DOI: 10.56511/JIPBS.2019.v6.i04.pp07-10

Journal of Innovations in Pharmaceutical and Biological Sciences (JIPBS)
ISSN: 2349-2759
Available online at www.jipbs.com

Research article

Antidiabetes activity of pirdot leaf water infusion extract (*Saurauia vulcani* Korth.) in type II diabetes rats induced by nicotinamide-streptozotosin

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Key words: Antidiabetic, Saurauia vulcani Korth, Water Infusion extract.

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Vol. 6 (4), 07-10, Oct-Dec, 2019.

Abstract

Objective: This study was conducted to determine the effect of pirdot leaf water infusion extract (*Saurauia vulcani* Korth.) to decrease blood glucose levels in type 2 diabetic rats induced by nicotinamide-streptozotosin. **Methods:** Pirdot leaf water infusion extract (*Saurauia vulcani* Korth) was obtained by infusion method. Animals in this study were type 2 diabetic rats that induced by nicotinamide 110 mg / kg BB and streptozotosin 65 mg / kg BW intraperitoneally. The antidiabetic activity test using pirdot leaf water extract was obtained in 3 different doses, namely 0.25 ml, 0.5 ml, and 1 ml were given orally once a day and observed for 28 days. **Results:** Pirdot leaf water infusion extract at dose of 0.25 ml, 0.5 ml, and 1 ml for 28 days had an antidiabetic effect in type II diabetic rats induced with nicotinamide-streptozotosin. The antidiabetic activity of pirdot leaf water doses of 0.5 mL, and 1 mL significantly different ($p < 0.05$) to negative controls and extracts of pirdot leaf water at a dose of 0.25 mL but it was not significantly different ($p > 0.05$) to glibenclamide in influencing the difference (Δ) of rat blood glucose levels. **Conclusion:** Pirdot leaf water infusion extract could reduce blood glucose levels in type 2 diabetic rats induced by nicotinamide-streptozotosin.

Introduction

Diabetes mellitus is a group of disorders of fat, carbohydrate and protein metabolism caused by lack of insulin secretion, lack of insulin sensitivity or both. Chronic hyperglycemia that occurs in people with diabetes mellitus was associated with long-term damage, dysfunction, and failure of various organ functions, especially the eyes, kidneys, nervous system, heart and blood vessels [1]. In Indonesia, the prevalence of diabetes mellitus patients in 2017 is around 10.3 million and will increase to 16.7 million by 2045 [2].

Diabetes mellitus is grouped into: type I diabetes caused by pancreatic beta cell damage caused by autoimmune disease or viral infection from patients, type II diabetes induce decreased insulin secretion and or insulin resistance, gestational DM, and other specific types of DM [1].

Pirdot leaf (Saurauia vulcani Korth) is one of the natural ingredients as an alternative medicine that has been widely used by the people of Simalungun, Toba, and Karo to treat various diseases. They use pirdot leaves as an antidiabetic drug by boiling 5-8 dried leaves in 1 liter of water until the remaining half of the portion is taken and then consumed twice to three times a day [3]. In vivo studies have been shown that pirdot leaf infusion extract has various activity such as antihyperglycemic activity using ethanol infusion extract [4], excision wound healing in hyperglycemic [5], antioxidant [6] and antihyperlipidemic mice [7]. This study was conducted to determine the effect of water infusion extract of pirdot leaf (*Saurauia vulcani*, Korth.) on blood glucose levels in type 2 diabetic rats induced by nicotinamide-streptozotosin.

Method

Preparation of pirdot leaf water infusion extract

Dried powder of pirdot leaf was extracted by the infundation method. Weighed pirdot leaf dried powder as much as 5 g, put into infundation pan, then added 50 mL water (1:10), then heated at 90ºC for 15 minutes (starting from the temperature reaches 90ºC) while stirring with stirrer. Then the infusion were filtered while warm with flannel filter cloth and stored in a container [8].

Phytochemical screening of pirdot leaf

Phytochemical screening carried out on pirdot leaf includes examining the chemical secondary metabolites of alkaloids, flavonoids, glycosides, tannins, saponins, triterpenoids, and steroids [9-11].

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Preparation of Nicotinamide solution (NA)
Nicotinamide were dissolved in 0.1 M citrate buffer (pH 4.5) [12].

Preparation of Streptozotosin solution (STZ)
Streptozotosin were dissolved in 0.9% NaCl solution [12].

Induction of diabetes test animals
Rat weighed 200-250 gram which to be induced were fasted for 18 hours. Weight and blood glucose levels were measured to determine the initial body weight and initial blood glucose level before NA-STZ induction. Nicotinamide solutions were injected with 110 mg / kg BB intraperitoneally, then 15 minutes later injected streptozotosin intraperitonially at a dose of 65 mg / kg BW. At Day 3 measured the blood glucose levels in rat, if blood glucose levels ≥ 200 mg / dL was considered as diabetes [12].

Antidiabetic activity test
The antidiabetic activity test using pirdot leaf water extract was made into 3 different doses, namely: 0.25 mL; 0.5 mL; and 1 mL given once a day orally. The animals test used in this experiment were male white rat that had been induced by nicotinamide-streptozotosin, it were divided into 5 groups and each group consisted of 5 animals, namely:

a. Group I were a negative control rats
b. Group II were a group of rats given a dose of 0.45 mg/kg BW of glibenclamide as a positive control.
c. Group III were test group of pirdot leaf water infusion extract at dose of 0.25 mL.
d. Group IV were a test group of pirdot leaf water infusion extract at dose of 0.5 mL.
e. Group V were a test group of pirdot leaf water infusion extract at dose of 1 mL.

The treatment was begun after the animal tested positive as diabetes rats, this is the first day of the treatment, every 4 days blood glucose levels are measured. It were tested for 28 days, and blood glucose were measured on days of 4, 8, 12, 16, 20, 24, and 28 [13].

The calculation the decreasing blood glucose effect using the formula:

Blood glucose level after induction – Blood glucose level at day t observation

Statistical analysis
The results of the research data were analyzed using the SPSS version 22.0 program. Data were analyzed using the Two Way ANOVA method. If there are significant differences, the analysis is continued with Duncan's Post Hoc test. Statistical analysis was carried out at 95% confidence level.

Results and discussion

Phytochemical screening of pirdot leaf water infusion extract
Phytochemical screening result showed that ethanol extract beetroot positively contains of Flavonoids, Saponins, Tanins and Glycosides.

Antidiabetic Acticity of pirdot leaf water infusion extract (*Saurauia vulcani* Korth.)
Streptozotosin can cause pancreatic β cell death through the process of alkylation of DNA, oxidative stress and nitric oxide (NO) production. The protective effect of nicotinamide on streptozotosin by inhibiting the action of poly ADP-ribose polymerase-1 (PARP-1), capturing free radicals and NO, increasing regeneration of β cells, and acting as a methyl group acceptor, which reduces DNA methylation [12].

The model of Type 2 DM rats by nicotinamide-streptozotosin induction is based on the protective effect of nicotinamide on streptozotosin β-cytotoxic effects, so this model has several advantages, namely: moderate hyperglycemia that did not require exogenous insulin to survive, b-cell reduction (–40%), reduce pancreatic insulin storage by 60%, and glucose intolerance due to impaired insulin secretion [12].

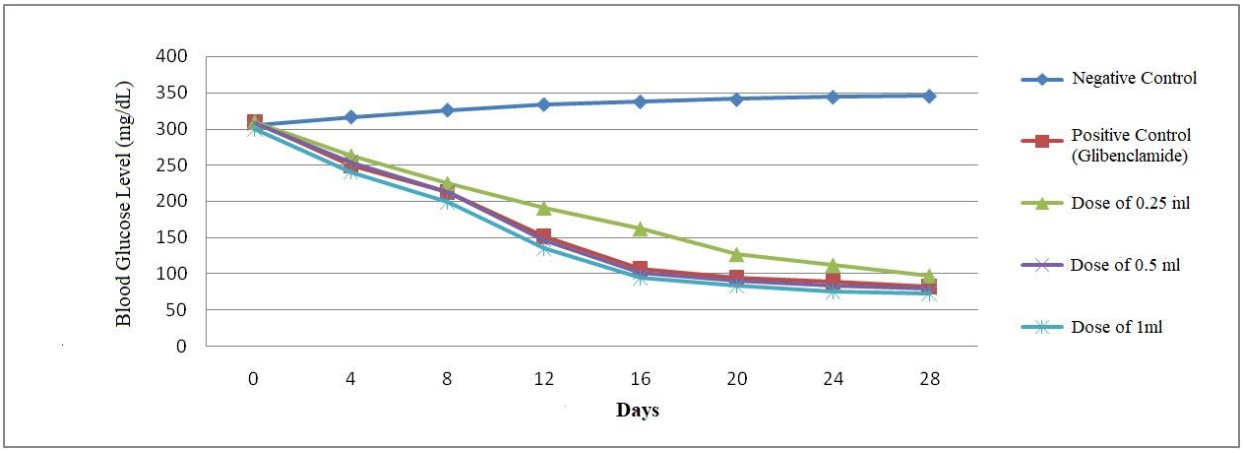


Figure 1. Mean Value of Blood Glucose Level After Treatment.

Pirdot leaf water infusion extract at doses of 0.25 mL, 0.5 mL and 1 mL could reduce blood glucose levels on day 4 to day 28th (Figure 1). Pirdot leaf water infusion extract at dose of 0.5 mL, 1 mL, and glibenclamide dose of 0.45 mg / kg BB showed a decrease blood glucose levels on day 4th, and it shown a decreased level of blood glucose to normal (<126 mg / dL) on the 16th day. Pirdot leaf water infusion extract at dose of 0.25 mL showed a decreased level of blood glucose on day 4, and decreased level of blood glucose to the normal level (<126 mg / dL) on the day 24th.

Figure 2 shows that on the 4th, 8th, 12th, 16th, 20th, 24th and 28th days, there were a decreased in blood glucose levels in the glibenclamide group at dose of 0.45 mg/kg BW, pirdot leaf water infusion extract at dose of 0.25 mL, 0.5 mL and 1 mL, while the negative control group experienced an increase in blood glucose levels, which can be seen from the bar graph which leads to a minus values. Pirdot leaf water infusion extract at dose of 0.5 mL, and 1 mL were significantly different ($p < 0.05$) to negative control and pirdot leaf water infusion extract 0.25 mL but it did not significantly different ($p > 0.05$) to glibenclamide in influencing the difference (Δ) blood glucose levels of rats.

The duration of administration affected the changes in blood glucose levels significantly ($p<0.05$) at each observation time, namely observations on day 4 on the 8th, 12th, 16th, 20th and 24th days (Table 1).

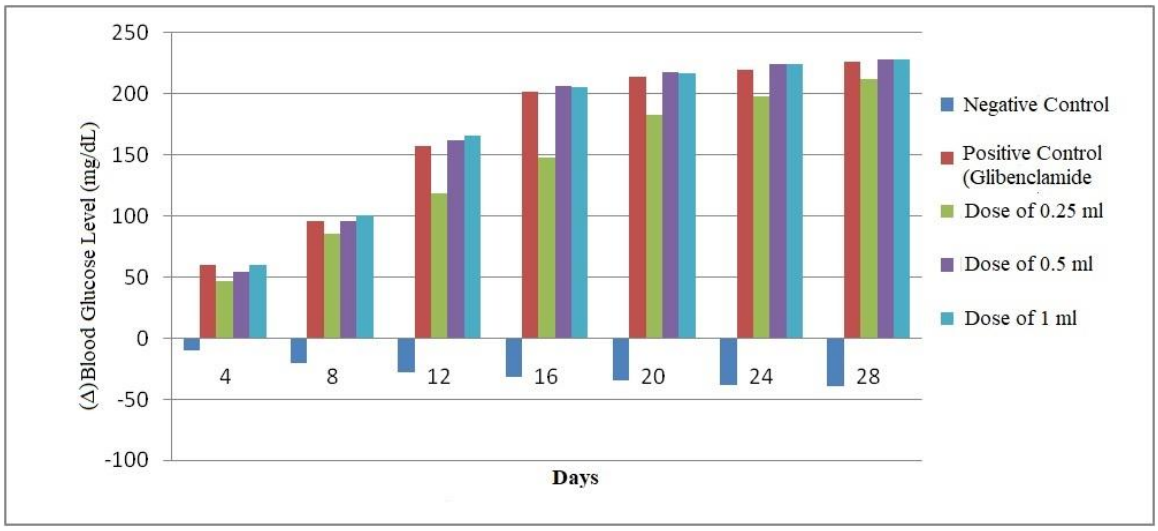


Figure 2. Mean value of Difference Graph (Δ) Blood Glucose Levels after treatment.

Table 1. Post Hoc Duncan Test of the Treatment Time Factor Against Difference (Δ) Blood Glucose Levels.

Days	n	Subset						
		1	2	3	4	5	6	7
Day 4	25	42.00						
Day 8	25		71.44					
Day 12	25			114.96				
Day 16	25				145.84			
Day 20	25					159.36		
Day 24	25						165.68	
Day 28	25							171.08

The antidiabetic effect of pirdot leaf water extract was due to the presence of secondary metabolites contained in pirdot leaf water infusion extract, it is consist of flavonoids, tannins, and saponins [4-6].

Flavonoids are polyphenols compounds found in many plants. Flavonoids can reduce blood glucose levels by increasing insulin secretion, reducing apoptosis, promoting pancreatic β cell proliferation, reducing insulin resistance and oxidative stress in muscles and fat, increasing glucose uptake in skeletal muscle and adipose tissue [14].

Saponins can reduce blood glucose levels by stimulating insulin secretion, increasing insulin sensitivity, regenerating pancreatic β cells, increasing liver glycogen storage, increasing peripheral glucose utilization, inhibiting α-glucosidase activity, inhibiting glycogen phosphorylase mRNA expression and glucose 6-

phosphatase, inhibiting gluconeogenesis, and increase the expression of Glut4 [15].

Tanins lowers blood glucose levels by increasing glucose uptake by mediating insulin signaling pathways, such as activation of PI3K (Phosphoinositide 3-Kinase), activation of p38 MAPK (Mitogen-Activated Protein Kinase) and Translocation of GLUT-4, inhibiting intestinal glucose absorption, increasing insulin secretion, induces β cell regeneration, and increases insulin activity [16].

Conclusion

Pirdot leaf water infusion extract (Saurauia vulcani Korth.) at dose of 0.25 mL, 0.5 mL and 1 mL could reduced blood glucose levels in type 2 diabetic rats induced by nicotinamide-streptozotosin and it showed dose dependent manner.

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