

Research Article

THE EFFECT OF ANNONA MURICATA LEAVES ON BLOOD GLUCOSE LEVELS SCRATCHING SWISS WEBSTER STRUCTURED BY ALLOXANT

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Abstract

Background: Oxidative stress and inflammatory responses have roles as destructive agents in exacerbating the pathological conditions of diabetes mellitus. The aim of this study was to determine the effect of the ethanol extract of *Annona muricata* leaf on reducing glucose levels in alloxan-induced Swiss Webster mice. **Methods:** This study used 25 Swiss Webster mice which were randomly divided into 5 groups: the Negative Control (NC), Positive Control (PC) group, the treatment group dose 150 mg, 300 mg, 600 mg. Histopathological features will be assessed using the NASH CRN score which will then be processed using SPSS version 24 using the Chi-Square test. While blood glucose levels will be tested using the Kruskal-Wallis test with the post hoc Mann Whitney U Test. **Results:** While blood glucose levels obtained at the pre-test (H0) compared with the posttest (H14) did not have a significant difference ($p = 0.542$). The 14th day of the test (H14) between the 5 dose groups did not have a significant difference ($p = 0.553$). **Conclusion:** There was no significant relationship in ethanol extract of *Annona muricata* leaves administration on mice blood glucose level.

Keywords: Alloxant, *Annona muricata*, glucose, mice.

INTRODUCTION

Diabetes Mellitus is a chronic metabolic disease characterized by increased blood glucose levels and can cause complications in various organs of the body if not given proper management¹. According to WHO data, the number of people with diabetes has almost doubled since 1980, increasing from 4.7% to 8.5% in 2014². Diabetes mellitus can cause serious complications in different organ systems in the body, such as the kidneys, eyes, heart, liver, and other organs³. Insulin resistance as the main cause of hyperglycemia and hyperinsulinemia is becoming the main cause of liver damage in diabetic patients^{4,5}. The liver as an insulin-sensitive organ, can be affected by the effects of oxidative stress induced by hyperglycemia, which can cause inflammation in liver tissue^{5,6}. Both oxidative stress and inflammatory response have roles as agents, destroyer in aggravating the pathological condition of diabetes mellitus^{7,8}. The aim of this study was to determine the effect of the ethanol extract of *Annona muricata* leaf on reducing glucose levels in alloxan-induced Swiss Webster mice.

METHODS

The design used in this study is a true experimental one. In this study, 25 male Swiss Webster mice were used which were put into 5 groups with different interventions. The ethics of this research have received information that it has passed the ethical review with the number KET-432/UN2.F1/ETIK/PPM.00.02/2019. This research was combined in a study entitled "Molecular, Cellular, and Histopathological Studies of the Effect of *Annona muricata* Extract on the Pancreas, Liver and Testis of Diabetes Mellitus Mice.

Research Sample Preparation

This study used 31 male Swiss Webster mice aged 12-14 weeks with a body weight of 30-40 grams, which were categorized into 5 groups, namely negative control group (given alloxan 40 mg/kg BW), positive group (given alloxan 40 mg/kg BW and given glibenclamide 0.65 mg/ml/head/day for 14 days), group low dose treatment (given alloxan 40 mg/kgBW and given ethanol extract of AM leaves 150 mg/kgBW/day for 14 days), medium dose treatment group (given alloxan 40 mg/kgBW and given AM leaf extract 300 mg/kgBW/day for 14 days), high dose treatment group (given alloxan 40 mg/kgBW and given ethanol extract of AM 600 mg/kgBW/day for 14 days).

Hematoxylin-Eosin Staining

First, all preparations were soaked by xylol I and II for each 5 minutes and followed by submersion in ethanol gradient series (70% and 90%) for 5 minutes. Then, the preparations were stained by soaking them into hematoxylin solution about 5-10 minutes, followed by rinsing them under water. After that, the samples were soaked into eosin solution about 3 minutes, followed by dehydrating them with stratified concentration alcohol (70%, 90%, and 100%) each 3-4x dye. Then, all preparations were dipped by xylol I and xylol II solutions about 5 minutes each. Lastly, the samples were dripped with one drop of entelan and covered again by cover glass.

Calculate Glucose Level

The first count is carried out on the day before dosing. Second, the calculation was carried out on the 14th day of treatment. Measurements were made using a Digital Blood Meter.

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Tabel 1. Hasil analisis Kruskal-Wallis

	n	Blood glucose levels	Value P
Group	NC	247(107-515)	>0,05
	PC	258(46-333)	
	LD	121(-76-294)	
	MD	197(-198-224)	
	HD	72(-47-402)	

Information: NC = Negative Control (given alloxan 40 mg/kgBW), PC = Positive Control (given alloxan 40 mg/kgBW and glibenclamide 0.65 mg/ml/head/day), LD=Low dose (given dose of soursop extract 150 mg/kgBW/day), MD=Medium dose (given dose of soursop extract 300 mg/kgBW/ days), HD = High Dosage (given a dose of soursop extract 600 mg/kgBW/day). Kruskal-Wallis test. Data is presented in Median (Minimum-Maximum)

DISCUSSION

Blood Glucose Levels in Mice

Data H0 with H14 did not show a significant difference, the data obtained showed a decrease in blood glucose levels in the dose group (LD, MD, HD). The effect of reducing blood glucose levels also occurred in previous studies, showing a decrease in blood glucose levels in streptozotocin-induced Wistar rats after being given AM leaf extract for 14 days. This is presumably due to the regeneration that occurs in pancreatic beta cells after being given AM leaf extract⁹. AM leaf extract showed antioxidant activity that was able to reduce pancreatic oxidative damage induced by streptozotocin¹⁰. (LD, MD, HD) showed results that were not different from the PC group that had received glibenclamide therapy. Therefore, in this study it was found that the administration of AM leaf extract had the effect of lowering blood glucose in mice such as the effect of glibenclamide therapy given to the PC group.

Conclusion

There was no significant relationship between the administration of AM leaf ethanol extract on alloxan-induced reduction in blood glucose levels of mice.

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