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The Effectiveness of *Aloe vera* Extracts Against Blood Glucose Levels and Repair The Proportion Pancreatic β Cells of The Hyperglycemic Rats

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Abstract— This research aims to determine the effectiveness of *Aloe vera* extracts. L decrease blood glucose levels and pancreatic β cell microscopic structure hyperglycemic rats.This Research used a CRD with five treatments and five replications. Each treatment in this study is consisted of a negative control (given distilled water), B as a positive control (75 mg/kg BW alloxan), C (100 mg/kg of extract of *Aloe vera* and 75 mg/kg alloxan), D (300 mg/kg of extract of *Aloe vera* and 75 mg/kg alloxan) and E (500 mg/kg BW leaf extract of *Aloe vera* and 75 mg/kg alloxan). Data were analyzed using analysis of variance followed by Duncan's multiple range test at 5% confidence interval. The results showed that the extract of *Aloe vera* very significant effect on blood glucose levels hyperglycemic rats. It can be concluded that the extract of *Aloe vera* of 100, 300, 500 mg/kg for 21 days effective in lowering blood glucose levels in hyperglycemic rats and the use of *Aloe vera* at a dose of 500 mg/kg for 21 days and can reduce pancreatic β cell nekrosa proportion to the percentage of 48%.

Keyword : *Hyperglycemic, β Cells, Aloe vera, Rats*

I. INTRODUCTION

High levels of glucose in the blood greatly affect the onset of hyperglycemic in the body. It is influenced by the lifestyle of the people who are less healthy by eating foods that contain high levels of fat and carbohydrates are high that it becomes a health issue most often discussed among people today. According Ganong (1997) blood glucose levels is a very important factor for the smooth working of the body. Blood glucose levels are determined by the balance between the amount of glucose into the blood stream and the amount of glucose out of the bloodstream. The main determinant of the blood glucose level is the amount of food intake, rate of glucose entry into cells, and the activity of liver glucostatic. Hyperglycemic is rising levels of glucose in the blood is indicated by an increase in the percentage of HbA1c.Hiperglikemia cause autooksidation glucose, glycation of proteins and activation of the polyol metabolic pathway which further accelerates the formation of reactive oxygen species (Lasdaukas M, 2008). Molecular modification in various tissues resulting in an imbalance between antioxidants protective (antioxidant defense) and an increase in production is an early bebas.Hal radical oxidative damage known as oxidative stress (Suhartono Eko Setiawan B and E, 2005).

Blood glucose levels increase with the absorption of glucose from food. Increased blood glucose levels occur because of tissue to absorb glucose from the blood and save it in the form of glycogen. When blood glucose levels rise, pancreatic β cells are stimulated to secrete the hormone insulin to lower blood glucose levels (Marks et al., 2000).

The entry of glucose from the intestinal epithelial cells into the blood causes increased blood glucose levels. Normal human blood glucose levels ranging from 80-100 mg / dL (Murray et al., 2003), whereas in mice blood glucose to normal levels ranged between 50-135 mg / dL (Malole and Pramod, 1989).

The use of herbal formulations and various native species that has been attempted for the treatment of diabetes mellitus and has obtained encouraging results from plant extracts in connection with antidiabetic activity, but only partially been explored, among these plants are plants that are easy to get that *Aloe vera*. Research aloe has been carried out by Afaf, *et. al* (2008) administration of ethanol extract

of aloe with doses of 100, 300 and 500 mg/kg to male rats diabetic activity, the results showed that blood glucose levels alloxan diabetic rats decreased after administration of ethanol extract of aloe for six days, but Afaf not see the microscopic structure of rat pancreatic β cells hyperglycemic other studies have also been conducted by Bashkar et al (2013) by the same method but this research measure blood glucose levels and see bilirubin heart, and do not measure the microscopic structure of the pancreatic β cells. While research Sema et al (2005) conducted a study using the gel and pulp of aloe, and glibenclamide for 15 days, but from the research results of *aloe vera* (gel and pulp) extract or glibenclamide no significant differences in glucose blood of mice treated with the use of gel and pulp of aloe, and glibenclamide compared with the control group were given PBS and also does not have a beneficial effect on pancreatic β cell microscopic structure of the rat. Therefore, the researchers want to do research on the effectiveness of the use of *Aloe vera* to decrease blood glucose level hyperglycemic rats.

II. METHODS

A. Tool

The tools used in this study is GlukoDr^{TM} Blood Glucose Test Meter (All Medicius, Korea), OHAUS scales with power weigh 2610 g, Erlenmeyer flask with 100 mL size, rat cages of 70 cm x 44 cm x 20 cm, oven, spuid 5 mL, gavage, and stationery.

B. Material

Materials used in this study were 25 rats (Rattus wistar) 3-month-old male with a body weight of 200-250 grams, pellet type 789-S production by PT. Charoen Phokpahan Medan-Indonesia, alloxan, *aloe vera* ethanol, distilled water, and 1% CMC (Sodium Carboxymethyl Cellose).

C. Study Design

This study used a completely randomized design (CRD). Treatment consists of: A = Rat normoglikemik given distilled water as a control, B = Rats were given 75 mg / kg alloxan as hyperglycemic rats), C = hyperglycemic rats were given 100 mg/kg of leaf extract of *Aloe vera* during 21 days, D = hyperglycemic rats were given 100 mg/kg of leaf extract of *Aloe vera* for 21 days and E = hyperglycemic rats were given 100 mg/kg of leaf extract of *Aloe vera* for 21 days. Leaf extract of *Aloe vera* during treatment is done orally (intubation of the esophagus) with doses 0,5ml / 100 g BW.

D. Data Collection Techniques

- Provision Animals Models

  This study used 25 rats (*Rattus wistar*)-month-old male with a mean body weight of 200-250 grams obtained from stables maintance of the Laboratory of Veterinary Clinical Pathology Department of the Faculty of Veterinary University of Syiah Kuala. Rats acclimatized for 7 days in the stable, the experiment, the cage is made of a plastic tub with a size of 70 cm x 44 cm x 20 cm with the top covered with wire mesh and lined hull bottom with a thickness of 3 cm. Experimental animals are given food in the form of pellets, type 789-S, eat and drink provided in *adlibitum*.

- Induction Alloxan In Rat (*Rattus wistar*) Males

  Before the treatment is done, all the rats were weighed for determination of alloxan dose using OHAUS scales with power weigh 2610 g. Giving alloxan be 1 (one) time on the first day of treatment in a dose of 75 mg / kg for 6 (six) days and continued with the use *Aloe vera* with different concentrations. The use of *Aloe vera* is done orally (intubation of the esophagus) for 21 (twenty one) days in treatment C and D. Animal control only given alloxan solvent and water. Provision of treatment carried out at 10:00 am before the animal is fed.

- Making and Giving Extract *Aloe vera* in male rats.

  Leaf extract of *Aloe vera* is obtained by finely grinding the leaves of *aloe* (length approximately 50 cm, thickness 2.5 cm) which had been cleaned and removed the thorns. Then add 70% ethanol was stirred for 30 minutes with a magnetic stirrer and allowed to stand for 48 hours. Results maceration filtered 3 times with buctner funnel lined with filter paper and accommodated erlenmeyer (Voigt, 1994).

The filtrate was evaporated by vacuum filtration results rotary evaporator. Further dilution with 1% CMC (Sodium Carboxymethyl Cellulose) to obtain a dose of 100 mg / BB, 300 mg / BB and 500 mg / BB (Afaf, 2008).

- Examination of Blood Glucose Levels

  Examination of the blood glucose levels of mice were fasted for 18 (eighteen) hours prior to the examination of blood glucose levels Santos *et al* refer to. (1978) performed 3 times. The first measurements performed on whole animal before treated and alloxan induced and the use of *Aloe vera*. Initial measurement is intended to ensure that the animal is an animal that is used normoglikemik. The second measurement is done after 6 days induction alloxan treatment, to ensure that the rats treated B, C, D, and E in a positive state of hyperglycemic. Alloxan hyperglycemic rats performed the use of *Aloe vera* every day for 21 days as much as 0.5 mg/100 g BB for each treatment. Glucose measurement is then performed on day twenty-one. Blood samples treated by taking blood on the tail in the rat tail flick and one day after the treatment ended in enthaunasia rats. Blood tests performed using GlukoDr^{TM} Blood Glucose Test Meter. Obtained blood dripped on GlukoDr^{TM} test strips, then after 11 seconds the blood glucose levels indicated on the screen GlukoDr^{TM} Blood Glucose Test Meter and after it is done reading the data. Blood glucose levels were observed to be in units of mg / dL.

- Decision-Making Organs and Histological preparations

  Rats make to of *enthaunasia* one day after treatment ended. After surgery carcass, organ pancreas is immediately taken and subsequent histological preparations were made using paraffin. Pancreas specimens were fixed in Bouin solution, then dehydrated using 70% alcohol series to absolute alcohol, clearing in xilol, infiltration and embedding in paraffin blocks 56-58 0C. Preparations are already at *embedding* slashed with a thickness of 4 microns using a rotary microtome. Each repetition in 4 incision made at intervals of 10 incision and placed on glass objects that have been treated with a solution of adhesive. Observation of pancreatic β cells nekrosa in mice stained with Gomori's staining method Chromium Hematoxylin Phloxin which refers to Gridley (1960).

  Observations nekrosa pancreatic β cells carried on with a light microscope at a magnification of 10 x 40. Each slice was observed by 3 field of view, so that at each repetition there are 12 field of view observation.

- Data analysis

  The data obtained from the study were analyzed using SPSS (version 18) and by analysis of variance. If there is a difference between treatments will continue with the analysis of Least Significant Difference test at 5% confidence interval (Yitnosumarto, 1991).

III. RESULTS AND DISCUSSION

A. Result

- Blood Glucose

Levels Analysis of variance on blood glucose levels of rats on a wide variety of treatment showed a treatment effect highly significant (P <0.01). Having followed by Duncan's multiple test, the results can be seen in Table 1.

Table 1 Multiple Range Test on The Mean Blood Glucose Levels

Treatment	Blood Glucose Level Mean mg/dL ($\bar{X}$ ±SD)		
	1st day	6th Day	21st Day
A. Water	80,2 ± 18,34	83,4 ± 14,04^{B}	83,4 ± 16,36^{A}
B. 75 mg/kg BB Alloxan & incubated in 21 days	80,2 ± 22,80	127 ± 27,42^{A}	141,4 ± 51,70^{B}
C. 100 mg/kg BB *Aloe vera*	72,6 ± 38,77	112,8± 26,78^{A}	89,2 ± 7,88^{A}

Extract and 75 mg/kg BB alloxan in 21 days			
D. 300 mg/kg BB *Aloe vera* Extract and 75 mg/kg BB alloxan in 21 days	89,8 ± 19,524	118,8± 13,59^{A}	83,8 ± 10,18^{A}
E. 500 mg/kg BB *Aloe vera* Extract and 75 mg/kg BB alloxan in 21 days	75,2 ± 21,01	126,2± 13,59^{A}	80,6 ± 7,43^{A}

Description: The capital letters A, B superscript in different way shows highly significant difference (P <0.01).

Table 1 shows the mean blood glucose levels in mice treated significantly different with treatment B (P <0.01) and was not significantly different and the treatment C, D, and E (P> 0.01).

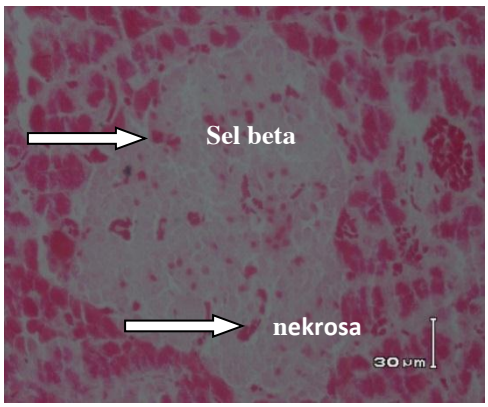
- Nekrosa Pancreatic β Cells

Pancreatic β cells of rats with nekrosa on various treatments can be seen in Figure 1. Analysis of variance of the pancreatic β cell nekrosa treated mice showed a highly significant effect of treatment (P <0.01). After continued with Duncan's multiple range test, the results can be seen in Table 2.

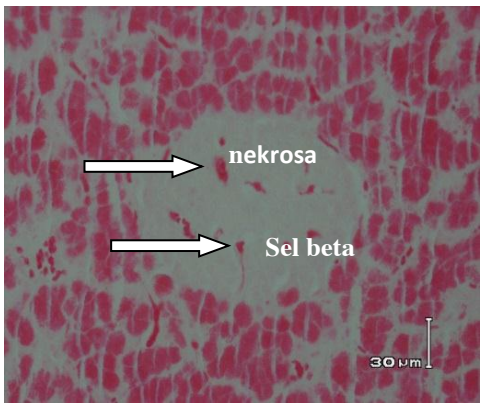
Table 1 The Proportion Mean β Cells Rat Nekrosa In Different Treatment

Treatment	The Proportion Mean β Cells Rat Nekrosa (X ±SD)
A. Water	0,4760 ± 0,0662^{A}
B. 75 mg/kg BB Alloxan & incubated in 21 days	0,8924 ± 0,0359^{D}
C. 100 mg/kg BB *Aloe vera* Extract and 75 mg/kg BB alloxan in 21 days	0,5916 ± 0,0956^{C}
D. 300 mg/kg BB *Aloe vera* Extract and 75 mg/kg BB alloxan in 21 days	0,5432 ± 0,0463^{C}
E. 500 mg/kg BB *Aloe vera* Extract and 75 mg/kg BB alloxan in 21 days	0,4805 ± 0,0696^{B}

Description: the different capital superscript (A, B) shows highly significant differences (P <0.01).



A



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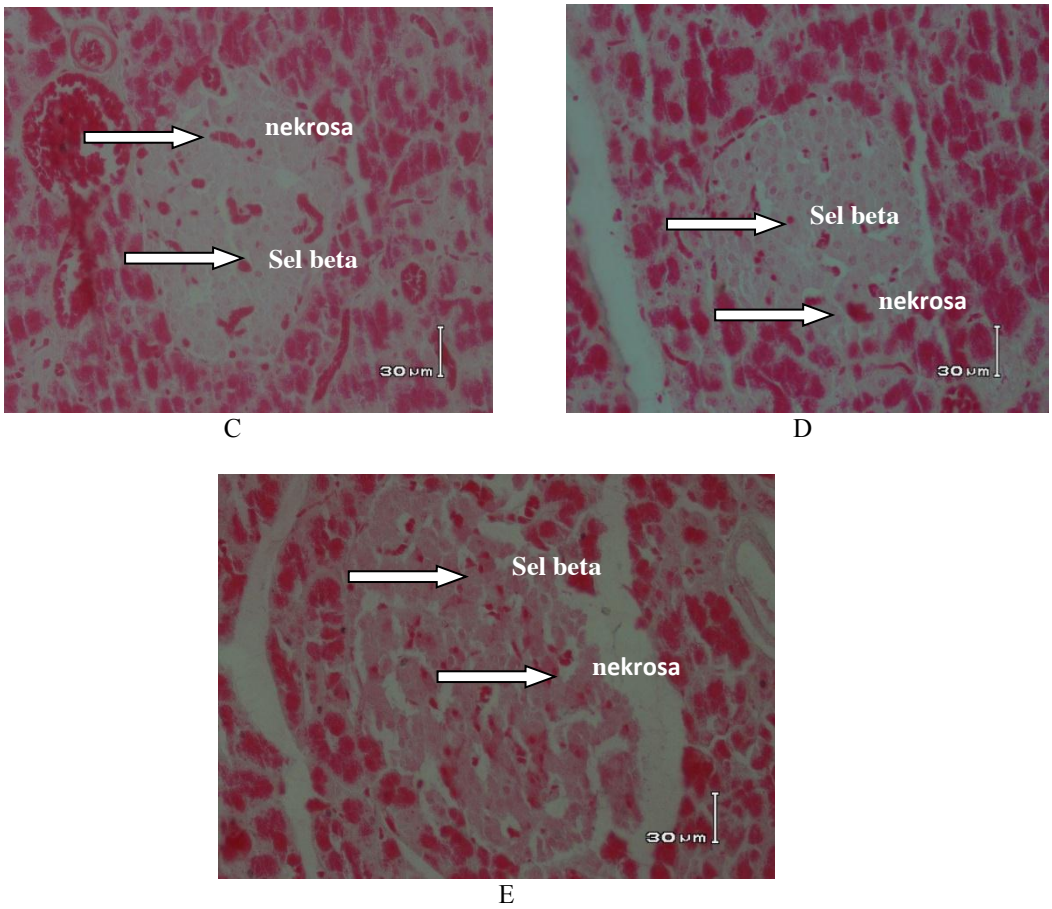

Figure 1. Rats' Pancreas Preparations In Various Treatment A (distilled water), B (75 Mg / kg BW alloxan and incubated for 21 Days), C (100 mg / kg *Aloe* Leaf Extract and 75 mg/kg alloxan Over 21 day), D (300 mg / kg *Aloe* Leaf Extract and 75 mg / kg alloxan Over 21 Days), E (500 mg / kg *Aloe* Leaf Extract and 75 mg / kg alloxan Over 21 Days). b is the beta cells of the pancreas, n is nekrosa pancreatic beta cells.

B. Discussion

- Blood Glucose Levels

From the results of statistical analysis showed that the mean blood glucose levels in treatment B (positive control) days prior to the one induced by alloxan 75 mg/kg BW was 80.2 mg/dL, on the sixth day after alloxan induced with 75 mg/kg BW glucose is increased to 127 mg/dL, and on day twenty-one was 141.4 mg/dL. Mean blood glucose levels of rats was higher than treatment A (negative control) on day twenty-one is 83.4 mg / dL. This suggests that elevated levels of glucose in treatment B had experienced hyperglycemia (elevated blood glucose levels) after injection of alloxan, as well as the treatment C, D, and E are also induced by alloxan. This condition is in line with research (Oyedepo, et al, 2013) which states that the increase in blood glucose levels in rats by intraperitoneal injected alloxan may occur >72 hours after alloxan injection, blood glucose levels of rats ≥ 200 mg/dL.

Mean blood glucose levels in rats induced by alloxan treatment C 75 mg/kg BW and accompanied by the administration of 100 mg/kg of *Aloe vera* on day twenty-one is 89.2 mg / dL. Mean blood glucose levels in rats induced by alloxan treatment D 75 mg/kg BW and accompanied by administration of 300 mg/kg BW leaf extract of *Aloe vera* on day twenty-one is 83.8 mg/dL. Treatment E flats rat blood glucose levels induced alloxan 75 mg/kg and with a leaf extract of *Aloe vera* 500 mg/kg is 80.6 mg/dL. This shows a decrease in blood glucose levels significantly with treatment B. Treatment B were significantly different with treatment C, D and E ($P < 0.01$).

This condition is due to the use of *Aloe vera* can lower bl ood glucose levels that act as antidiabetic and antioxidant. According Afaf, *et al* (2008) the effects of antioxidants is to prevent oxidation of glucose

and reduce the potential for enzymes that play a role in the transfer of phosphate groups on the glucose which is the initial stage of the glycosylation process. The use of *Aloe vera* can lower blood glucose kadara and increase glycogen in the liver as well as *Aloe vera* may increase the activity of pancreatic β cells in stimulating the biosynthesis and secretion of insulin.

- Nekrosa Pancreatic β Cells

The mean proportion of pancreatic β cell nekrosa in treatment B (negative control) induced alloxan 75 mg / kg BW for 21 days ie 0.8924 significantly different with treatment A is 0.4760 (Table 2). Increased nekrosa in treatment B cells (negative control) (Table 2 and Figure 1) resulted in the production of insulin deficiency resulting in increased blood glucose levels of mice (Table 1), this condition is in line with Guyton and Hall (1997) claim that if the pancreatic β cells damaged the production of insulin deficiency. Insulin deficiency can interfere with the metabolism of glucose is berjumlahnya glucose enter the cells and reduced the use of glucose by the network. This condition causes an increase in blood glucose levels and pancreatic β cells become damaged.

A decrease in blood glucose levels and the proportion of β cell nekrosa rats gradually affect blood glucose levels hyperglycemic mice, and the results of the study also obtained the result of increased doses of *Aloe vera* is given, can reduce the proportion of rat pancreatic β cell nekrosa, it is thought the higher the extract of *Aloe vera* applied, the higher the active ingredient contained in the extract of *Aloe vera* to reduce the proportion of β cell nekrosa treated rats. This is in line with Steencamp and Stewart, (2007), the content of *Aloe vera* can reduce levels of glucose in the blood and can improve the microscopic structure of the β cells of the pancreas is a polysaccharide acemannan and glucomannan, Aloe emodin, glycoproteins, flavonoids, vitamins and minerals.

Glucomannan is a soluble fiber that play a role in improving insulin sensitivity and decrease insulin requirements by helping insulinisasi network more effectively so that there was no increase in blood glucose levels significantly. Just like other water-soluble fibers, *glucomannan* will increase the viscosity of the stomach so that the lower the rate of glucose absorption, causing changes in hormone levels in the gastrointestinal tract such as gastric inhibitory polypeptide (GIP), glucagon, and somatostatin which affects the digestive tract motility, nutrient absorption, and secretion insulin (Bender, 2007). *Acemannan* (B-1,4) -linked acetylated mannan) is the main carbohydrate in Aloe vera (Aloe vera) that most of its content is mannose which can be used as a hypoglycemic therapy (Steencamp and Stewart, 2007). Aloe emodin is an organic compound that activates antrokuinon class levels of insulin signaling as absorbent insulin-beta and substrate-1, phosphatidyl inositol-3 kinase and increases the rate of glycogen synthesis by inhibiting glycogen synthase kinase 3 beta, so it is very useful to reduce the blood sugar ratio, antiseptic and burn treatment (Juprimalino, 2012).

C. Conclusion

The use of *Aloe vera* in mice treated can lower blood glucose levels hyperglycemic rats. And the use of aloe vera *Aloe vera* at a dose of 500 mg/kg for 21 days can reduce pancreatic β cell nekrosa proportion to the percentage of 48%.

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