



**Effects Analysis Leaf Extract Breadfruit (*Artocarpus
altilis* (Park.) Fosberg) Against Insulin Resistance in Rat
(*Rattus norvegicus*) Obese**

Study on Cell Morphology of Langerhans Island

Wahyudin^{a*}, Muh Nasrum Massi^b, Rosdiana Natzir^c, Gemini Alam^d, Hendra
Stevani^e

^a*The doctoral program university medical hasanuddin*

^b*Department of Microbiology, Faculty of medicine university hasanuddin*

^c*Department of Biochemistry, Medical Faculty of Hasanuddin University*

^d*Pharmaceutical Faculty of Hasanuddin University*

^e*Department of clinical nutrition university medical faculty of Hasanuddin, Polytechnic pharmaceutical
Makassar*

Abstract

The state of obesity is closely related to insulin resistance that leads to type 2 diabetes incidence of exposure to high concentrations of glucose cause increased apoptosis of pancreatic Langerhans Island. *A. altilis* plants have traditionally been used by the people of Indonesia for treating diabetes mellitus. The objective of this study was to determine the concentration of leaf extract of *A. altilis* which can improve insulin resistance in rats (*Rattus norvegicus*) who are obese by looking at the morphology of Langerhans islet cells. The method used is eksperimntal laboratory to study design Randomized Controlled Trial (RCT). Rats were divided into five groups, with each group consisting of 5 rats, then given a high-fat meal (open source) for fattening or obese.

* Corresponding author.

Weight measurement to assess that the rats had been obese and the fasting blood sugar (GDP) by using the tool GlukoDR tests to ensure that the mice had increased blood glucose and insulin resistance. Group I as a negative control group, the group II as a positive control group using metformin HCl, group III as 5% of the test group, Group IV as the test group, 10% and V as a test group of 15%. HE staining was done to see the number of islets of Langerhans cells of each group. Data analysis was performed using One Way Anova to see the differences between the groups with 95% confidence level. All data were analyzed with SPSS version 21.0 (SPSS, Inc. Chicago, IL). Results revealed that no difference in the number of Langerhans islet cells in the negative control with extracts of *A. altilis* 5%, 10% and 15%. ($P = 0.000$) in which 10% extract has the same effect with metformin and extract 15% had a greater effect of metformin ($p = 0.000$). In conclusion, the extract *A. altilis* can increase the number of Langerhans islet cells in obese mice. So it can be taken into consideration *A. altilis* use in the prevention of insulin resistance.

Keywords: *A. Extracts altilis*; obesity; islands of Langerhans; insulin resistance.

1. Introduction

Increasing incidence of obesity is followed by the numbers increase in the incidence of type 2 diabetes Insulin resistance is a condition that is defined as a reduced response to normal circulating insulin plays an important role in the development of type 2 diabetes mellitus [1]. According Bastard and his colleagues [2], obesity is a risk factor for type 2 diabetes, dyslipidemia and cardiovascular disease. In obese individuals, adipose tissue releases a number of non esterified fatty acids, glycerol, hormones, cytokines, proinflammatory and other factors involved in the development of insulin resistance. Several studies have demonstrated the role of insulin in glucose homeostasis pathway, controls blood pressure and vascular reactivity, where these factors contribute in the definition of metabolic syndrome [3,4]. In individuals with diabetes mellitus, there is a change histpatologis on the island of Langerhans. These changes can occur quantitatively as a reduction in the number, size, or in kualitati such as necrosis, degeneration, and amyloidosis. Damage to the pancreatic beta cells causes the body cannot produce insulin, causing blood glucose levels to rise (a state of hyperglycemia). The condition can result in the formation of hyperglycemia by reactive oxygen species (ROS = reactive oxygen species). Excessive ROS can cause oxidative stress and can exacerbate the damage pancreatic beta cells. From the test results of the qualitative content of the active substance in the leaf extract of *A. altilis* known that the leaf extract of *A. altilis* contained active substances are compounds of phenols, flavonoids, alkaloids and saponins [5]. In the phytochemical test methanol extract of dried leaves of *A. altilis*, conducted Maharani and his colleagues [6], concluded that the methanol extract of leaves of *A. altilis* contain alkaloids, flavonoids, tannins, phenols and saponins. Polifinol role as an antioxidant thought to be able to protect pancreatic β cells from the toxic effects of free radicals that are produced under conditions of chronic hyperglycemia and tend to increase insulin secretion. Quercetin supplementation as one class of polyphenols will improve the status of inflammation

2. Materials and Methods

The subjects were male rats, Wistar strain and has a normal activity, do not marry as many as 25 animals were divided into 5 groups, each consisting of 5 male rats. Materials used in the form of leaves that are still green and

not yellow from *Artocarpus plant altilis* (Park.) Fosberg taken at \pm 9-10 hours of the morning of Gowa regency, South Sulawesi. Test animals used were male rats, healthy, 4 months old Wistar strain weighing 150 to 200 g, then do fattening to get obese mice. 25 animals Male rats were divided into 5 groups each consisting of 5 male rats, in which group I as a negative control group, the group II as a positive control group using metformin HCl, group III as the test group 5%, Group IV as the test group 10% and group V as a test group of 15% .. 25 test animals adapted for 7 days, then given a high-fat meal (open source) to get a rat obesity and insulin resistance by checking levels of GDP. After 14 extract *A. altilis* in each group, HE staining to see the number of cells in the Langerhans islands in each group. Data analysis was performed using one way ANOVA test to see differences between the groups with 95% confidence level. All data were analyzed with SPSS version 21.0

3. Results and Discussion

The results of the study the effects of extracts of *A. altilis* the number of cells in the Langerhans islands statistical analysis are presented in Table 1

Table 1: Average number of islets of Langerhans cells Interagency Group Post Test.

Group	Cells number in average	SD
Negative control	26,04	2,07
Positive control	161,04	26,12
<i>A. altilis</i> 5%	75,06	14,43
<i>A. altilis</i> 10%	152,6	11,19
<i>A. altilis</i> 15%	249,06	11,45

In table 1 there is a difference in the average number of cells in the test group 5%, 10% and 15%, with the highest number of cells in the test group 15%. While the average number of cells in the positive control group and the test group 10% showed no significant differences. In Table 2 there are differences in the number of cells in the Langerhans islands between the positive control, negative control ($p = 0.000$). On the negative control there is a difference with all treatment groups, and between the positive control group and the extract of *A. altilis* 10% no significant differences ($p > 0.05$).

Results showed no effect of extracts of *A. altilis* in increasing the number of cells in the islets of Langerhans, which at a concentration of 10% has the same effect as metformin, and the concentration of 15% which has the effect of a higher increase in the number of cells in the islets of Langerhans.

Table 2: Differences Between Langerhans cell counts Island Post Group Test

Group	Different cell number	SD	P
Negative control–Positive control	-135,00	9,59	0,000
Negative control – <i>A. altilis</i> 5%	-49,20	9,59	0,000
Negative control – <i>A. altilis</i> 10%	-126,20	9,59	0,000
Negative control – <i>A. altilis</i> 15%	-223,20	9,59	0,000
Positive control – <i>A. altilis</i> 5%	85,80	9,59	0,000
Positive control – <i>A. altilis</i> 10%	08,80	9,59	0,370
Positive control – <i>A. altilis</i> 15%	-88,20	9,59	0,000
<i>A. altilis</i> 5% - <i>A. altilis</i> 10%	-77,00	9,59	0,000
<i>A. altilis</i> 5% - <i>A. altilis</i> 15%	-174,00	9,59	0,000
<i>A. altilis</i> 10% - <i>A. altilis</i> 15%	-97,00	9,59	0,000

A. altilis extract the active compounds that play a role in the homeostasis of blood glukosa is not known clearly. But suspected that the acetone-water-soluble compound that is a class of polyphenols unknown type. The active compounds of this class of polyphenols that act as antioxidants that can prevent and reduce free radicals in the way it reacts directly on free radicals [7]. Polyphenols can improve antioxidant enzymes such as superoxide dismutase (SOD), catalase and glutathione peroxidase, which plays a role in preventing damage to cell DNA β and the effect of anti-inflammatory prevent cell damage β pancreas by inhibiting oxidative stress (Lee, YM, and his colleagues., 2009) , Polyphenol compounds, in an attempt to cure diabetes will increase the insulin produced by the pancreatic β cells by changing the metabolism Ca^{2+} (Hii and Howell, 1985). Increasing the number of cells in the islets of Langerhans of the pancreas in treatment group, allegedly because of their bioactive compounds in extracts of *A. altilis* are polyphenols, these bioactive compounds can act as antioxidants. Antioxidants are involved in the repair process of damaged cells. Cell damage caused by the free radicals can be overcome with the antioxidants that serve as agents of decline and lowering oksidator before damaging the cell so that the cell damage can be reduced, Robinovith and his colleagues [8] polyphenols are known to play a role capturing free radicals or function as natural antioxidants [9]. The antioxidant activity allows the polyphenols to

capture or neutralize free radicals (such as ROS or RNS), so as to improve the situation of damaged tissue in other words the inflammatory process can be inhibited [10].

In the pancreatic islets of Langerhans cells, the polyphenols as antioxidants tend to increase insulin secretion. Several epidemiological studies have shown that consumption of polyphenol-rich fruits can reduce the risk of diabetes mellitus-2 [11]. Quercetin supplementation as one class of polyphenols will improve the status of inflammation, plasma insulin levels and fat levels in obese mice [12]. Polifinol role as an antioxidant thought to be able to protect pancreatic β cells from the toxic effects of free radicals that are produced under conditions of chronic hyperglycemia. According Kaneto and his colleagues. [13], the provision of antioxidants can improve pancreatic β cell mass and keep the insulin content in it. In general, a decrease in oxidative stress can reduce insulin resistance and inhibit the pancreatic β cell damage. Arrest of free radicals by the polyphenolic compounds contained in extracts of *A. altilis* causing delays magrofag activity so as decreased phagocytic Langerhans islet cells of the pancreas. Polyphenols are reported to have antidiabetic activity that is able to regenerate cells in the Langerhans island [14-16]

4. Conclusion

A. altilis extract can increase the number of cells in the islets of Langerhans, which at a concentration of 10% has the same effect with metformin, and in knsentrasi 15% had a higher effect in increasing the number of cells in the islets of Langerhans. so it can be considered for use in the prevention *A. altilis* insulin resistance.

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