natural ingredients such as breadfruit plants.

Breadfruit (*Artocarpus altilis*) has many benefits. In the West Indies, yellowing breadfruit leaves are used as tea to

treat diabetes, high blood pressure and asthma⁴. Secondary metabolite compounds isolated from *Artocarpus* species such as prenylflavones including artocarpins which have biological activities such as antibacterial⁵, antiviral, antifungal, antitubercular, antiplatelet, antidiabetic, cytotoxic, antiinflammatory⁶, skin whitening, antioxidant, antiandrogen, antiparasmodial, neuraminidase inhibitor and wound healing activity⁷. Based on the above literature, it is necessary to do research on the effect of Breadfruit (*Artocarpus altilis* (Parkinson) Fosberg) leaf infusion on blood glucose levels in male mice (*Mus musculus*) Diabetes Mellitus Type 2.

METHODS AND MATERIALS

Preparation of Plant Samples

Breadfruit leaves used are fresh and old leaves. Sampling was carried out purposively without comparing with the same plants from other areas. Samples were taken from Lau Cih Village, Medan Tuntungan District, Medan City, North Sumatra. Breadfruit leaves were identified by the Herbarium Medanense Department of Biology, University of North Sumatra (No.5108 / MEDA / 2020).

Making Breadfruit Leaves Infusion

Breadfruit leaf powder is weighed as much as 10 g, put into an infusion pan and moistened with distilled water twice the weight of breadfruit leaf powder which has been weighed, namely 20 ml. The powder and distilled water that had been mixed in the infusion pan were added with 100 ml of distilled water, then heated using a water bath for 15 minutes starting from the time the temperature was 90°C. The results of the infusion are filtered while hot using a flannel cloth, to get the 100 ml infusion juice you can add distilled water through the dregs until you get 100 ml.

Phytochemical Screening of Breadfruit Leaves Infusion

Phytochemical screening tests were carried out on breadfruit leaf infusions to determine the presence of secondary metabolite compounds.

Preparation of Alloxan Monohydrate 200 mg / kg BW

A total of 200 mg of alloxan monohydrate was put into a 10 ml fluidized flask, dissolved in a cold solution of 0.9% NaCl. Enough volume up to the mark.

Preparation of Test Animals

The experimental animals used in this study were male white mice weighing 20-30 g. In the alloxan induction method, 25 mice were divided into 5 groups, each group divided by 5 mice. Before the test was adapted for 1 week, healthy mice were selected which were characterized by a stable or increased body weight.

Group 1: 1% w / v Na-CMC suspension

Group 2: Glibenclamide suspension dose of 0.65 mg / kg BW

Group 3: An infusion of breadfruit leaves 300 mg / kg BW

Group 4: An infusion of breadfruit leaves 400 mg / kg BW

Group 5: An infusion of breadfruit leaves 500 mg / kg BW

Antidiabetic Activity Test of Breadfruit Leaves Infusion with Alloxan Induction Method

As many as 25 male white mice with a body weight of approximately 20-30 g which had been fasted and their body weight was determined, fasting blood glucose levels were determined, then each mice were induced by alloxan at a dose of 200 mg / kg BW intraperitoneally. The mice were given food and drink as usual, and the behavior of the mice and body weight was observed. The mice used were mice with blood glucose levels ≥ 200 mg / dl. Diabetic mice that can be used and have their blood glucose levels measured are grouped into 5 groups, each of which consists of 5 mice. Each group was given treatment for 2 consecutive weeks. Furthermore, the measurement of blood glucose levels was measured on the 3rd, 5th, 7th, 9th, 11th, 13th and 15th days using a glucometer measuring instrument.

Data analysis

The research data were analyzed using the analysis method of variance (analog ANOVA) with a confidence level of 95% and continued with the Tukey test to see the real differences between treatments. This statistical analysis used the SPSS version 23.0 program.

RESULTS AND DISCUSSION

Phytochemical Screening

The results of phytochemical screening show that there are secondary metabolite components found in the breadfruit leaf infusion can be seen in table 1.

Table: 1. Results of Phytochemical Screening of Breadfruit Infusion

No.	Screening	Reagent	Breadfruit Leaf Infusion
1	Flavonoid	Mg + HCl + AmilAlkohol	Positive
2	Alkaloid	Mayer	Negative
		Bouchardat	Negative
		Dragendorff	Negative
3	Saponin	Foam Test	Positive
4	Tanin	FeCl ₃ 1%	Positive
5	Steroid/Triterpenoid	Lieberman-Buchard	Negative

The phytochemical screening test was carried out to determine the components of the secondary metabolite compounds found in plants. Based on Table 1, it shows that the results of phytochemical screening contained in the breadfruit leaf infusion consist of flavonoids, saponins and tannins. Secondary metabolite compounds have a function in biological activities, especially in the health sector⁸.

Flavonoids are included in polyphenolic compounds found in all parts of plants such as leaves, roots, bark, pollen, nectar, flowers, fruit and seeds which have the potential as

anti-inflammatory, anti-cancer, allergy, antioxidant and antimicrobial activity and have the ability to reduce risk of cardiovascular disease⁴.

Saponins are glycosides in plants and consist of sapogenin groups (steroids or triterpenoids), hexose, pentose, or uronic acid groups. Saponins have antimicrobial effects⁹, diuretics, analgesics, promote wound healing¹⁰ and play a role in accelerating and clotting red blood cells¹¹.

Tannins are also known as tannic acid and galothanic acid. Tannins in breadfruit leaves can protect the intestines from

unsaturated fatty acids by binding to body protein and will coat the intestinal wall in the form of compaction of the mucus layer of the digestive tract so that fat absorption is inhibited. Tannins have astringent properties, accelerate the healing of wounds and inflamed mucous membranes, overcome indigestion, and fever¹².

Result of Breadfruit Leaves Infusion Antidiabetic Activity Test

The results of the antidiabetic activity test of breadfruit leaf infusion were carried out by the alloxan induction method by observing the blood glucose levels of mice for 2 weeks starting on the 3rd day to the 15th day can be seen in Table 2.

Table 2. Blood Glucose Levels of Mice Using the Alloxan Method

Blood Glucose Levels of Mice Using the Alloxan Method					
Treatment of Mice	Group 1 1% w / v Na- CMC suspension	Group 2 Glibenclamide suspension dose of 0.65 mg / kg BW	Group 3 An infusion of breadfruit leaves 300 mg / kg BW	Group 4 An infusion of breadfruit leaves 400 mg / kg BW	Group 5 An infusion of breadfruit leaves 500 mg / kg BW
BGLFasting	90.2	93.2	89.2	92.4	89.8
BGLAfter Alloxan Induction (mg/dl)					
Day 3 th	350.4	318.6	324.2	318.2	332.2
Day 5 th	337	274.6	277.2	264.8	282
Day 7 th	304.6	150.2	251.6	240	255.6
Day 9 th	264.6	120.6	178.4	166.8	177.8
Day 11 th	237.6	106.4	151	140.8	151.4
Day 13 th	230.4	86.6	132.6	120.8	136.8
Day 15 th	216.8	79.6	107.6	95.6	107.2
Mean	277.34	162.37	203.22	192.43	206.14

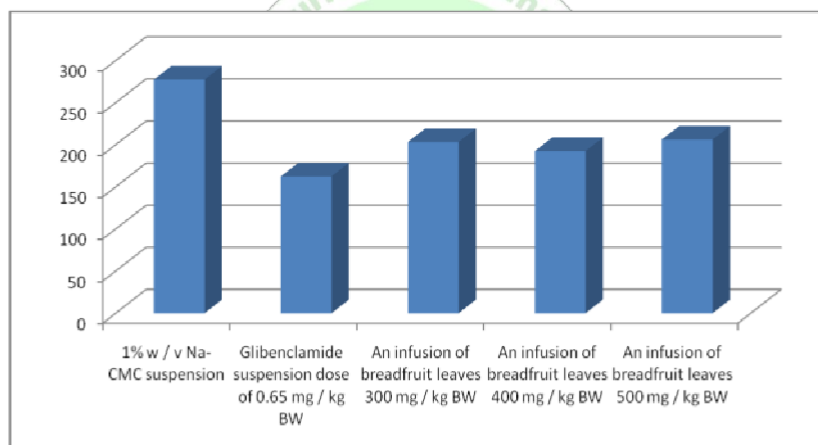


Figure: 1. BGL Graph of Alloxan Induction Test Method

Based on Table 2 and Figure 1. It can be seen that after alloxan administration, blood glucose levels of male mice in all groups experienced an increase or diabetes. After testing all treatments, it showed a decrease in blood glucose levels in each group. In group 1 still showed higher blood glucose levels than the other groups. This is because in group 1 is included in the negative group (negative control) without any treatment. In the glibenclamide group, the effect of reducing blood glucose levels was not different from those in groups 3, 4, and 5. The infusion of breadfruit leaves at a dose of 300 mg / kg BW, 400 mg / kg BW and 500 mg / kg BW showed a decrease in blood glucose levels. not significantly different with glibenclamide administration. This is due to the presence of secondary metabolites found in breadfruit leaf infusion which has an antidiabetic effect.

Breadfruit leaves have traditionally been widely used in treating liver cirrhosis, hypertension and diabetes¹³. The leaves, bark, and fruit have an effect in lowering blood glucose by inhibiting the activity of α -amylase, α -glucosidase, and sucrase through glucose diffusion throughout the body². Secondary metabolite compounds isolated from Artocarpus species such as prenylflavones including artocarpins which have biological activities such as antibacterial, antiviral, antifungal, antitubercular, antiplatelet, antidiabetic, cytotoxic, anti-inflammatory⁵, skin whitening, antioxidant, antiandrogen, antiplasmodial, neuraminidase inhibitor and wound healing activity⁶. Based on previous research¹⁴, it was stated that the breadfruit leaf extract showed strong antioxidant activity. Investigation of the antiluciferase activity of phenolic-rich extracts plays a role in reducing diabetes. It has been shown that senescence leaves are used to prepare tea to lower blood pressure and can also be considered to control diabetes, treat liver

disease and fever, and have antioxidant and anti-tumor effects. According to previous studies¹⁵,

This is due to the antioxidant activity of breadfruit leaves¹⁶. One way ANOVA test on day 3 to day 15 there is a difference in the reduction in glucose levels because the significant value is <0.05.

CONCLUSIONS

Based on these results, it can be concluded that the breadfruit leaves infusion has an effect on reducing blood glucose levels in white male mice with type 2 diabetes mellitus.

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