

ANTIDIABETIC ACTIVITY OF ETHANOL EXTRACT OF *Phrynium pubinerve* Blume LEAF IN ALLOXAN-INDUCED DIABETIC RATS (*Rattus norvegicus*)

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ABSTRACT

Phrynium pubinerve Blume is a original plant of North Sulawesi that is widely used by local residents as a wrapper of rice. Plant leaves contain alkaloids and terpenoids. Alkaloids compounds have long been studied and used in the treatment of antidiabetes. The mechanism of action alkaloids in lowering blood glucose is by increasing insulin secretion, increasing glucose uptake by adipose tissue and skeletal muscle tissue, inhibits intestinal glucose absorption and inhibits hepatic glucose production. So even terpenoida compounds. The antidiabetic activity of terpenes has been widely recognized and has the same properties as alkaloids. The aim of this study was to know the effect of *Phrynium pubinerve* Blume leaf on the effect in decreasing blood glucose level on alloxan-induced diabetes mellitus rats.

The design of this study was laboratory experimental with post-test only control group design. The experiment was conducted in vivo using experimental animals. Blood glucose levels were determined every day for 10 days. Dose *Phrynium pubinerve* Blume seeds dry extract administered orally. Used of 30 male rats divided into negative control group, positive control with Glibenlamide 0,65 mg/Kg BW, the P1-P4 group treated with leaf extract with doses was 625; 250; 2500 and 4500 mg / KgBB.

Testing results showing that four levels dose extract elusan leaf able to decreasing blood glucose levels, after gave elusan leaf extract treatment for 10 days. Data analysis result-test, using with T-test there was significantly on dose elusan leaf 2500 mg/kg body weight (P3) on the decreasing blood glucose levels on white rattus has α value = 0,000. Conclusion: Results of research showing that dose was very effected that is intervention treatment elusan leaf dose of 2500mg/kgBW. Suggestion so that can be done continued research of acut toxicity test.

Word Key: Phynium pubinerve Blume, blood glucose, aloxan.

INTRODUCTION

Diabetes is a set of metabolic diseases characterized by the occurrence of hyperglycemia and caused by abnormalities of insulin secretion, insulin work, or both. Chronic hyperglycemia in diabetes causes damage, dysfunction, and organ failure especially the eyes, kidneys, nerves, heart, and blood vessels. There are several pathogenic processes involved in the development of diabetes, such as autoimmune damage of the pancreatic beta cells so that insulin deficiency. The prevalence of people with diabetes mellitus is always increasing from year to year. According to Riskesdas 2013 data,

prevalence of diabetes mellitus in North Sulawesi has increased from 1.6% to 3%.

Various Types of native plants from North Sulawesi can be used as medicine. Some efficacious as antidiabetes, for example tarutuk, gedi, pakoba, mandanginan, jambura, boyoba, doludo, tagalolo and red balacai. The use of herbal medicine can reduce the side effects of drugs and is relatively safer because it is a natural substance that can be well tolerated by the human body.

Left of elusan (*Phrynium pubinerve* Blume) has a local name of rice leaf is a native plant of North Sulawesi that is used by local communities as a wrapper of rice.

Some studies have been done on the leaves of elusan as a wound healer, even juice from the leaves can be used to treat the eyes that are irritated or infected. Ren Li et al have studied the leaves of elusan and succeeded in isolating the essential oil from the leaf of elusan which after testing has high antioxidant power with good antimicrobial ability. This leaf has the potential as a preservative in food and as an antibiotic development biomarker.

Left of elusan contain alkaloids and terpenoids. alkaloids compounds have long been studied and used in the treatment of antidiabetes. The mechanism of action of alkaloids in lowering blood glucose is to increase insulin secretion, increase glucose uptake by adipose tissue and skeletal muscle, inhibit intestinal glucose absorption and inhibit hepatic glucose production. So it is with terpenoida compounds. The antidiabetic activity of terpenes has been widely recognized and has the same properties as alkaloids.

Research conducted by Wakur, et al (2013) in Minahasa Selatan, leaves Elusan can heal new wounds, as well as research by Kinho Forestry Research Institute of North Sulawesi (2010) leaves Elusan can be used as an antidote due to snake or insect bites. According to the conscience at the Forestry Research Institute of Manado traditionally leaves used as a wrapper of rice and rice to be durable and smells fragrant.

The results of interviews with several local residents residing in several villages in Southeast Minahasa and Minahasa districts were found to be boiling water leaves elusan empirically has long been used as an antidiabetic drug taken once a day by brewing 3-5 leaves of elusan in boiling water and drink while still warm. Even some locals have felt the benefits of

leaf elusan as an antidiabetic drug. The high interest of the community using traditional medicine to treat the disease indicates the conscious society will benefit and the safety of traditional medicine.

Based on the description above, it is necessary to test the activity of leaf antidiabetes of Elusan (*Phrynium pubinerve blume*) and it is hoped that the result of this research will give information to the public about the benefits of leaves of Elusan. Based on the above problem the question arises: "Does Elusan leaf extract (*Phrynium pubinerve blume*) have antidiabetic activity? and Is there any effect of dose of Elusan leaf extract (*Phrynium pubinerve blume*) to antidiabetic activity? and what is the effective dose of Elusan leaf extract (*Phrynium pubinerve blume*) that has antidiabetic activity?"

METHODOLOGY

Animals : Adult albino rats, males weighing 200-300 grams were used in this study. all rats had to go through the acclimatization stage for 14 days before starting the study. Rats were fed feeding standard and drinking water daily during the study.

Plant Extracts: Elusan leaves were obtained from Patar Village, Airmadidi District, North Minahasa District. Fresh green leaves are taken in the morning, then dried in a place protected from direct sunlight, mashed and sieved with a smooth degree of matching until the weight of 4-5 kg of powder is obtained. 10 parts of Elusan leaf powder soaked with 75 parts ethanol 95%, cover and leave for 5 days then strain and evaporated using Rotary Evaporator until obtained by thick extract without smell of ethanol. Then the resulting extracts were examined phytochemical content.

Glibenclamide: Glibenclamide was used as a positive control in this study produced by PT. Indofarma Indonesia. Single dose of Glibenclamide provokes a brisk release of insulin from pancreas. It acts on β -cell membrane leading to enhance calcium flux across it, hence degradation, the given oral dose is 0,65 mg/Kg BW.

Induction Of Diabetes: All rats measured baseline blood sugar levels were then given Aloxsan (Sigma Aldrich) at a dose of 100 mg/KgBB intra-peritoneal and then observed for 7 days to maximize the diabetogenic effect in rats with known measurements of blood sugar levels.

Experiment: This study used 30 rats divided into 6 treatment groups.

Group 1 (KN) , The negative control group given a 0.5% CMC suspension

Group 2 (KP), The positive control group treated with doses of glibenclamide 0,65 mg/KgBW

Group 3 (P1), The treatment group was given *Phynium pubinerve* Blume leaf extract at a dose of 625 mg/KgBW

Group 4 (P2), The treatment group was given *Phynium pubinerve* Blume leaf extract at a dose of 1250 mg/KgBW

Group 5 (P3), The treatment group was given *Phynium pubinerve* Blume leaf extract at a dose of 2500 mg/KgBW

Group 6 (P4), The treatment group was given *Phynium pubinerve* Blume leaf extract at a dose of 4500 mg/KgBW.

All treatment groups measured baseline blood sugar levels and were subsequently induced with aloxsan and left for 7 days to maximize the diabetogenic effect. On the 8th day each treatment group was administered peroral ethanol extract of elite leaf once daily for 10 days. Blood sugar measurements were performed using the Autocheck tool and blood samples were taken through the tail.

RESULTS AND DISCUSSION

Based on the result of the research of blood glucose level of mice in the animal treatment group test showed blood glucose levels on the 1st, 4th and 10th days in the four treatment groups, showed variation of increase and decrease of blood glucose level, this was caused by difference of response of each animal group and individual test against pancreatic beta cell destruction caused by aloxsan diabetes-inducing agents. The negative control group given with 0.5% CMC, on day 4 the mean value of blood glucose levels of 191 mg / dL and day 10 increased to 207.4 mg / dL. This shows that the group of tested animals given CMC 0,5% did not decrease blood glucose level because CMC 0,5% did not have the effect of lowering blood glucose level after mouse had hyperglycemic.

The positive control group given glibenclamide, a decrease in blood glucose levels, occurred after day 10 of 144.8 mg / dL compared to day 4 of 158 mg / dL. This happens because of the effects of glibenclamide as one of the drugs that can increase insulin secretion by pancreatic beta cells.

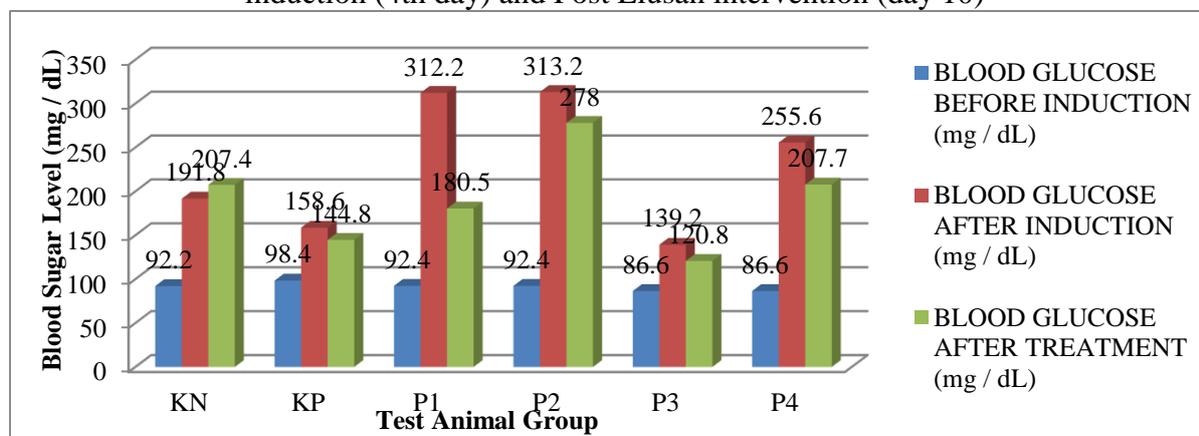
Decrease in blood glucose levels also occurred in the treatment group of Elusan leaf extract. For the dose group 625mg / kgBW where the results showed the blood glucose level on day 4 was 312mg / dL and the 10th day fell to 180.5 mg / dL. Group dose 1250 mg / kgBW; 2500 mg / kgBB and 4500mg / kgBW of blood glucose on the 4th day for each group were 313.2 mg / dL decreased to 278 mg / dL; 139.2 mg / dL decreased to 120.8 mg / dL and 255.6 mg / dL fell to 207.7 mg / dL. This proves that the elan leaf ethanol extract has a hyperglycemic effect.

Research on natural materials has been widely practiced and is useful as an antidiabetic drug. Plants Phynium pubinerve Research that shows the same results conducted by Sukmawati, et al 2015 in Palu research on Antibi-dation Test Exhibition Ethanol Ambon Banana Leaves (*Moses paradisiaca* L.) Against Ratus White (*Rattus norvegicus* L.) Induced Karangenan, concluded that ethanol extract Ambon banana leaves (*Musa paradisiaca* L.) have anti-inflammatory activity against caragenan-induced white rats. The dosage of ethanol extract of ambon banana leaves (*Moses paradisiaca* L.) which can be used to give anti-inflammatory effect is 750 mg / KgBB.

extract of Elusan leaf showed decreased blood glucose level when compared with negative control and positive control. Significant decrease value occurred in the treatment group dose 625 mg / KgBB. The result of statistic test of data using T test with 95% confidence level, on Antidiabetes Activity from Elusan Lean (*Phrynium pubinerve* Blume) ethanol extract on male rats (*Rattus norvegicus*) induced by Aloxsan, showed significant effect on dosing 2500 mg / kgBB to the decrease in blood sugar levels in white rats, which obtained the value of $\alpha = 0.000 < 0.05$, meaning that the leaves of elusan have the effect of lowering blood sugar levels in white male mice.

The results of the study in Graph 1 showed that all treatment groups of ethanol

Graph 1. Distribution of Examination Result of Pre-Blood Sugar Level (day 1, Aloxsan induction (4th day) and Post Elusan intervention (day 10)



Conclusions and recommendations

The results showed that there was antidiabetic activity of elusan leaf extract (*Phynium pubinerve* Blume) in white rat in induction of aloxsan. Significant differences in blood glucose levels decreased in the dose of 2500 mg / kgBW with the value of $\alpha = 0.000$. Research Suggestion: Providing effective information to the community about the results of this study. This study

may proceed to further studies of acute toxicity trials.

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