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***THE POTENTIAL OF NGOKILO LEAVES EXTRACT
(STACHYTARPHETA MUTABILIS. VAHL) AS A LOWERING OF
BLOOD GLUCOSE LEVELS OF WHITE MICE (RATTUS
NORVEGICUS)***

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Abstract

Diabetes is a disease, in which the body cannot produce enough insulin so that there is excess sugar in the blood which becomes toxic to the body. Ngokilo plants are believed to be able to lower blood sugar levels because of the antioxidants and polyphenols contained therein. The objective of this study was to determine the potential of the ethanol extract of Ngokilo leaves (Stachytarpheta mutabilis, Vahl) as a lowering blood glucose levels in white mice (Rattus norvegicus). The tests were carried out by an experimental method using Swiss Webster male mice (Rattus norvegicus) aged 2-3 months with a body weight of 30-40 grams as test animals. This study used four dosage ratios of ngokilo leaf extract, namely 1: 20: 40: 60 and control used aquadest. The results showed that the ethanol extract of Ngokilo leaves had an F value of 27.033 > F Table 2.60. It indicates that the independent variable (the difference in the concentration of ethanol extract of Ngokilo leaves) was proven to have a significant effect on the dependent variable (blood sugar levels).

Keywords: *Diabetes mellitus; Ethanol extract; Ngokilo leaves*

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INTRODUCTION

Diabetes mellitus (DM) is a disease characterized by hyperglycemia and disorders of carbohydrate, fat and protein metabolism which are associated with absolute or relative deficiency of insulin activity and/or secretion (Forouzanfar *et al.*, 2016). *Diabetes mellitus* is familiarly called the silent killer because DM can attack all organs of the body and cause various complaints. Diseases that will arise due to DM include visual impairment, cataracts, heart disease, kidney disease, sexual impotence, wounds that are difficult to improve and gangrene, lower respiratory tract infections, blood vessel disorders, stroke and others. Not surprisingly, DM sufferers who have severely amputated their body parts due to decay (Trisnawati, 2013).

Diabetes mellitus is a disease that has a serious impact on human health (Rahmawati *et al.*, 2014). Diabetes is a metabolic disorder of glucose distribution by the body (Rohilla & Ali, 2012). Diabetics are characterized by insulin that is not produced in the appropriate amount or the body is unable to use insulin effectively, as a result the blood sugar levels excess (Sangala *et al.*, 2011). The lack of insulin activity causes the failure of glucose transport from plasma to cells (Hasanah *et al.*, 2017). Glucose that is absorbed during the meals is not metabolized at a

reasonable rate so that it collects in the blood (hyperglycemia) and is excreted into the urine (glycosuria) resulting in osmotic diuresis and an impact on increased urinary production (polyuria) (Agung *et al.*, 2017). In addition, abnormalities in glucose metabolism as a result of the lack of insulin activity also result in loss of fluids and trigger thirst (polydipsia) (Dewi, 2009).

Diabetes mellitus can lead to serious complications, such as hypoglycemia, which is a condition in which blood sugar levels drop dramatically due to too much insulin in the body, these symptoms include blurred vision, fast heartbeat, headaches, trembling, cold sweat, and dizziness. Diabetic ketosidosis (KAD) is a medical emergency situation as a result of a very high increase in blood sugar content, it occurs when the body cannot use glucose as a fuel source, as a result the body processes fat and produces ketones as a source of energy. It can lead to accumulation of dangerous acids in the blood resulting in loss of body fluids, coma, shortness of breath, and death. *Hyperosmolar hyperglycemic state* (HHS), occurs as a result of a very high spike in blood sugar levels of a specific duration. Symptoms are characterized by acute metabolic disorders characterized by hyperglycemia, hyperosmolarity, and loss of body fluids without ketoacidosis (Zamri, 2019).

Uncontrolled diabetes can also lead to other serious complications, namely: 1). Disorders of the eye (diabetic retinopathy), damage to the blood vessels in the retina and the potential to cause blindness in the eye. 2). Damage to the blood vessels in the eye caused by diabetes also increases the risk of visual problems, such as cataracts and glaucoma. 3). Kidney damage (diabetic nephropathy) can lead to kidney failure, moreover, it can end in death if not treated properly, the patient is obliged to carry out regular dialysis or kidney transplantation. 4). Nerve damage (diabetic neuropathy), high blood sugar in the blood can interfere with blood vessels and nerves in the body, especially in the legs, it occurs when the nerves are damaged either by direct impact of high blood sugar or because blood flow to the nerves decreases. The damaged nerves will cause sensory disturbances such as tingling, numbness, or pain, and can affect the digestive tract and cause gastroparesis, such as nausea, vomiting, and feeling full when eating. 5). In men, complications of diabetes mellitus can cause erectile dysfunction / impotence. 6). Germs and fungi will be very easy to reproduce in diabetics especially complications of diabetes mellitus can cause erectile dysfunction / impotence. 6). Germs and fungi will be very easy to reproduce in diabetics especially when the self healing ability decreases, due to the

impact of diabetes, the patient's feet are at risk for easy injury and infection as a result of gangrene and diabetic ulcers. 7). Cardiovascular disease, high blood sugar levels can cause damage to blood vessels in the body, it can cause the disruption of blood circulation in all bodies as well as in the heart. The complication of diabetes mellitus that affect the heart and blood vessels include heart disease, stroke, heart attack, and atherosclerosis. 8). The number of people with diabetes mellitus is increasing every year, it is estimated that in 2045 people with diabetes will reach 629 million people. This figure is sourced from a report by the International Diabetes Federation (IDF) in 2015 which said that the number of diabetes sufferers was 415 millions, in 2017 it was 425 millions. In Indonesia itself, based on Riskesdas from 2013 to 2018 the prevalence of Diabetes Mellitus (DM) increased from 6.9 percent to 8.5 percent which means around 22.9 millions of the prevalence of Diabetes Mellitus (DM). Diabetes mellitus is the most common cause of death in Indonesia. There is an increasing trend in the prevalence of this disease from year to year. Currently there are many drugs to cure the disease but this disease causes complications that are not easy to be controlled (Parisa, 2016).

There have been many treatments tried to cure diabetes, especially type 2 diabetes which is due to insulin deficiency

or insulin resistance because the insulin receptors in the visceral adipose tissue decrease or their structure changes as a result of not responding to insulin. Starting from seeing a doctor, using herbal medicines, and trying various replacement treatments. The treatment with chemicals certainly has many side effects and negative effects. What can be done now is not only carrying out preventive measures such as regular exercise, drinking lots of water, reducing the intake of those with high glucose content and also carrying out curative actions through herbal treatments (Sampath *et al.*, 2012). Generally, the use of conventional medicine is estimated to be more comfortable than the use of modern medicine. It is since the conventional medicine has fewer side effects than modern medicine (Patel & Goyal, 2012). However, accuracy in using conventional drugs is still needed to minimize side effects, namely: correct drug, correct dose, correct time of use, correct method of use, not misused, and the right choice of drugs for special diseases (Dewi *et al.*, 2019).

Ngokilo plant is a shrub with soft stems belonging to the genus Acanthaceae. It has thick, long-rounded and slightly hairy leaves with jagged edges. Ngokilo is included in the vile glass plant which contains high potassium in the leaves, as a result it is believed to be able to smooth urine and destroy stones in the bile, kidney

and bladder. In the matter of curing diabetes, this plant has not been studied much, as a result it has not been known yet that its content is trusted by the public to treat diabetes. As a diabetes medicine, people generally use 3 fresh leaves to consume as fresh vegetables (Sulaeman, 2017).

Diabetes is a disease that is very risky and feared, so many alternative treatments are carried out (Care, 2015). In the traditional way, ngokilo plant has considerable efficacy in treating diabetes, therefore it is very significant to conduct a research on the ability of ethanol extract from Ngokilo leaves (*Stachytarpheta mutabilis*. Vahl) to lower the blood glucose content in mice.

MATERIALS AND METHODS

This research was carried out in June to August 2019. Sampling of ngokilo leaves in Jagran Village, Karanggeneng District, Lamongan Regency. The extract making and the treatments were carried out at the Environmental Health Laboratory of the Environmental Health Study Program, Faculty of Health Sciences, Lamongan Islamic University.

This research method was experimental, a method implemented to reveal the causal relationship between two or more variables by controlling the influence of other variables. This method

was done by deliberately giving independent variables to the object of a research to determine the response in the dependent variable. Research used Ngokilo leaves which were used as an extract to treat type 2 diabetes mellitus.

Research procedure

Making Ngokilo leaf extract by maceration method by adding ethanol solution for 24 hours (Sutopo *et al.*, 2017). It stirred every 2 hours. Then filtered with a funnel padded a filter paper and then evaporated at a temperature of 800 C with a rotor speed of 35 rpm for 30 minutes and the results were taken in the form of Ngokilo leaf extract.

Increasing the blood glucose levels (hyperglycemia) in mice (*Mus musculus*) by intraperitoneal injection using alloxan monohydrate at a dose of 175 mg/kg with an injection volume of 0.5 ml/kg as many as 2 times.

Application of Ngokilo leaf extract to Swiss Webster male mice aged approximately 2-3 months.

Checking blood sugar done by glucometer kit (Cahyaningrum *et al.*, 2019).

Tools and Materials

The tools used are scales, pH meter, measuring cup, knife, filter paper, blender, dropper, stirring rod, infusion pan, cylinder vessel, filter, plastic, petri dish, measuring

cup, enlemeyer tube, funnel, filter paper, weighing scale. Bunsen analytic, tongs, horn spoon, mouse cage, injection splut, blood sugar checker, mice food containers, cotton wool, tissue. Ngokilo leaves. Aquades, ethanol liquid, NaCl, Alloxan.

Data Collection and Analysis Techniques

Data were collected by observing blood sugar levels before and after being given treatments.

Data analysis was performed using one way ANOVA with an alpha of 0.05%. This analysis aimed at determining the difference in the effect of giving Ngokilo leaf extract in each treatment. Then the Least Significant Differences (LSD) test with alpha 0.05% was performed which aimed at seeing the differences in each treatment that can reduce blood sugar levels in mice.

RESULTS AND DISCUSSION

Ngokilo Leaf Extract Dosage Formulation (*Stachytarpheta mutabilis*. Vahl)

The doses of Ngokilo leaf extract given to mice were adjusted their body weight. The test mice were male, Swiss Webster, aged 2-3 months and weighing 30-40 grams. The ratio used in this treatment is 0: 1: 20: 40: 60

In this study, the ethanol extract of the leaves of Ngokilo was given orally, so that 1% of the extract was used. The calculation formula is Dose Volume = Weight of Mice x Percent of Feeding.

Based on (Kustini, 2019b) The treatment were carried out on mice were as follows: Group A: given distilled water 1

ml/100 gBB, Group B: given an extract dose of 11, 25 mg/100 gBB in 1 ml/100 gBB, Group C: extract dose 112.5 mg/100 gBB in 1 ml/100 gBB and Group D: extract dose of 337.5 mg/100 gBB in 1 ml/100 gBB.

The doses formulation of Ngokilo leaf ethanol extract can be seen in table 1 as follows.

Table 1. The Doses Formulation of Ngokilo Leaf Ethanol Extract (*Stachytarpheta mutabilis*. Vahl)

Treatment	Dose	Number of mice
K	0.4 ml distilled water	5
P1	4.5 mg / 40 grBB at 0.4 distilled water	5
P20	90 mg / 40 grBB at 0.4 distilled water	5
P40	180 mg / 40 grBB at 0.4 distilled water	5
P60	240 mg / 40 grBB at 0.4 distilled water	5

Table 1 shows that the treatments used are doses of 4.5, 90, 180 and 240 mg/40 grBB, it is expected to provide a real picture of the effect of Ngoliko leaf extract to lower the blood sugar in mice.

In Table 1, it can be seen that the different doses of ngokilo leaf extract will be given to mice according to treatment.

Each treatment was repeated 5 times, namely 5 mice.

Application of Ngokilo Leaf Extract

The value of the average blood sugar levels of alloxan-induced diabetes mellitus mice after giving ethanol extract of Ngokilo leaves (*Stachytarpheta mutabilis*. Vahl) within 7 days is presented in table 2.

Table 2. Lowering the glucose levels of Swiss Webster strains Male Mice *Diabetes mellitus (Musmusculus)* Induced by Alloxan in 8 (eight) treatment groups

Treatment Groups	Initial Glucose Levels (mg / dl)	Glucose Levels Before Treatments (mg / dl)	Glucose Levels After Treatment (mg / dl)	Difference
K	100.4	100.2	100.4	-0.2
P1	107	147.8	145.2	2,6
P20	103.4	149.6	132.2	17.4
P40	96.6	136.8	100.6	36.2
P60	96.4	140.6	83.4	57.2

In table 2, it is explained that the average value of blood sugar levels of diabetes mellitus mice that induced by alloxan after giving ethanol extract of Ngokilo leaves (*Stachytarpheta mutabilis*. Vahl) for 7 days, there was a significant decrease in each treatment compared to the control. The lowest decrease in blood glucose levels in mice was in the P1 group, namely the treatment by giving the ethanol extract of leaves of ngokilo doses 4.5 mg/40 grBB at 0.4 distilled water, that is, there was a decrease in blood sugar levels

by 147.8 to 145.2 mg/dl, in the P20 group a dose of 90 mg/40 grBB at 0.4 distilled water there was a decrease in blood sugar levels from 149.6 mg/db so 132.2 mg/dl, group P40 dose 180 mg/40 grBB in 0.4 distilled water there was a decrease in blood sugar levels from 136.8 mg/dl to 100.6 mg/dl, P60 group dose of 240 mg/40 grBB in 0.4 aquades contained decreased blood sugar levels from 140.6 mg/dl to 83.4 mg/dl. The control group that was given distilled water as much as 0.4 cc had a slight increase in blood sugar levels.

Figure 1. Comparison of blood sugar levels before and after treatment

From Figure 1 above, it is explained that the biggest difference between blood glucose levels is at P60, the fourth treatment used a dose of 240 mg / 40 grBB mice. It can be interpreted that in larger doses it contains an active compound that has a higher level so that it can prevent higher blood glucose levels from rising. It is in accordance with the research that single doses of 100, 150 and 200 mg/kgBB of the leaf extract of Sambung Hidup leaves given

can reduce blood sugar levels in mice. The decrease in blood sugar levels was assumed caused by the endogenous factors of each white mice which had individual characteristics and was heavily influenced by some non-physical and environmental factors. The fate of the drug, given Ngokilo leaf extract as a positive control, can be influenced by the pathological factors that can make the drug go down or rise. Decrease the effect of the

drug was assumed as result of poor absorption in the gastrointestinal tract, blood vessels or increased excretion through the kidneys (Nurhidayah, 2015).

Based on (Cahyaningrum *et al.*, 2019; Simanjuntak, 2018) states that the destruction of insulin-producing pancreatic β cells is due to alloxan which is an oxygen-derived pyrimidine derivative. Alloxan can induce a multiphase blood glucose response when injected into the experimental animals, followed by changes in plasma insulin concentrations and accompanied by changes in β cell

ultrastructure in the sequence until necrotic cell death occurs. The results of the study, when compared with the glucose level of the negative control group, it showed that all treatment groups increased their blood sugar levels, namely in the range of more than 200 mg/ dL, where the normal blood glucose levels of mice were around 62.8 mg/dL to 176 mg/dL.

Furthermore, the one way ANOVA test was carried out to determine whether there was a significance level of blood sugar using different treatment doses.

Table 3. ANOVA test results on the difference in concentration between treatments

	Sum of Squares	Df	Mean Square	F	Sig.
Between Groups	12960,560	4	3240,140	27,033	.000
Within Groups	2397,200	20	119,860		
Total	15357,760	24			

Based on table 3, the results of the One Way ANAVA test show that the F count is 27,033 greater than the F table, which is 2.60. it means that there is a significant difference in blood sugar levels of mice in each treatment.

The follow-up test was carried out using a paired T test to see any differences in blood sugar levels between before and after treatment

Table 4. Paired T Test Results for Differences Before and After Treatment

		Mean	Std. Deviation	Std. Mean Error	95% Confidence Interval of the Difference		t	df	Sig. (2-tailed)
					Lower	Upper			
Pair 1	Before after	2.26400E 1	23.45897	4.69179	12.95661	32,32339	4,825	24	.000

In table 4 it is explained that the results of the Paired T Test show that the T Count is 4,825 > than the T Table of 1.71. It showed that there was a significance level of glucose in mice between before and after treatment. The ethanol extract of Ngokilo leaves showed an effect on lowering blood sugar in diabetes mellitus-induced mice by alloxan.

According to research (Kustini, 2019a) which stated that there was a significant difference in blood sugar levels before and after the treatment. The administration of an ethanol extract of Ngokilo leaves showed a significant effect on lowering blood sugar in alloxan-induced diabetes mellitus mice.

The lowering blood sugar levels in diabetic mice that had been induced by alloxan after presenting ethanol extract of Ngokilo leaves was due to ethanol extract of Ngokilo leaves which had an astringent function, namely could emphasize intestinal mucous membrane protein and create a protective layer of the intestine, so that it prevented sugar intake so the blood glucose did not increase very highly, in addition it is also able to accelerate the discharge of blood, by speeding up the circulation related to the performance of the heart and by speeding up filtration and excretion of the kidneys so that there is an increase in urine production, the rate of excretion of glucose through the kidneys

increases, resulting in a decrease in glucose levels in blood. Accelerate the release of glucose by increasing metabolism or entering into fat deposits. The pancreas is involved in this process to make insulin (Widowati, 2018; Dasopang, 2018).

As research conducted by (Cahyaningrum *et al.*, 2019) that degenerative diseases such as diabetes mellitus can be prevented through ingredients that have antioxidant activity. Plants contain many natural flavonoids, and one of the functions of flavonoids is to prevent diabetes and its complications. The presence of flavonoids in amla (*Phyllanthus emblica* L) is estimated to have potential as an antidiabetic. Research by (Widowati, 2018) stated that the provision of antioxidant compounds can ward off free radicals so that oxidative stress in diabetes mellitus can be reduced. Which in vitro the flavonoid compound has been proven to be a natural antioxidant that can trap free radicals.

The leaf extract also contains alkaloid and flavonoid compounds which have antioxidant properties that can suppress free radical activity. Flavonoids worked by inhibiting the enzymes alpha amylase and alpha glucosidase which were useful in breaking down carbohydrates into monosaccharides that can be absorbed by the intestine. Therefore, blood glucose levels do not rise after eating food or drinks

with sugar or compounds that can be broken down into sugar. This effect is estimated to reduce blood sugar levels in people with diabetes mellitus (Soelistijo *et al.*, 2015; Novita *et al.*, 2020).

CONCLUSION

From the experiment on the potential of Ngokilo leaf ethanol extract on reducing blood glucose levels in white mice, it can be concluded that the ethanol extract of Ngokilo leaves was able to lower blood sugar levels in white mice. For 4 treatment doses, the best was P60, that was, with an initial glucose level of 140.6 mg/dl to 83.4 mg/dl.

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