

The Effect of Breadfruit Leaf Extract (*Artocarpus Altilis*) on Fasting Blood Sugar Levels among Diabetes Mellitus (DM) Type 2 Outpatient at Biru Public Health Center of Bone Regency, Indonesia

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Diabetes is a disease that can reduce the quality of life of patients and lead to death. Based on Indonesian Basic Health research, the prevalence of diabetes mellitus has increased over several years. Breadfruit leaves contain antioxidant compounds that can lower blood sugar by inhibiting glucose transport in the gastrointestinal tract and stimulating insulin secretion in pancreatic beta cells. The study aimed to assess the effect of giving Breadfruit Leaf Extract on reducing Fasting Blood Sugar among type 2 Diabetes Mellitus Patients. The study used a quasi-experiment study with a randomized pretest-posttest, design with the control group. It involved 39 outpatients for type 2 diabetes mellitus at Biru Public Health Center of Bone Regency, who had suffered from Diabetes for 1-4 years. The sample was divided into 2 groups by simple random sampling, 19 respondents for the intervention group and 20 respondents for the control group. Data collected were the socio-demographic characteristics and fasting blood sugar levels. In the intervention group, breadfruit leaf capsules were given at a dose of 500 mg 1x1 for 21 days, while the control group was only given health education. The data were analyzed using the Chi-Square test, paired t-test, independent t-test, Wilcoxon Signed Rank Test, and Mann-Whitney. The majority of respondents aged 46-55 years were 53.8% in both groups, 74.4% were female, while the majority of BMI status had normal nutritional status as much as 41%. There was a change in FBS levels in the intervention group before (263.31 ± 134.43) and after (174.84 ± 84.99) intervention (p -value = 0.000). there was a change in FBS levels in the group before (181.35 ± 91.36) and after (147.45 ± 79.25) intervention (p -value = 0.001). it is known that there is a significant difference in changes in fasting blood sugar levels of patients with diabetes mellitus in the intervention group (-88.47 ± 88.01) and the control group (-33.90 ± 53.53) with (p -value = 0.024). The test results show that the content of flavonoids and other non-nutritive substances in breadfruit leaves has an effect on lowering the FBS of patients with diabetes mellitus and can be used as an alternative medicine in patients with diabetes mellitus.

Keywords: Breadfruit Leaf Extract; Diabetes Mellitus; Fasting Blood Sugar.

Diabetes mellitus (DM), commonly called Diabetes, is a chronic disorder of the body's metabolism due lack of insulin hormone in the body that cannot be used effectively in regulating blood sugar balance, thereby increasing the concentration of sugar levels in the blood (hyperglycemia).¹ Diabetes is a disease that can reduce the quality of life of patients and lead to death. Treatment that is carried out in the long term and continuously will have an impact on the finances of the diabetes mellitus patient because the cost of treating diabetes mellitus requires large costs.²

Diabetes mellitus can cause serious health problems caused by high blood sugar (hyperglycemia), such as hypercholesterolemia, in which cholesterol concentration in the blood exceeds the standard value.³ Diabetes mellitus, especially type 2, is very at risk of suffering from dyslipidemia and increases the risk of cardiovascular disease.⁴ In general, cardiovascular disease (CVD) is a disease related to the heart and blood vessels such as coronary heart disease, stroke, and hypertension.⁵

The prevalence of diabetes mellitus based on Basic Health Research continues to increase from 2007 as much as 1.1%, in 2013 as much as 1.5%, and in 2018 the prevalence of Diabetes Mellitus at the age of 15 years and over is 2.0%.⁶ The prevalence of diabetes mellitus in 2018 for all ages is 1.5, age 55-64 years is the age with the highest prevalence of diabetes mellitus, which is 6.3% and most suffers by women.⁶ In South Sulawesi, the prevalence of Diabetes Mellitus for all age groups is 1.3%, while for ages 15 years and over it is 1.83%. According to the 2018 Riskesdas in Bone Regency, the prevalence of diabetes mellitus is 2.17%.⁷

There are many programs in lowering blood glucose levels of people with diabetes mellitus. Innovations continue to be created in the treatment of diabetics, one of which is creating capsules/plant extracts to lower blood glucose and total cholesterol levels. Many studies have been conducted to test for the best drug discovery for people with diabetes mellitus. Since ancient times, the Indonesian people have used breadfruit fruit or leaves as a treatment to be able to help several types of diseases, including high blood pressure, diabetes, heart disease. Breadfruit leaves are rich in phenolic compounds, flavonoids, saponins and tannins.

The content of flavonoids in breadfruit leaves is a compound that is responsible for the activity of reducing glucose levels.⁸ The phenolic content in breadfruit leaves acts as an antioxidant where phenolic acts as an electron donor which further ends the radical chain reaction by converting free radicals into more stable cells .

A study aimed at the effectiveness of breadfruit leaves in lowering blood glucose levels and maintaining the sperm count of mice by The results of the study found that breadfruit leaf extract was able to reduce blood glucose levels and the most effective concentration was the treatment of breadfruit leaf extract at a dose of 100 mg/kg bw given for 21 days with an effectiveness of 66.77%.⁹ Junedi (2021) also conducted a study of breadfruit leaf extract in humans with pre-diabetes mellitus, the results of this study showed a change in the intervention group after giving breadfruit leaf extract for 28 days showing changes in fasting blood glucose levels of 16.16 mg/dl compared to control group ($p=0.00$), decreased total cholesterol level by 33.54mg/dl ($p=0.00$).¹⁰

The content of flavonoids which act as antioxidants that can inhibit the formation of free radicals by neutralizing the increase in Reactive *Oxygen Species* (ROS) due to diabetes and is able to regenerate damaged pancreatic cells and supported by previous research in pre-DM patients there is a significant relationship between the administration of leaf extract Breadfruit to decrease blood glucose and lipid profile, the researchers are interested in conducting further research to determine the effect of breadfruit leaf extract (*Artocarpus altilis*) on fasting blood glucose in outpatient diabetes mellitus patients.

MATERIAL AND METHODS

This research used quasi-experimental with a *randomized design pretest-posttest with control group* to obtained the data. In this research design, 2 treatment groups were used, namely the intervention group and the control group which had met the inclusion such as patient has been diagnosed by medical doctor, had suffering Diabetes for 1-4 years, taking diabetic oral drug and willing to consume breadfruit leaf extract every day for 21 days. All respondents then were randomized using a simple random sampling. The

total sample was 39 respondents and divided into 19 respondents in the intervention group and 20 respondents in the control group.

This research was conducted in the working area of Biru Public Health Center of Bone Regency, South Sulawesi Province, Indonesia. The study was conducted during April-June 2022. The time for implementing the intervention or data collection was carried out within 3 months. This research has obtained ethical approval from ethic commission of Faculty of Public Health,

Hasanuddin University with the number: 1953/UN4.14.1/TP.01.02/2022.

The variable in this study was fasting blood sugar (FBS) level which was taken by venous blood as much as 3cc by trained laboratory personnel and analyzed at independent health laboratory of Bone Regency. Before taking blood samples, the health worker (the research team) instructed respondents to fast from 11.00 p.m. in the evening until tomorrow morning during the blood test (07.00 a.m.). The officer explained about the

Table 1. Distribution of research subjects based on the general characteristics of respondents

| Variable | Intervention | | Control | | total | | P Value* |
|-------------------------------------|--------------|------|---------|----|-------|------|----------|
| | n(19) | % | n(20) | % | n(39) | % | |
| Age (Years) | | | | | | | |
| 36-45 | 4 | 21.1 | 5 | 25 | 9 | 23.1 | 0.885 |
| 46-55 | 10 | 52.6 | 11 | 55 | 21 | 53.8 | |
| 55-65 | 5 | 26.3 | 4 | 20 | 9 | 23.1 | |
| Gender | | | | | | | |
| Man | 7 | 36.8 | 3 | 15 | 10 | 25.6 | 0.118 |
| Woman | 12 | 63.2 | 17 | 85 | 29 | 74.4 | |
| Education | | | | | | | |
| Elementary School | 3 | 15.8 | 2 | 10 | 5 | 12.8 | 0.948 |
| High school graduate | 4 | 21.1 | 5 | 25 | 9 | 23.1 | |
| finished high school | 6 | 31.6 | 7 | 35 | 13 | 33.3 | |
| College | 6 | 31.6 | 6 | 30 | 12 | 30.8 | |
| Work | | | | | | | |
| Housewife | 10 | 52.6 | 10 | 50 | 20 | 51.3 | 0.549 |
| Farmer | 1 | 5.3 | 0 | 0 | 1 | 2.6 | |
| Retired | 1 | 5.3 | 0 | 0 | 1 | 2.6 | |
| Employee | 6 | 31.6 | 7 | 35 | 13 | 33.3 | |
| Businessman | 1 | 5.3 | 3 | 15 | 4 | 10.3 | |
| Family Head Job | | | | | | | |
| Housewife | 1 | 5.3 | 0 | 0 | 1 | 2.6 | 0.168 |
| Farmer | 4 | 21.1 | 1 | 5 | 5 | 12.8 | |
| Retired | 2 | 10.5 | 0 | 0 | 2 | 5.1 | |
| Employee | 5 | 26.3 | 9 | 55 | 14 | 35.9 | |
| Businessman | 7 | 36.8 | 10 | 50 | 17 | 43.6 | |
| Length of Suffering from DM (Years) | | | | | | | |
| 1-2 years | 10 | 52.6 | 14 | 70 | 24 | 61.5 | 0.265 |
| 3-4 years | 9 | 47.4 | 6 | 30 | 15 | 38.5 | |
| BMI | | | | | | | |
| Underweight | 1 | 5.3 | 0 | 0 | 1 | 2.6 | 0.469 |
| Normal | 7 | 36.8 | 9 | 45 | 16 | 41 | |
| Overweight | 7 | 36.8 | 5 | 25 | 12 | 30.8 | |
| Obesity I | 3 | 15.8 | 6 | 30 | 9 | 23.1 | |
| Obesity II | 1 | 5.3 | 0 | 0 | 1 | 2.6 | |

Source: Data processed, 2022

*Chi-Square Test

Table 2. Changes in fasting blood sugar levels between intervention and control groups

| Variable | Before(mean ± SD) | After(mean ± SD) | P Value | D |
|---------------------|-------------------|------------------|---------|---------------|
| Intervention (n=19) | 263.31 ±134.43 | 174.84±84.99 | 0.000* | -88.47 ±88.01 |
| Control (n=20) | 181.35 ±91.36 | 147.45 ±79.25 | 0.001** | -33.90 ±53.53 |
| P Value | 0.051**** | 0.415**** | | 0.024*** |

Source: Data processed, 2022

*paired T test

**Wilcoxon

***Independent T test

****Mann-Whitney

informed consent after the respondent understood and was willing to sign the informed consent, the health worker would take blood from the cubital vein, either on the right or left arm.

Preparation Method of Breadfruit Leaf Capsule

Breadfruit leaves 60 kg were cleaned then aerated and then chopped/sliced finely, then put into the drying room with a cooling system of 180C for 3x24 hours then put into the crusher to make it fine (simplicia), 9 kg is obtained, then in the maceration stage, simplicia is put in a container by adding a water solvent (reverse osmosis) with a ratio of 1:10 added 500 liters of water for 3 hours, stirring every 28 minutes, then entering the spinner/sparator at a speed of 2800rpm/minute for 10 minutes so that it is separated between residue and filtrate. The residue was discarded and the filtrate was dried with a Freeze dryer (HaiCuan brand) using a temperature of -60 °C (sublimation method) for 36 hours to obtain 1000gr of solid extract. The dry extract was weighed on a digital scale weighing 500 mg and put in a capsule by the internal quality control team from *Ismut Fitomedica Indonesia Corps.* (PT IFI).

Capsule was given to the sample with a dose of 1x1 for 21 days. In the intervention group, breadfruit leaf capsules were given at a dose of 500 mg 1x1 for 21 days and education using leaflet media was also given, while the control group was only given education using leaflet media. The control of consumption breadfruit leaf extract capsules was using via WhatsApp and cell phone and door to door during the research period with the integrated service pos (*posbindu*) of public health centre to re-monitor the respondent's condition and to prevent hypoglycemia. In addition to measuring FBS we also measure weight using a weight scale, height using a standardized microtoice,

and for the characteristics of respondents using a questionnaire. The data analysis used Chi-Square test, paired t-test, independent t-test, Wilcoxon Signed Rank Test, and Mann-Whitney.

RESULTS

Based on the characteristics of the respondents in general, including age, gender, education, occupation, length of suffering from DM and BMI. Based on the age group, the majority of respondents aged 46-55 years as much as 52.6% in the intervention group, while in the control group as much as 5 5%. The gender of the respondents was mostly female, in the intervention group 12 people (63.2%) and 17 people in the control group (85%). The education level of respondents is mostly high school and college education, for high school education in the intervention group as much as 31.6% and in the control group 35%, while in college education in the intervention group as much as 31.6% and in the control group 30%. Occupational status of most respondents worked as housewife, each in the intervention group as much as 52.6% and in the control group as much as 50%. The occupation status of the household heads of most respondents worked as entrepreneurs, in the intervention group as much as 36.8% and in the control group as much as 50%. The most respondents suffered from DM, namely 1-2 years, in the intervention group by 52.6% and in the control group by 70%. Most of the respondents had a normal BMI, in the intervention group it was 36.8% and the control group was 45%.

The mean results before and after the intervention of each variable and changes in the two groups are shown in the table above which shows

the pre post-test intervention group FBS variable (mean±SD) 263.31±134.43 and 174.84 ±84.99 (*p* value = 0.000) in the control group. *pre-post test* (mean±SD) 181.35±91.36 and 147.45 ±79.25 (*p* value = 0.001). The change in the difference in FBS levels in the intervention group was -88.47±88.01 while the control group was -33.90±53.53 (*p* value = 0.024), it can be concluded that there was a significant difference between the two intervention and control groups (*p* = <0.05).

DISCUSSION

Diabetes mellitus is a disease characterized by the development of hyperglycemia and disorders of carbohydrate, lipid, and protein metabolism associated with absolute or relative lack of insulin action and secretion. Symptoms reported by people with diabetes mellitus include polydipsia, polyuria, polyphagia, weight loss, and tingling.¹¹

The results showed that the status of patients with diabetes mellitus for 1-2 years was the most among all samples. The majority of the sample ages are 46-55 years. BMI in the intervention group was mostly with normal nutritional status and overweight, while in the control group the dominant nutritional status was normal. In this study, the sample of DM patients was mostly women, and the sample work was housewife.

Diabetes Mellitus has several risk factors including age, education level, gender, smoking, genetic factors, and stress. Age and education level are one of the risk factors that have an effect on diabetes mellitus. In previous studies, it was found that there was a relationship between education level and the incidence of diabetes mellitus, people with a low level of education were 1.27 times more likely to suffer from diabetes mellitus than educated people.¹²

The results of research in developed countries show that the age group at risk of developing Diabetes Mellitus is 65 years and over. In developing countries, the age group at risk for diabetes mellitus is 46-64 years old because at that age there is glycosuria. Fatmawati's research shows that age is a significant variable on the incidence of Diabetes Mellitus.¹³

It has been discussed previously that the average sample in this study is women. Although

there is no direct relationship between gender and the incidence of diabetes, it is related to age, body mass and race. Diabetes is very closely related to the incidence of obesity because as you get older you are more prone to obesity than men, this is because the composition of the percentage of body fat mass in women is much higher than men, of course this is enough to explain why women suffer from diabetes more than men.¹⁴

Nathan & Delahanty stated that there is a work relationship with the incidence of diabetes that the absence of work makes the body less mobile and can trigger obesity. This will lead to insulin resistance. This situation causes body tissues to become less sensitive to the effects of insulin. So that the sugar in the blood has difficulty leaving the blood and entering the cells.¹⁵

Type 2 diabetes mellitus is not caused by a lack of insulin secretion, but because insulin target cells fail or are unable to respond to insulin normally. This condition is commonly referred to as "insulin resistance". A lot of insulin resistance occurs as a result of obesity and lack of physical activity and aging. In patients with type 2 diabetes mellitus, there can also be excessive hepatic glucose production but there is no autoimmune destruction of Langerhans B cells such as type 2 diabetes mellitus.¹⁶

Some of the risk factors that cause type 2 diabetes mellitus are age, obesity, food intake, lifestyle, genetics, etc. as much as 80-85% obesity can affect the occurrence of diabetes mellitus, as evidenced by a nursing study, women with a BMI of 23-24.9 kg/m² have 4-5x risk of diabetes mellitus.¹⁷

Flavonoids improve the pathogenesis of diabetes and its complications through the regulation of glucose metabolism, hepatic enzymes activities, and a lipid profile. The mechanism of flavonoid has a similar activity as metformin like induced an insulin independent 5' adenosine monophosphate-activated protein kinase (AMPK) pathway which slows the oxygen consumption of adenosine diphosphate by stimulating GLUT 4 translocation and expression in isolated mitochondria.¹⁸ Blood glucose can be reduced by anti-aging gene sirtuin 1. Sirt 1 is essential to prevent inflammation and Sirt 1 inactivation may induce nonalcoholic fatty liver disease (NAFLD) that may corrupt pancreas function. In this case,

flavonoids can act as activators for sirtuin 1, in regulating blood glucose levels.^{19,20,21}

The results of the study for the level of FBS in the intervention group decreased by -88.47 ± 88.01 while the control group -33.90 ± 53.53 (p value = 0.024), it can be concluded that changes in FBS in the intervention group decreased (-88.47 gr) while in the control group there was a decrease in FBS. a decrease in FBS by (-33.90 g), there was a significant difference between the two intervention and control groups ($p = <0.05$).

This is in line with a study that looked at the effect of the flavonoid content of methanol extract and ethyl acetate extract of breadfruit (*artocarpus altilis* (park.) fosberg) leaves and their activity on reducing glucose levels in vitro. The total flavonoid content of ethyl acetate extract and methanol extract was 0.5554% and 0.3727% by weight of the sample, respectively. A 50% decrease in glucose levels occurred in the treatment of 36,114 ppm ethyl acetate extract and 39,448 ppm methanol extract. The decrease in glucose levels after the ethyl acetate extract and methanol extract were added was probably due to the glucose solution forming a complex of glucose with flavonoids. The OH groups located at numbers 3' and 4' on flavonoids are thought to be able to bind glucose which makes the glucose levels in the standard solution decrease. The remaining glucose that is not bound by flavonoids will react with Nelson's reagent and form a brick red precipitate then the addition of arsenomolybdate reagent produces molybdine which is greenish blue, then its absorption is measured with a UV-Vis spectrophotometer.²²

Then the research conducted by Tandil *et al.*, in 2017 looked at the effect of the ethanol extract of breadfruit leaves (*artocarpus altilis* (Parkinson *ex fazorn*) on reducing blood glucose levels, total cholesterol and the histopathological description of the pancreas of male white rats (*Rattus norvegicus*) hypercholesterolemia - diabetes from the findings The results show that there are secondary metabolites in the ethanolic extract of breadfruit, breadfruit leaf extract with an effective dose of 200 mg/kgBW has an effect on blood glucose levels and total cholesterol levels, a dose of 400 mg/kgBW regeneration of rat pancreas tissue.²³

The same thing in a study conducted by Putra, JD *et al.* (2014) who saw the effect of giving dried extract of breadfruit leaves (*artocarpus altilis*) on blood glucose levels in diabetic white rats from these findings. Normality test using Shapiro-Wilk and data analyzed by One Way Anova test and showed a significant difference ($p: 0.000 < 0.05$).²⁴ The results of the analysis by post hoc test showed a significant difference between the treatment group dose 1 and dose 2 ($p < 0.05$). The conclusion of this study was that dried breadfruit leaf extract had several effects on blood glucose levels in rats with diabetes mellitus, and there was a significant difference in blood glucose levels between the treatment groups that had been given a dose of 2 and 3 doses of dried breadfruit leaf extract.

CONCLUSIONS

Breadfruit Leaf Capsules can reduce fasting blood sugar level of diabetic patients. The content of flavonoids and other non-nutritive substances plays a role in reducing fasting blood sugar levels in diabetes mellitus patients. Breadfruit leaf capsules are potential recommended as an alternative treatment in reducing the incidence of type 2 diabetes mellitus.

Recommendations

Giving Breadfruit Leaf Capsules can reduce the FBS of diabetic patients. The content of flavonoids and other non-nutritive substances plays a role in reducing FBS levels in diabetes mellitus patients.

Conflict of Interest

The author declares that he has no conflict of interest.

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