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Effect of Breadfruit (*Artocarpus Altilis*) Leaf Extract on Blood Pressure in Obese Adults in Makassar, Indonesia

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Obesity has become a global public health and nutrition problem. Obese people will have a variety of diseases, one of which is high blood pressure. Therefore, this study aims to determine the effect of breadfruit leaf extract on blood pressure in obese adults in Makassar City. An experimental study was conducted involving a double-blind, randomized controlled trial with pretest and posttest assessments, which included 36 obese respondents. The intervention group received breadfruit leaf extract in the methodology, while the control group received a placebo capsule. Blood pressure was monitored using a digital tension device. Data analysis was performed using SPSS 13, including paired tests, independent tests, Wilcoxon and Mann-Whitney tests. Systolic and diastolic blood pressure were lower in the intervention control group before and after the intervention (p=0.015 and 0.018) with a difference (p=0.105) (p>0.05) of -3 systole and -3.5 diastole. Mean analysis for the intervention and control groups in systolic blood pressure revealed a p-value of 0.628, signifying no significant difference between the groups (p>0.05). While the control group's systolic and diastolic blood pressure before and after the intervention (p=0.007 and 0.003) (0.05) showed a difference (p=0.271) (p>0.05) with a decrease in the control group's systole -8.39 and diastole -3.22, there was no statistically significant difference between the two intervention and control groups—only a decrease. Giving breadfruit leaf extract capsules to the intervention group with obese respondents and high blood pressure showed a decrease in blood pressure after giving breadfruit leaf extract capsules. People with high blood pressure can consume breadfruit leaf decoction or extract.

Keywords: Arcoupus Artilis; High Blood Pressure; Obesity.

Obesity is an excessive or abnormal accumulation of fat that can interfere with health.1. Obesity results from an imbalance in the caloric intake and energy expenditure equation, wherein caloric consumption exceeds energy demands or utilization (energy expenditure). This surplus of energy within the body leads to the accumulation of adipose tissue. One of the medical conditions prevalent among individuals grappling with obesity is hypertension.

Hypertension, a prevalent chronic health condition, affects a significant portion of the global populace and is linked to an elevated risk of heart attacks, arteriosclerosis, strokes, and kidney failure.

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Projections suggest that by 2025, as many as 30% of adults worldwide will grapple with hypertension. Factors such as a sedentary lifestyle, stress, obesity, and excessive sodium intake are contributing variables that elevate the likelihood of developing high blood pressure.[2].

The term "silent killer" refers to hypertension since it can go years without symptoms before developing into other illnesses such as heart failure, diabetes, peripheral artery disease (PAD), and cerebrovascular disease (stroke).[3].

Ethnobotany has a significant impact on drug and food discovery. The practices of traditional communities regarding their relationship with plants in their daily lives can lead to research by scientists looking for evidence of local knowledge. Artocarpus altilis, known locally as breadfruit, is one of Indonesia's most widely utilized plants. Artocarpus altilis belongs to the Moraceae or mulberry family.[4].

Breadfruit is one of the Indonesian plants used for disease treatment and prevention. The plant known as the breadfruit is widespread throughout practically all of Indonesia. The fruit of the breadfruit plant, which is high in fiber, is the component the community has traditionally used. Another breadfruit component used for illness treatment and prevention is the leaves.[5.] Artocarpus altilis also possesses several proven therapeutic qualities; for instance, its leaves have historically been used to treat diabetes, hypertension, and liver cirrhosis.[4].

Tropical and subtropical areas are home to the breadfruit plant Artocarpus altilis. The tea made from the withering leaves is traditionally used to alleviate hypertension. In a rat model of hypertension brought on by the hormone angiotensin II, tea made from the plant's leaves significantly reduced mean arterial pressure (40–50 mmHg).[3].

With a variety of diseases that will be felt for people with obesity, such as high cholesterol, low HDL, and high blood pressure, as we know, various types of traditional medicines will give good effects and little risk for the body if consumed, using herbal medicines will provide a slight risk because it uses natural raw materials based on products made by Prof. Dr. Nurhaedar jafar, Apt, M.Kes. related to breadfruit leaf extract.

MATERIALS AND METHODS

Ethics

This study was approved by the Health Research Ethics Committee of Hasanuddin University with a recommendation for ethical approval number 3004/UN4.14.1/TP.01.02/2023. Respondents' participation in this study was voluntary, and respondents who agreed to participate had filled out informed consent.

Study Design and Respondents

The design of this research study is an experiment with a double-blind design, Randomized controlled trial, pre and post-on obese patients conducted from May 2023-June 2023 at Makkasau Health Centre Makassar City. The population in this study were people in the Makassau Health Centre area with obese nutritional status ranging in age from 25-60 years. The sample of this study was 36 people, with 18 people in the intervention group and 18 in the control group.

Preparation of Breadfruit Extract

The prepared material was then placed in a drying room with a cooling system set at 180°C for three cycles of 24 hours each. The finely chopped product was then processed in a crusher to create a substance known as simplicia, resulting in a yield of 9 kg. The simplicial was deposited into a container and combined with a water solvent (reverse osmosis) at a ratio of 1:10, incorporating 500 liters of water. The mixture was left to macerate for three hours, stirring intervals of every 28 minutes.

Subsequently, the macerated material underwent separation using a spinner/separator at a speed of 2800 revolutions per minute for 10 minutes. This process effectively distinguished between the residue and the filtrate. The residue was discarded, and the filtrate underwent drying using a HaiCuan freeze dryer. The drying process employed a temperature of -60 ºC through the sublimation method and lasted for 36 hours, producing 1000 grams of solid extract.

The obtained dry extract was carefully weighed using a digital scale measuring 500 mg. The internal quality control team from Ismut Fitomedica Indonesia Corps. (PT IFI) then encapsulated the dry extract.

Data Collection

This study used anthropometry measurement tools such as BA digital scales to

measure body weight and fat percent and Microtoice to measure height. Dietary measurement tools used were the Food Recall 24 hours and questionnaires. They were measuring high blood pressure using a digital tensimeter. The intervention group was given breadfruit leaf extract capsules, and the control group was given a placebo. The placebo for the control group is filled with lactose. During the data collection phase, respondents in the intervention group consumed two capsules of breadfruit leaf extract per day for 21 days (42 capsules per respondent), while the control group consumed one placebo capsule daily for the same duration, totaling 21 capsules per respondent.

Blood Pressure Measurement

Blood pressure measurements were taken by health workers using a digital tension device and taken in a sitting position two times. Prehypertension 130/80 - 139/80 and hypertension >140/80.

Statistical Analysis

In this research, data analysis is done using SPSS software version 13 by IBM corporate. The confidence level in this study is 95%, and the significance level is 0.5. The first analysis is the normality test of data using the Kolmogorov-Smirnov test. If the data is normal, the paired t-test is carried out, and the independent t-test, if the data is not normal, then uses the Wilcoxon and Mann-Witney tests.

RESULTS

Respondent Characteristics

The characteristics of the respondents are shown in Table 1. This study involved 36 respondents, evenly split between the intervention and control groups, each with 18 respondents. The majority of the intervention group (38.9%) and control group (44.4%) respondents were between 26 and 35 years old. In the intervention group, there was an equal gender distribution (50% male, 50% female), while the control group had a higher proportion of females (61.1%). In terms of education, the intervention group had mostly high school graduates (33.3%), whereas

Table 1. Characteristics of Respondents

Variables	Intervention		Control		p*
	N	%	N	%	
Age (Years)					
26-35	7	38.9	8	44.4	0.185
36-45	2	11.1	4	22.2	
46-55	5	27.8	6	33.3	
56-60	4	22.2	0	0	
Gender					
Male	9	50	7	38.9	0.502
Famale	9	50	11	61.1	
Education					
Finished Primary School	2	11.1	3	16.7	0.403
Completed Junior School	2	11.1	4	22.2	
Completed High School	6	33.3	2	11.1	
Higher Education	1	44.4	3	50.0	
Jobs					
Work	14	77.8	14	77.8	1.000
Not Working	4	22.2	4	22.2	
Abnominal					
e”90 Male	9	50.0	7	38.9	0.502
e”80 Famale	9	50.0	11	61.1	
IMT					
Overweight	5	27.8	3	16.7	0.423
*O*besity	13	72.2	15	83.3	

Source: Primary Data, 2023

the control group consisted mainly of junior high school graduates (22.2%). The majority of both groups were employed (77.8% in each). Abdominal circumference analysis revealed that 50% of the intervention group had measurements e"90 for males and e"80 for females, while 61.1% of the control group had measurements e"80 for females. As for BMI, 72.2% of the intervention group and 83.3% of the control group were classified as obese.

Overview of Respondents' Examination

Table 2, shows the Blood Pressure variable most respondents have Hypertension Blood Pressure levels, in the control group as much as 55.5% to 55.6%, and 5 normal 22.8%. While in the intervention group 55.5% became 56.5%, and 1 normal 5.6% after the intervention.

Analysis of Mean Before and After Blood Pressure Intervention and Change in Each Group

Table 3 presents the pre-intervention mean analysis for both the intervention and control groups in systolic blood pressure, revealing a p-value of 0.628, signifying no significant difference between the groups ($p>0.05$). In the post-intervention phase, the p-value remains above 0.05 at 0.371, indicating no significant disparity between the groups. Similarly, for diastolic blood pressure, the pre-intervention analysis yields a p-value of 0.083, while the post-intervention analysis results in a p-value of 0.057, both exceeding the significance threshold ($p>0.05$). In summary, there is no substantial distinction between the intervention and control groups regarding diastolic blood pressure in both the pretest and posttest phases.

Regarding systolic blood pressure, the intervention group exhibited a mean of 146.05 ± 12.41 before the intervention, which decreased to 142.61 ± 11.63 after, resulting in a statistically significant p-value of 0.015 ($p<0.05$). In contrast, the control group's pre-post measurements indicated a shift from 147.72 ± 15.72 to 139.33 ± 13.71, with a p-value of 0.007 ($p<0.05$). The calculated change (") in systolic blood pressure showed a decrease of -3.44 ± 8.44 in the intervention group and -8.39

Table 2. Overview of Blood Pressure Respondents in each group before and after the intervention

Variable	Control group				Intervention group			
	Pre-test		Post-test		Pre-test		Post-test	
	N	%	N	%	N	%	N	%
High Blood Pressure								
Pre-hypertension	5	27,8	3	16,7	8	44,4	7	38,9
Hypertension	13	55,5	10	55,6	10	55,5	10	55,5
Normal			5	27,8			1	5,6

Source: Primary Data, 2023

Table 3. Comparison of Mean (Before-After) Triglyceride Levels Between Intervention and Control Groups

	Variable	Before (mean ± SD)	After (mean ± SD)	p value	Difference
Blood Pressure					
Systole	Intervention	146,05±12,41	142,61±11,63	0,015	-3,44±-8,44
	Control	147,72±15,72	139,33±13,71	0,007	-8,39 ± -3,83
		p value =0.628	p value =0.371		p value=0.105
Blood Pressure					
Diastole	Intervention	90,11±7,56	86,61±7,57	0,018	-3,5±3,38
	Control	89,44±5,46	86,22±5,68	0,003	-3,22±-3,36
		p value =0.083	p value=0.057		p value=0.271

Source: Primary Data, 2023

± 3.83 in the control group, but the p-value was 0.105 ($p>0.05$), suggesting no significant difference between the two groups.

For diastolic blood pressure in the intervention group, the mean values shifted from 90.11 ± 7.56 before the intervention to 86.61 ± 5.7 after, with a p-value of 0.018 ($p<0.05$). The corresponding " diastolic blood pressure was -3.5 ± 3.38. In the control group, the diastolic values went from -3.22 ± 3.66 before to after, with a p-value of 0.271 ($p>0.05$). These results indicate that diastolic blood pressure changes were similar in both groups, with no significant difference observed.

DISCUSSION

The sample consisted of obesity and hypertension blood pressure measurements in this study were carried out 2x repeatedly to ascertain whether the blood pressure results were by the measurement standards in 21 days in the morning using a digital device carried out directly by the general Makassau puskesmas officer in charge of this study to measure the respondent's blood pressure before the intervention, during the intervention, and after the intervention. Therefore, it is guaranteed that the implementation is by the SOP in measuring blood pressure.

The results of this study proved that the respondents' blood pressure decreased after giving breadfruit leaf extract capsules, and systole blood pressure was -3.44 mmHg. There was a slight decrease in blood pressure in the intervention group before the intervention, while the control group decreased by -8.39 mmHg. While in diastole, the control group was -3.22, and the test group was -.3.5. The control group that experienced a decrease was also caused by respondents who were still taking hypertension medication. Seven respondents were still taking hypertension medication, which allowed the control group respondents to experience a decrease in hypertension of 8.39 mmH. There is in accordance by research conducted in America showing that intravenous administration of breadfruit leaf water extracts at 1 mg/ml at an infusion rate of 1 ml/hour for 45 minutes was shown to reduce mean arterial pressure (20-30 mmHg), which was significant.[3]. Research conducted in India also showed that breadfruit can reduce blood pressure.[5]. Research conducted in Indonesia shows that breadfruit root decoction can regulate high blood pressure.[6]. Research at the University of the West Indies uses breadfruit leaves as an antihypertensive drug.[7].

Regarding medication adherence, several samples took anti-hypertension medication in both the intervention and control groups. Two people in the intervention group took medication, while in the control group, there were 11 people, which could lead to more significant results in the control group. Experienced a decrease compared to the intervention group, based on the journal, which stated that there was an influence of medication adherence on reducing the incidence of hypertension

The breadfruit leaf extract in this study is young breadfruit leaves that are dried, then processed in the form of extracts and encapsulated by the freeze dryer process (HaiCuan brand) using a temperature of -60 ºC (sublimation method) for 36 hours to obtain a capsule-shaped solid extract.[8].

Extraction is withdrawing a desired active substance from a raw material using a specific solvent chosen where the desired substance can dissolve. Raw materials come from plants or animals that are collected, cleaned, washed, dried, and powdered. The result of extraction is called an extract. Extracts contain not only one element but various elements, depending on what raw materials are extracted and the extraction conditions.[9]

Alkaloids, flavonoids, essential oils, and other groups are active compounds in different simplisia. Choosing the best solvent and extraction technique will be easier if you are aware of the active compounds that simplisia contains. Rhizomes and leaves of soft simplisia, easily absorbed by solvents, do not need to be powdered until smooth before the extraction process. Hard-dried natural ingredients such as seeds, bark, and root bark are challenging to absorb by solvents, so they must be powdered until smooth.[10]

One of the fruits commonly processed into fried snacks known as 'breadfruit chips' in Indonesia, breadfruit Artocarpus altilis, is also utilized in traditional medicine. Breadfruit leaves treat various conditions, including diabetes, high blood pressure, kidney disease, enlarged spleen, liver disease, and hepatitis. Additionally, the flavonoid content in breadfruit leaves helps prevent increased blood cholesterol levels.[11]

Breadfruit has many benefits, from fruit leaves, and can be used as traditional medicine either processed in capsules or naturally, such as boiled. Breadfruit contains Artocarpus and papain enzymes; its leaves contain quercetin, camphor phenols, and gamma-aminobutyric acid, which can lower blood pressure.[12]

So, breadfruit leaf extract was tested to reduce blood pressure in obese adults. The results of the above study showed the management of blood pressure. Caps given to control group respondents and intervention groups were expected to lower blood pressure, and it was proven that it could reduce blood pressure for 21 days, given intervention or treatment. Then breadfruit leaves (Artocarpus altilis) are one of the traditional medicines widely known to the Indonesian people. Flavonoids, hydrocyanic acid, acetylcholine, tannin, riboflavin, saponin, phenol, quercetin, kaempferol, and potassium are the chemical content of breadfruit leaves that are efficacious as a medicine for diseases such as kidney, heart, high blood pressure, liver, enlarged spleen, diabetes, asthma, and cancer.[13]

Several theories underlie the potential anticancer mechanisms of flavonoids. One theory suggests that flavonoids serve as oxidants, initiating cancer cell apoptosis by triggering DNA fragmentation, starting with releasing a DNA chain due to reactive oxygen compounds like hydroxyl radicals formed through Cu(II) redox reactions. Flavonoids are known to mobilize these copper compounds from intra- and extracellular sources, focusing on chromatin.[14,15]

Another theory highlights flavonoids' antioxidant properties, mainly shielding against Reactive Oxygen Species (ROS). In a third theory, flavonoids are thought to hinder cancer cell proliferation by inhibiting protein kinase activity, disrupting the signal transmission pathway from the cell membrane to the nucleus.[16,17]

A fourth theory suggests that flavonoids can inhibit receptor tyrosine kinase activity, which is crucial in the growth of malignancies. Quercetin, a flavonoid derivative, is utilized as a dietary supplement and has been promoted by the American Cancer Society for its potential in disease prevention, including cancer. However, concrete clinical evidence for its effectiveness in cancer prevention or treatment in humans remains scarce, and at normal dietary levels, quercetin is generally considered safe.[13,18]

Traditional medicines as an alternative to medicine are considered safer regarding side effects and toxicity.[19,20]. The results of research by Fita Dwi Amira from the Department of Pharmacy, Faculty of Mathematics and Natural Sciences, University of Indonesia, show that breadfruit leaf extract, which consists of 30% flavonoid compounds, does not cause poisoning in the body. The parts of the breadfruit plant that are commonly used as medicine are the fruit and leaves. However, what is most often used as herbal medicine is the leaves.19

Breadfruit leaves are made into a drink to cure high blood pressure, heart disease, and diabetes because they contain quercetin and potassium.[21]. In India, breadfruit leaves can reduce high blood pressure and relieve asthma.[19]. Currently, part of the breadfruit plant that is most widely used for medicine is the leaves. Quercetin, a derivative of flavonoids, has antihypertensive properties, namely widening the narrowed blood vessel channels and improving blood circulation.[22].

CONCLUSIONS AND RECOMMENDATIONS

Giving breadfruit leaf extract capsules to the intervention group with obese respondents and high blood pressure showed a decrease in blood pressure after giving breadfruit leaf extract capsules. People who have high blood pressure can consume breadfruit leaf decoction or breadfruit leaf extract. Artocarpus altilis is a herbal plant that is high in flavonoids and is able to cure various types of other diseases including lowering high blood pressure, with herbal treatment it will not give side effects, previous research has carried out toxicity tests which say that breadfruit leaves do not have bad effects if consumed even though routinely.

Limitations of the study

The number of respondents in this study was still small so that the comparison between the intervention group and the control group was not too large. Monitoring of respondents in taking the breadfruit leaf extract capsules was not done every day and the respondents' diet was also not monitored. Breadfruit leaf extract is not yet

licensed for over-the-counter sale, so breadfruit leaf water decoction can be a more applicable recommendation in everyday life.

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Conflict of Interest

No conflict of interest.

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