

Original Research Article

Ameliorative Effect of Plant Extract of Suruhan (*Peperomia pellucida*) on Renal Histological Abnormality in Alloxan-Induced Hyperglycemic Mice

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Abstract: Diabetes mellitus, characterized by hyperglycemia, is a major risk factor of kidney disease. The study aimed to determine whether suruhan plant (*Peperomia pellucida*) claimed to have anti-diabetic properties, can improve renal histological abnormalities in alloxan-induced hyperglycemic mice. Male albino mice (n=25) were grouped into five (5 mice each). Group 1 treated with alloxan at the dose of 150 mg/kg BW (as negative control). Group 2 was given alloxan and glibenclamide of 0.65 mg/kg bw (as positive control). Group 3, 4 and 5 were treated with alloxan and plant extracts at the dose of 56, 112 and 168 mg/kg BW respectively. Injection of alloxan was done 3 times in 6 days and the plant extract was given every day for 35 days. Results showed that plant extract of suruhan significantly reduced histological abnormalities of renal tubular and glomerular cells. In conclusion plant extract of suruhan is potent to be used as anti hyperglycemic agent and diabetes-related complication.

Keywords: Diabetes mellitus, antihyperglycemia, suruhan, *Peperomia pellucida*, alloxan, glibenclamide, renal histology.

INTRODUCTION

High level of blood sugar or hyperglycemia is one of the characteristics of pancreatic metabolic disorders that cause diabetes [1]. Chronic prolonged hyperglycemia may lead to severe damage to the tissue and vascular system leading to serious complications such as neuropathy and kidney disease [2, 3]. To address the diabetes-related complications a common strategy is to lower blood sugar levels, one of the most commonly used techniques is to apply a well-known standard drug - glibenclamide. Unfortunately, the use of this drug still leaves concerns about its side effects [4].

In an effort to find drugs to lower blood sugar levels that are free from side effects, the search for safe natural ingredients continues. There are many medicinal plants known to have antidiabetic properties such as *Momordica charantia* L., *Pterocarpus marsupium* Roxb., and *Trigonella foenum graecum* L. [5]. In Southeast Asia, especially in Indonesia, one of the medicinal plants commonly used as an anti-diabetic herb is 'suruhan' an Indonesian vernacular name of *Peperomia pellucida* L. Kunth. [6].

However, there is a lack of research report on the efficacy of *P. pellucida* to treat kidney histological damage related to hyperglycemia. This study aims to determine whether the suruhan plant can be used to cure kidney histological damage due to hyperglycemia in alloxan-induced mice.

MATERIALS AND METHODS

Plant Materials

Plant materials used in this study were the whole parts of suruhan (*P. pellucida*) collected from suburb of Bandar Lampung, Indonesia. The weeds were washed with tap water and rinsed using aquadest. After air dried, the whole plant was sliced into small pieces, and then soaked in 96% ethanol for 24 hours. After being macerated for four times, the macerate evaporated using rotary evaporator under low pressure at 50°C until brownish-viscous extract formed.

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Animals and Experimental Design

Male albino mice aged 3-4 months, weighing between 30-40 g, were obtained from Lampung Veterinary Center, Bandar Lampung, Indonesia. Before being treated for research, the animals were acclimated for one week, maintained under room temperature, fed with a standard laboratory diet and water ad libitum. By using a completely randomized design, 25 male albino mice were grouped into five (5 mice each). Group 1 treated with alloxan at the dose of 150 mg/kg bw (as negative control). Group 2 was given alloxan and glibenclamide of 0.65 mg/kg bw (as positive control). Group 3, 4 and 5 were treated with alloxan and plant extracts at the dose of 56, 112 and 168 mg/kg bw respectively. Alloxan was given 3 times in 6 days and suruhan plant extracts were given once daily for 35 days.

Alloxan Induction and Extract Administration

The hyperglycemic condition of the experimental animals was made by intraperitoneally injecting 0.5 ml of alloxan monohydrate (Sigma Aldrich, Cat.No.A7413-10G) at the dose of 120 mg/kg body weight after the mice were fasted for 8 hours. Before and after alloxan injection, blood glucose levels of each animal were measured using strip glucometer (from Roche, Germany).

Histological Preparation

After 35 days of treatment, necropsy was carried out by sacrificing the mice under chloroform anesthetic. Then the kidneys were taken and put in a container containing a 10% buffer formalin solution. The histological preparations of the kidney were made using the paraffin method with Hematoxylin Eosin staining. The histological slides then observed under light microscope with 400x magnification.

Study Parameters

The criteria for kidney damage were based on the total damage scores of renal tubules and glomerulus (with a range of 0-6). The histological damage to each of these organs can be divided into 4 levels, namely: 0 = all cells appear normal; 1 = inflammatory cell infiltration; 2 = swelling of the bowman's capsule cells; 3 = necrotic cells

Statistical Analysis

One-way ANOVA and LSD were applied in analysis of the effects of treatment on blood sugar levels of experimental mice. Meanwhile, to analyze the data on the impact of the treatment on tubular damage and renal glomerulus in mice, the Mann Whitney test was used.

RESULTS AND DISCUSSION

Blood glucose levels of mice before (baseline) alloxan injection and after treatments are presented in Table 1. It is clear that in comparison to the negative control group, blood glucose level of mice treated with plant extract of suruhan decrease significantly ($p < 0.05$). However, the highest effect of the order extract was shown by the lowest concentration (56 mg/kg bw.) rather than the highest.

Table-1: Blood glucose levels of mice before and after given treatments

Treatments	Blood glucose (mg/dL)
Baseline (normal mice)	75.96 ± 2.23 ^a
C +tive (alloxan + glibenclamide)	77.80 ± 3.114 ^a
C -tive (alloxan)	183.60 ± 16.426 ^d
P1 (alloxan + suruhan 56 mg)	78.40 ± 5.273 ^a
P2 (alloxan + suruhan 112 mg)	95.60 ± 7.335 ^b
P3 (alloxan + suruhan 168 mg)	115.80 ± 7.855 ^c
Values are presented as mean ± SD; values followed by the same superscript are not statistically different at $\alpha = 0.05$ by LSD test	

Ameliorative effects of plant extract of suruhan against the tubular and glomerular cells damage of test mice are shown in Table-2. The results of Mann Whitney U Test against mean scores of the renal tubular and glomerular cells damages are presented in Table-3 and 4 respectively.

Table-2: Effects of treatments on the mean scores of tubular and glomerular cells damage in mice kidney.

Treatments	Mean damage scores	
	Tubular cells	Glomerular cells
C -tive (alloxan + glibenclamide)	2.84	2.38
C +tive (alloxan)	2.12	1.36
P1 (alloxan + suruhan 56 mg)	0.96	0.7
P2 (alloxan + suruhan 112 mg)	1.7	1.04
P3 (alloxan + suruhan 168 mg)	1.5	1.04

Table-3: Results of Mann Whitney U Test (p value) against mean scores of renal tubular cells damages

Group	P1	P2	P3	C +ive	C -ive
P1	-	0,107	0,083	0,008*	0,008 *
P2	0,107	-	0,592	0,504	0,008 *
P3	0,083	0,592	-	0,068	0,008 *
C +ive	0,008*	0,504	0,068	-	0,007 *
C -ive	0,008*	0,008*	0,008*	0,007*	-

Table-4: Results of Mann Whitney U Test (p value) against mean scores of renal glomerular cells damages

Group	P1	P2	P3	C +ive	C -ive
P1	-	0,196	0,233	0,109	0,011 *
P2	0,196	-	0,822	0,511	0,014 *
P3	0,233	0,822	-	0,448	0,014 *
C +ive	0,109	0,511	0,448	-	0,070
C -ive	0,011*	0,014*	0,014*	0,070	-

This study results confirm the efficacy of the *P.pellucida* plant as antidiabetes as reported by Hamzah et al. (2012) and accordingly confirm traditional claims that suruhan plant can be used as antidiabetic drug [7].

The antidiabetic properties of *P. pellucida* are thought to be because this plant is rich in flavonoids, saponins, alkaloids, terpenoids, steroids and tannins. Because, as is known, plants that are proven to be efficacious as antidiabetic, usually contain these compounds. [8-10].

The findings of this study (Tables 2, 3 and 4) indicate that the histological damage to renal tubules and glomerulus of mice due to alloxan injection has recovered by the treatment of plant extract of *P. pellucida*. This fact indicates the functioning of the antioxidant compounds in this plant extract [11-12]. Antioxidant phytochemicals are natural ingredients that have been found to be very useful in the prevention of various chronic diseases [13].

As reported by Shah et al.(2017) plant extract containing antioxidant from *Sida cordata* potential to be used as nephroprotective agent [14]. Nephroprotective effect of phytochemical having antioxidant properties has also found in of *Combretum micranthum* plant [15].

CONCLUSION

Plant extract of *Peperomia pellucida* is revealed to reduce glucose levels and ameliorate histological cells damages of kidney in alloxan-incude mice. It suggests that plant extract of suruhan potent to be use as antidiabetes and its related complication.

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