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Antidiabetic Effect of Ethanol Extract of Keji beling Leaves (*Strobhilantes crispa*) in Rats Induced by Streptozotocin

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Abstract
Diabetes Mellitus (DM) type 2 is a chronic disease characterized by increased glucose levels in the body due to insulin resistance or inadequate insulin production. This study aims to determine the antidiabetic potential of keji beling (Strobhilantes crispa) leaf extract. This research is different from other studies which used Alloxan as a diabetes inducer. In this study, Streptozotocin was used as a DM inducer. After treatment, information was obtained that keji beling (S. crispa) extract could reduce blood glucose levels in type 2 DM rats. Experimental research used 30 male Wistar rats divided into six groups consisting of normal group, negative control (HFD and Streptozotocin), positive control (Glibenclamide), dose group I (150 mg/kg BW), dose II (300 mg/ kg BW), and dose III (450 mg/kg BW). Based on the research results, it is known that S.crispa leaf extract can reduce blood glucose levels in mice induced by Streptozotocin and has the potential to act as an antihyperglycemic in type 2 DM.

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INTRODUCTION

Diabetes Mellitus (DM) type 2 is the most common form of diabetes, usually affecting adults, but also in children and adolescents. DM is a global pandemic that is spreading very quickly throughout the world. Indonesia on in 2021 it is ranked 5th with a diabetes prevalence rate of 10.6% of the population (IDF, 2021). Type 2 DM is a chronic disease characterized by increased blood sugar levels in the body due to insulin resistance or inadequate insulin production. Due to high glucose levels in diabetes, it can cause damage to tissues and organs such as the brain, eyes, feet, kidneys, heart and vascular system (Hartanti & Budipramana, 2020).The main characteristics of DM that can trigger complications are hyperglycemia and hyperlipidemia. Hyperglycemia and hyperlipidemia are responsible for the development of diabetes and its complications such as atherosclerosis, hepatotoxicity, and nephrotoxicity. Therefore, it takes effort controlling blood sugar levels to delay the development of complications in diabetes mellitus patients (Sun et al., 2021).

The number of cases and deaths due to diabetes and its complications increases from year to year. Thus there must be an effort to control glucose levels. One of the efforts made to treat diabetes is by using medicinal plants. A lot of research and drug development has been carried out, including the search for medicinal compounds from natural ingredients (Ruswanto et al., 2018). One of them is keji beling leaves (Strobhilantes crispa). Natural compounds from plants have the potential to become alternative new therapeutic agents for treating diabetes

and have fewer side effects. Lots of plants The drug has been studied for its antihyperlipidemic effects on diabetes activity mellitus and confirmed in animal models (Ojuade et al., 2021).

One of the plants that can used to treat diabetes mellitus is a keji beling plant (Strobhilantes crispa) especially on leaf part Ethanol extract of keji shard leaves (S. crispa) has antidiabetic activity in white rats (Rattus norvegicus) induced by alloxan (Palit, F et al., 2018). The results of the phytochemical test for keji beling leaf extract were positive contains active compounds flavonoids, alkaloids, saponins, triterpenoids, steroids and tanninsn (Natanael et al., 2017). Strobilanthes crispa is traditionally used medicinally in Malaysia and Indonesia as an antidiabetic, diuretic, or antilytic agents and laxatives to treat constipation (Ghasemzadeh, A et al., 2015).

This study aims to determine the effect of ethanol extract of keji beling (S. crispa) leaves on the blood glucose levels of streptozotocin-induced diabetic rats. Antidiabetic research on keji beling leaves (S. crispa) is important to provide scientific evidence regarding the use and development of keji beling leaves (S. crispa) as a diabetes medication. This research is different from other studies which used Alloxan as a diabetes inducer. In this study, Streptozotocin was used as a DM inducer. After treatment, information was obtained that keji beling (S. crispa) extract could reduce blood glucose levels in type 2 DM rats.

METHOD

Antidiabetic testing refers to a modified study (Ojuade et al., 2021). Diabetic rats were induced by intraperitoneal administration of streptozotocin (50 mg/kg BW) dissolved in 0.01 M citrate buffer pH 4.5. After 3 days, mice with severe hyperglycemia (fasting blood glucose = 200 mg/dL) were selected and used for research. Diabetic mice were randomly selected and divided into 6 groups (n=5) of animals. Group I was not treated or was a normal control. Group II as a negative control group, diabetic mice were given 5% Na-CMC. Group III positive control, diabetic rats were given glibenclamide at a dose of 0,09 mg/kg BW. Groups IV, V, and VI were diabetic rats who were given ethanol extract of keji beling leaves at doses of 150, 300, and 450 mg/kg rat body weight. Each group was given treatment for 14 days. Blood glucose levels were measured on days 0, 7 and 14. Blood glucose was monitored using a glucometer (Ojuade et al., 2021).

RESULTS AND DISCUSSION

The keji beling (Strobhilantes crispa) leaf samples used in this research were determined at the Phytochemical Pharmacognosy Laboratory, Faculty of Pharmacy, Indonesian Muslim University with number: 0027/C/UD-FF/UMI/IV/2023. Determination was carried out with the aim of finding out the correct identity of the sample studied, namely the keji beling plant (Strobhilantes crispa) (Hasnaeni, 2019). Keji beling (S.crispa) leaf extract was extracted using the maceration method and an extract yield of 3.3% was obtained.

Figure 1. Sample keji beling (Strobhilantes crispa)

In vivo testing was carried out on male Wistar mice aged 2 months. This research has received ethical approval from the Health Research Ethics Committee Dr. Moewardi Number: 1.757/VII/HREC/2024. Tests were carried out to determine the antidiabetic potential of keji beling leaf extract (S. crispa). In this test, it was discovered that the ability of keji beling (S. crispa) leaf extract to reduce glucose levels. During testing, experimental animals were given high fat diet (HFD). In table 1 you can see the results of measuring the body weight of mice during testing.

Table 1.The results of measuring the body weight of mice

Groups	Body Weight						
	H0	H7	H14	H21 Induced STZ	H24	H31	H39
N	181±1.58	189.2±1.92	197.6±1.82	205.2±1.92	209.8±2.39	218.2±2.39	225.8±2.77[a]
K-	180.6±3.36	188.2±4.09	212.2±3.11	234.6±4.22	226±5.34	217.8±5.97	208.8±5.26[b]
K+Gli	180±1.58	188±1.58	211.4±2.97	234.4±2.07	225.8±2.59	229.4±2.30	233.2±2.86[a,c]
P1	179.6±2.41	187±2.24	211±2.24	234.2±3.03	225.2±3.49	228±3.67	232.2±3.49[a,c]
P2	180.2±2.59	187.8±2.77	211.6±3.05	234±3.54	224.8±3.56	229±3.39	235.2±3.96[c]
P3	181.4±2.70	189.4±2.88	213±3.16	236.2±2.86	228.2±3.70	232.8±3.70	239±3.81[c]

The results of body weight measurements showed an increase in body weight in all treatment groups.

The results of measuring the average fasting blood sugar levels of mice are presented in table 2 and figure 2.

Table 2. The results of measuring the average glucose levels of mice

No	Groups	Levels glukosa		Mean decrease in fasting blood glucose levels
		Before STZ induction	After STZ induction	
1	Normal	66,91	67,62	68.76±0.85
2	Kontrol (-)	264,39	266,9	268.11±1.30
3	Kontrol (+)	269,78	110,32	105.77±3.07
4	P I	273,74	131,67	128.54±1.97
5	P II	266,55	102,85	100.00±2.09
6	P III	278,42	95,02	93.52±2.14

Table description :
1. Normal group
2. HFD DM
3. HFD DM → Glibenclamid 0,09 mg / 200 gr
4. HFD DM → Exstract 150 mg / Kg
5. HFD DM → Exstract 300 mg / Kg
6. HFD DM → Exstract 450 mg / Kg

The highest average blood glucose levels of mice measured 3 days after STZ induction were in the control group administered dose III (450 mg/kg) with a level of 278.42. mg/dL, treatment group dose I (150 mg/kg) with a glucose level of 273.74 mg/dL, treatment group dose II (300 mg/kg) with a glucose level of 266.55 mg/dL, control group worth 269 .78 mg/dL and the negative control group was 264.39 mg/dL.

However, after 14 days of treatment with the drug and extract, the mice's blood glucose levels decreased as can be seen in Figure 2.

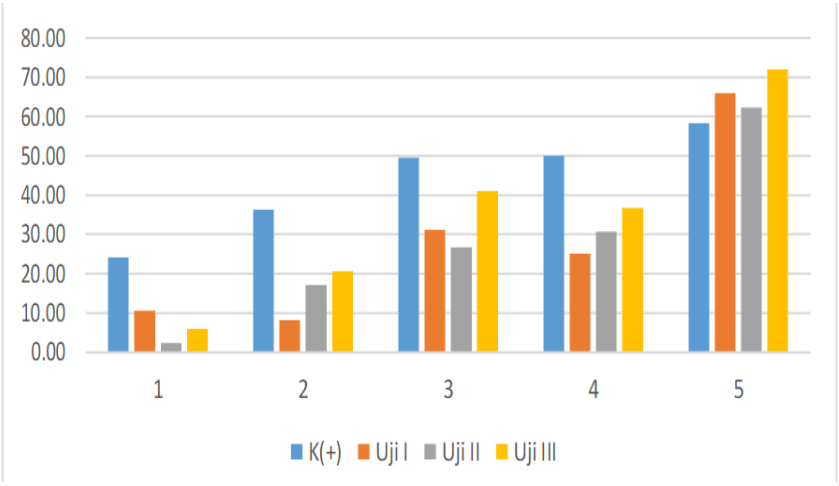

Figure 2. Percentage Decrease in Fasting blood glucose levels

Figure 2 shows a graph of the percentage decrease in fasting blood glucose levels. The average decrease in blood glucose levels in mice in the extract group dose II and dose III showed a decrease in blood glucose levels that were close to the blood glucose levels in the positive control group, namely the group given the drug glibenclamide at a dose of 0.09 mg/200 g.

The average decrease in fasting blood glucose levels of mice in the negative control group was 268.11 ± 1.30 mg/dL, the positive control group was 105.77 ± 3.07 mg/dL, the dose I treatment group was 128.54 ± 1.97 mg/dL, the dose II treatment group was 128.54 ± 1.97 mg/dL. 100.00 ± 2.09 mg/dL, and the dose III treatment group was 93.52 ± 2.14 mg/dL, while the Normal group had blood glucose levels at the beginning and after the end of the measurement, namely 68.76 ± 0.85 mg/dL.

Measurement of initial glucose levels, namely 3 days after STZ induction, showed that all treatment groups and positive and negative control groups showed glucose levels that were above normal, Monitoring glucose levels normal mice, namely 70-90 mg/dL and mice. It is said to be diabetes when the rat's blood glucose level exceeds 115 mg/dL (Panjuatiningrum et al. 2009). Based on the observation results, it can be seen that the decrease in fasting blood glucose levels in the extract group at a dose of 300 mg/kg BW and a dose of 450 mg/kg BW exceeded the average blood glucose levels in the control group given the drug glibenclamide. This shows that keji beling (S. crispa) has the effect of lowering blood glucose levels in test animals. This research is different from other studies which used Alloxan as a diabetes inducer (Palit, F et al., 2018). In this study, Streptozotocin was used as a DM inducer. After treatment, information was obtained that keji beling (S. crispa) extract could reduce blood glucose levels in type 2 DM rats.

CONCLUSION

Research provides information about the antidiabetic potential of keji beling (S. crispa)leaves due to its ability to reduce blood glucose levels in mice with type 2 DM.

RECOMMENDATIONS

It is important to carry out further research to find out more in-depth effects regarding the antidiabetic potential of Keji Beling leaf extract (S. crispa). The effects and potential use of Keji Beling leaves in the treatment of diabetes mellitus.

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