Original article:

Extract Ethanol of Poguntano in Alloxan Induced Diabetic Rats

Widjaja SS[1], Rusdiana[2]

Abstract

***Back Ground*:** Diabetes mellitus is a group of metabolic disease with high blood glucose level above 150 mg/dL over a prolonged period. The elevated of blood glucose, free fatty acid and insulin resistance will cause the endothelial dysfunction, hemostasis disturbances that lead to micro and macrovascular complications. Poguntano (Picria fel-terrae Merr) from family Scrophulariaceae found in most part of Indonesia, has been used as traditional plant for treatment of diabetes. ***Objective**:* The purpose of this study was to investigate the effect of extract ethanol of Poguntano in alloxan induced diabetic rats. ***Method*:** Fifteen male Wistar rats with body weight of 150-200 gr were given intra peritoneal injection of 150 mg/kg Alloxan to induce diabetes. These were divided into three groups (control diabetic, group given insulin and group given Extract ethanol of Poguntano 200 mg/Kg body weight) and one control normal control. The duration of study was 4 weeks; blood glucose and Endothelin-1 were measured for all groups. ***Results** :* Extract ethanol of Poguntano 200 mg showed significant results ($p<0.001$) in lowering blood glucose in Alloxan induced diabetic rats compared to control diabetic, but did not show superior to insulin group ($p=0.892$). Endothelin-1 showed statistical significant between group with normal rats and diabetic control rats. ($p=0.009$) but did not in the other groups. Levels of Endothelin-1 was higher in the diabetic control group with the median 1.95 (1,78-3.1). ***Conclusion*:** In our study we found that extract ethanol of Poguntano showed significant hypoglycemic activity and lowering the Endothelin-1 level in alloxan induced diabetic rats.

Keywords: blood glucose; anti-diabetic; poguntano; diabetic rats; endothelin-1.

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Introduction

Diabetes Mellitus is a group of chronic metabolic disease resulting from the defect in insulin secretion or resistance with high blood glucose above 150 mg/dL.[1,2] The elevated of blood glucose, free fatty acid and insulin resistance will cause the endothelial dysfunction, hemostasis disturbances and later thrombosis[3]. Diabetic complications developed due to prolonged hyperglycemia, dyslipidemia and genetic susceptibility,[4] and these can increased the mortality and morbidity rate of the diabetes.[3] Complications as cerebro and cardiovascular incidences, are major cause of death in diabetic patients.[1] Endothelial dysfunction is a prominent feature of cardiovascular diseases and also plays an important role in both micro and macrovascular complications of diabetes.[5,6] Strong vasodilator Nitric Oxide was decreased and endothelin-1 (vasoconstrictor) was increased in early stage of diabetes, this will impaired the vasorelaxation[7.] as the disease progress the activation of this endothelial system will leads to structural alteration, thrombosis and developed plaque in the vessel wall, fibrosis and inflammation[7,8,9] The activation of Endothelin-1 also stimulate the proliferation of vascular smooth muscle cell.[9] These all suggested ET-1 might play a major role in diabetic vascular complications.[7,10] The mainstay treatments of diabetes are control diets, exercise and medicine [11,12,13] A variety of traditional medicine has been used empirically to treat diabetes and Indonesia is a country rich of plenty medicinal plants.[14,15] Poguntano (Picria fel-terrae Merr) from family Scrophulariaceae, one of the medicinal plants found in North Sumatera has been used to treat diabetes, fever, malaria and cancer, the anti hyperglycemic effect has been proved empirically.[16,17,18,19,20]

1. Sry Suryani Widjaja, Biochemistry Department, Faculty of Medicine, USU, Medan, Indonesia, email:srysuryani@gmail.com
2. Rusdiana, University of Sumatera Utara Medical School, Biochemistry Department

Correspondence to: Sry Suryani Widjaja, Biochemistry Department, Faculty of Medicine , USU, Medan, Indonesia, email:srysuryani@gmail.com

The purpose of this study was to investigate the hypoglycemic and endothelial cell dysfunction of extract ethanol of Poguntano in alloxan induced diabetic rats.

Methods

This is an experiment study using male Wistar rats 4-8 weeks, weight 150-250 gr, under ethical approval from committee ethics University of Sumatera Utara.

Preparation of Plants Extract

Identification of Picria fel-terrae Lour. leaves was performed in Bogoriense Herbarium, LIPI, Jakarta, Indonesia. Extraction was done using maceration technique with ethanol 96%.[21]

Animals and Treatment

In this study fifteen wilstar male rats with body weight of 150-250 gr were given intra peritoneal injection of 150 mg/kg Alloxan monohydrate (Sigma Chemical Company) to induce diabetes.[22,23] Alloxan (2, 4, 5, 6-tetraoxypyrimidine; 2, 4, 5, 6- pyrimidinetetrone) an oxygenated pyrimidin derivative when administered to rodents will destroys cell Beta selectively in pancreas causing insulin dependent diabetes also known as alloxan diabetes.[24] The alloxan diabetes was confirmed when blood sugar concentration above 200mg/dL.

Twenty wilstar male rats were divided into four groups:

Group I normal control rats with no treatment

Group 2 diabetic control rats with no treatment

Group 3 diabetic rats received 1 unit of lantus Insulin

Group 4 diabetic rats received oral extraxt ethanol Poguntano 200 mg/kg

The duration of study was 4 weeks; blood glucose and Endothelin-1 were measured for all groups.

Statistical Analysis

The data were analyzed using Analysis of variance (ANOVA),SPSS (Statistical Product and Service Solutions) 17.0.

Results

Table 1. Blood glucose levels of alloxan-induced diabetic rats

Treatment Group	T0 (mg/dL)	T1w (mg/dL)	T4w (mg/dL)
Control	102	93	95
Diabetic control	374	271	312
Group Insulin	583	430	197
Poguntano 200 mg	435	209	133

In the group giving Extract ethanol Poguntano 200 mg, blood glucose started to come down after first week of treatment, and is better seen after four weeks of treatment.

Table 2 . Analysis one way anova of blood glucose at week four after treatment

		n	Mean ± SD	p
Variabel	Control	3	95.00 ± 3.00	< 0.001
	Diabetic Control	3	312.67 ± 60.01	
	Insulin	3	107.67 ± 49.66	
	Poguntano 200 mg	3	127.33± 15.04	

one way anova. post-hoc LSD: control vs control diabetes p<0.001; control vs insulin p=0.710; control vs poguntano 200 mg p=0.352; control diabetes vs insulin p<0.001; control diabetes vs poguntano 200 mg p<0.001; insulin vs poguntano 200 mg p=0.566

Extract ethanol of Poguntano 200 mg showed significant results (p<0.001) in lowering blood glucose in Alloxan induced diabetic rats at four week after treatment compared to control diabetic group without treatment, but did not show superior to insulin group (p=0.892).

Table 3. Analysis Kruskal Wallis for Endothelin-1

		n	Median (Minimum-maksimum)	p
Variabel	Control	5	0.05 (0.00-0.22)	0.015
	Control diabetes	5	1.95 (1.78-3.10)	
	Insulin	5	0.35 (0.14-1.06)	
	Poguntano 200 mg	5	0.55(0.00-1.27)	

Kruskal-Wallis. post-hoc Mann-Whitney test : Control vs control diabetes p=0.009; Control vs insulin p=0.0161; Control vs poguntano 200 mg p=0.072; control diabetes vs insulin p=0.009; control diabetes vs poguntano 200 mg p=0.009; insulin vs poguntano 200 mg, p=0.917

Endothelin-1 showed statistical significant between group with normal rats and diabetic control rats. (p=0.009) but did not showed significant results in the other groups. Levels of Endothelin-1 were higher in the diabetic control group with the median 1.95 (1.78-3.1) than the other groups.

Discussion

The main stay treatment of diabetes is diet, exercise and drugs. Drugs including insulin has been studied and used worldwide. A variety of traditional medicine has been proved empirically in lowering the blood glucose. This study showed the effect of lowering blood glucose in diabetic rats with extract ethanol

Poguntano 200 mg at 4 weeks after induction, this has also been done by Urip et al, by using extract hexane of Poguntano in diabetic rats.[16] Endothelin-1 was higher in the group with diabetic without any treatment this has been proved also by Krasimir Kostov et al, they showed the elevated of serum endothelin-1 in diabetes type 2 patients.[25] In our study the extract ethanol of Poguntano also lowering the level of Endothelin-1 in alloxan induced diabetic rats, this showed a promising study to prevent endothelial dysfunction in alloxan induced diabetic rats

Conclusion

In our study we have found that extract ethanol of Poguntano showed significant hypoglycemic activity and lowering the Endothelin-1 level in alloxan induced diabetic rats.

Conflict of interest: None

Acknowledgments

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