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The Effect of Cinnamon Bark Extract (*Cinnamomum burmannii*) on Blood Glucose Levels in Hyperglycemic Rats

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ABSTRACT

Diabetes mellitus is a disease in the form of a metabolic disorder characterized by blood sugar levels that exceed normal limits. In diabetes, there is an increase in blood sugar (hyperglycemia) which occurs due to abnormalities in insulin secretion by the pancreas. The cinnamon bark plant (*Cinnamomum burmannii*) is one of the plants that contains antidiabetics. The aim of this research is to determine the effect of cinnamon bark extract on the blood glucose levels of hyperglycemic rats. This research is an experimental research with a Post Test-Only Control Group design using 30 rats divided into five groups, namely K(-) distilled water, K(+) Alloxan induction, then continued administration of cinnamon bark extract (*Cinnamomum burmannii*) P1 (Dose 100 mg/kgBW), P2 (Dose 200 mg/kgBW) and P3 (Dose 300 mg/kgBW) for 30 days. Checking blood glucose levels using the enzymatic glucose method. The results showed that cinnamon bark extract (*Cinnamomum burmannii*) had an effect on reducing blood glucose levels ($p<0.05$).

Keywords: Hyperglycemic, Cinnamon Bark Extract, Antidiabetic

INTRODUCTION

Diabetes mellitus is a disease in the form of a metabolic disorder characterized by blood sugar levels that exceed normal limits. In diabetes, there is an increase in blood sugar (hyperglycemia) which occurs due to abnormalities in insulin secretion by the pancreas [(1)]. Diabetes is a chronic disease that occurs due to the pancreas being unable to secrete enough insulin hormones or the body being unable to effectively use the insulin hormone it produces. The normal level of fasting blood glucose in serum is 110-126 mg/dL [(2)]. The prevalence of type 1 diabetes mellitus sufferers in Indonesia in 2022 will reach 41.8 thousand people. Indonesia is the country with the most type 1 diabetes sufferers in ASEAN and is ranked 34th out of 204 countries on a global scale [(3)]. One of the factors that influences the high prevalence of type 1 diabetes mellitus cases is age. The majority of people with type 1 diabetes mellitus are in the age range 29-69 years with 26,781 cases. Meanwhile, there were 13,311 sufferers under the age of 20 years and 1,721 people aged 60 years and over [(3)].

Type 1 diabetes mellitus is an autoimmune disease that involves the destruction of pancreatic β cells to produce insulin. As a result, the pancreatic glands are unable to produce insulin [(4)]. Type 1 diabetes mellitus sufferers experience insulin deficiency so they require additional insulin from outside at all times to regulate the supply and glucose levels in the blood so that they remain stable[(5)]. The incidence of type 1 diabetes mellitus, which is characterized by

destruction of pancreatic β cells, is caused by genetic and environmental factors. Genetic factors, namely the occurrence of mutations and activation of the HLA-DQ8, HLA-DRB1*04:01 and HLA-DRB1*04:05 haplotypes in HLA (Human Leukocyte Antigen) class II which is at risk of developing autoimmunity against pancreatic beta cells. This type of haplotype is often associated with triggering autoantibodies to insulin and is susceptible to type 1 diabetes mellitus[(6)]. Then, environmental factors that trigger type 1 diabetes mellitus, namely, infection by viruses (DNA viruses from the Herpesviridae and Parvoviridae families and RNA viruses from the Togaviridae, Paramyxoviridae, Retroviridae, and Picornaviridae families), vitamin D deficiency, nutrition during infancy, and oxidative stress[(7)]. Type 1 diabetes mellitus is called juvenile-onset diabetes because this type of DM usually occurs before the age of 25 years and is characterized by an increase in blood glucose levels[(3)].

The condition of hyperglycemia occurs when the glucose level in plasma is ≥7.0 mmol/L (126mg/dL), with a glucose level of 110-126 mg/dL (6.1 to 7.0 mmol/L) is said to be a condition of glucose tolerance[(8)]. Treating diabetes sufferers using antidiabetic pharmacological drugs has side effects. Antidiabetic drugs (metmorphine) have side effects, namely nausea, dizziness, tremors and hypoglycemia[(9)]. Pharmacological therapy for type 1 diabetes mellitus using antihyperglycemic drugs such as pramlintide has the side effects of anorexia, nausea, vomiting and headaches. If pramlintide is given together with insulin, it will cause hypoglycemia. Apart from that, antihyperglycemia drugs such as incretin mimetic drugs such as liraglutide also have side effects such as nausea, appetite suppression, abdominal distension and dyspepsia[(10)].

To avoid the side effects of using drugs that come from pharmacology, you can use one of the herbal plants which has the potential to act as an anti-diabetic and antioxidant. One of the herbal plants that contains antidiabetic and antioxidant substances is cinnamon (*Cinnamomum burmannii*). Cinnamon bark extract contains antidiabetic substances in the skin so it can reduce blood sugar levels in hyperglycemic mice[(11)]. The main bioactive compounds contained in cinnamon bark (Cinnamomum zeylanicum) are Methylhidroxy Calcone Polymer (MHCP), cinnamaldehyde, and procyanidin type-A polymers or proanthocyanidin which have antidiabetic capabilities by reducing blood sugar levels, inhibiting the activity of the α-glucosidase enzyme. , and activates glycogen synthesis, increases glucose uptake, activates insulin receptor kinase and inhibits insulin receptor dephosphorylation [(12)]. Based on this, researchers are interested in examining the effect of cinnamon bark extract (*Cinnamomum burmannii*) on blood glucose levels. The use of cinnamon bark (*Cinnamomum burmannii*) in this research is hoped to make cinnamon bark a preventative for diabetes.

MATERIALS & METHODS

Materials

Alloxan (Sigma-Aldrich); 96% ethanol (Merck); Sterilized water dor injection (Otsu-WI); Aquades (Aquabidest); 70% alcohol; Betadine; Glucose Strips (Autocheck); Glucometer (Glukocheck); Handschoen; Cinnamon bark ethanol extract. Rat (*Rattus novergicus*)

Method

This research is an experimental laboratory research using the Post Test-Only Control Group design which uses experimental animals, namely male Wistar rats as research objects. The research sample was 40 rat which were then divided into 5 experimental groups, namely, negative control group (K-), positive control group (K+) alloxan induction, treatment group (P1) dose of 100 mg/kg BW, treatment group (P2) dose 200 mg/kgBW, treatment group (P3) dose 300 mg/kgBW.

a. Alloxan Induction

The induction process for experimental animals male rat (*Rattus novergicus*) will begin by restricting food for 30 hours before injection. The rats were not given food; however, they were only given water to drink. After the fasting period, the rat will be manually restrained and receive an intraperitoneal injection of 100 mg/kgBW alloxan in the rat's lower right abdomen properly. Next, the rats were placed back in their cages with water and commercial food ad libitum [(13)].

b. Making cinnamon bark extract
Cinnamon bark extra is made using the maceration method with a mixture of 96% ethanol. A total of 1000 g of cinnamon bark (*Cinnamomum burmannii*) is soaked in 96% ethanol with a volume of 1000 ml for 72 hours until it settles. Maceration will be carried out for 3 days in a shaded room and dark container protected from direct sunlight and then stirred periodically. The soaking product or macerate is put into an evaporation flask. The extraction results are put into a glass bottle and the extract results are stored in a refrigerator or freezer [(14)].

c. Phytochemical Test of Cinnamon Bark Extract (*Cinnamomum burmannii*)
The phytochemical test of cinnamon bark extract was carried out using qualitative analysis with the aim of maintaining the stability of the existing compounds contained in cinnamon bark extract. The chemical components that will be evaluated from cinnamon bark extract are the alkaloid test, phenol, terpenoid and flavonoid tests using Dragendorff's reagent, FeCl3 and vanillin sulfuric acid respectively[(15)].
d. Examination of Blood Glucose Levels
Checking blood glucose levels using the enzymatic glucose method. The rats were placed in the place provided. The tip of the rat's tail was cleaned using 70% alcohol, then cut slightly. The blood glucose strip on the device is attached to the blood until the empty space on the strip is filled. Then wait a moment and numbers will appear on the glucometer monitor screen.

STATISTICAL ANALYSIS

Data were analyzed with the SPPS-20 program. For data that is numerical and categorical, the Shapiro Wilks test will be used to determine the normality of the data as a condition for using One-Way ANOVA.

RESULT

a. Phytochemical test of cinnamon bark extract (*Cinnamomum burmannii*)
Test analysis of secondary metabolite compounds contained in the ethanol extract of cinnamon bark (*Cinnamomum burmannii*). Analysis was carried out qualitatively to determine the interpretation of the presence of chemical components in the form of flavonoids, phenolics, saponins, triterpenoids, steroids and alkaloids in the ethanol extract of cinnamon bark (*Cinnamomum burmannii*). In the phytochemical test of cinnamon bark extract, the following results were obtained.

Table 1. Content of secondary metabolite compounds in cinnamon bark extract (*Cinnamomum burmannii*).

Extract	Bioactive Compounds	Description	Observation result
Cinnamon Bark Extract (*Cinnamomum burmannii*)	Flavonoids	+	Orange
	Phenolic	+	Blackish blue
	Saponin	+	There is foamy
	Triterpenoid	+	there is a red ring
	Steroids	+	there is a green ring
	Alkaloid	+	there is a white precipitate

+: This compound is contained in the sample

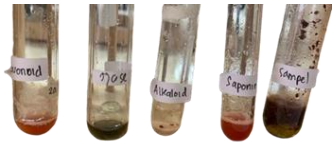

Figure 1. Flavonoids; Phenolic; Alkaloid; Saponin; control

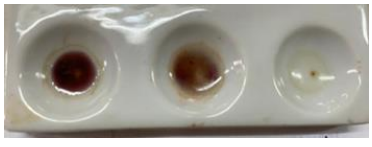

Figure 2. Steroid; Triterpenoid; control

b. Rat Blood Glucose Levels in All Groups

In the research group, blood glucose levels were measured with the aim of seeing the effect of cinnamon bark extract on blood glucose levels. The results of measuring blood glucose levels were subjected to statistical analysis using One-Way Anova

Table 2. Results of measuring blood glucose levels (mg/dL) for all Group.

Groups	n	$\bar{x}$ ± SD (mg/dL)	p *Value*
Negative Control (Aquades)	6	93.83 ± 8.24	<0.001
Positive Control (alloxan)	6	512.67 ± 102.34	
P1 (Dose 100 mg/kgBW)	6	221.67 ± 62.65	
P2 (Dose 200 mg/kgBW)	6	421.50 ± 56.49	
P3 (Dose 300 mg/kgBW)	6	557.17 ± 24.87	

Based on table 2, it can be seen that the positive control group animals induced by alloxan experienced an increase in the average blood glucose level, namely 512.67 ± 102.34 (mg/dL). The treatment group given cinnamon bark extract experienced a decrease in the average blood glucose levels in groups P1 (100 mg/KgBW) and P2 (200 mg/KgBW) compared to the positive control group (K+). However, the average blood glucose level increased again in the P3 group which was the highest dose (300 mg/KgBW). Based on the results of statistical analysis, cinnamon bark extract had a significant effect on the blood glucose levels of hyperglycemic rats ($p<0.05$).

DISCUSSION

Examination of the blood glucose levels of rat was carried out to see the effect of cinnamon bark extract on rat with hyperglycemia. Blood glucose levels were checked on day 31 using the glucose-oxidase method. Blood was taken from the rat's tail which was cut using sterilized scissors. Based on the results of examination of blood glucose levels, it shows that cinnamon bark extract can act as an antidiabetic agent due to a decrease in the average blood glucose level in alloxan-induced hyperglycemic rat. A decrease in the average blood glucose level occurred in treatment groups I and II who were given cinnamon bark extract (*Cinnamomum burmannii*) at a dose of 100 mg/KgBW and 200 mg/KgBW. However, in treatment group III with a dose of 300 mg/kgBB there was an increase in blood glucose levels. The best average reduction in blood glucose levels occurred in dose group I compared to dose group II.

The average decrease in blood glucose levels occurred in the group of rat that were given cinnamon bark extract orally. Based on the results of phytochemical tests carried out in the Organic Natural Chemistry Laboratory, Andalas University, it was proven that cinnamon bark contains chemical components in the form of flavonoids, phenolics, saponins, triterpenoids, steroids and alkaloids. This is reinforced by the opinion of Astuti[(16)] et al., that cinnamon bark contains antidiabetic substances which come from the flavonoid group such as cinnamaldehyde and MHCP (Methyl hydroxyl chalcone polymerase).

The flavonoid group MHCP compounds, according to research by Hoehn and Stockert[(17)], have the ability to reduce blood glucose levels by functioning as molecular mimics, thereby triggering insulin receptor activation. This is in accordance with the opinion of Emilda [(12)], who states that the Methylhidroxy Calcone Polymer (MHCP) compound has an insulin-like effect. MHCP is able to activate insulin receptor kinase, inhibit insulin receptor dephosphorylation, activate glycogen synthesis and increase glucose uptake. Based on research by Kubota[(18))] et al, insulin receptors are expressed on liver cell membranes, because the liver is able to promote glucose storage into glycogen and reduce glucose output.

This is in accordance with the opinion of Singh[(19)] et al, that the insulin receptor is also expressed on the membranes of skeletal muscle cells, adipocytes and cardiomyocytes because it is able to

stimulate glucose transport through GLUT 4 translocation. GLUT-4 is responsible for glucose uptake. stimulated by insulin into muscle and adipose cells. About 80% of glucose is transported to muscle cells. The GLUT4 glucose transport system can be regulated to maintain blood glucose homeostasis in cells[(20)]. The MHCP compound contained in cinnamon bark extract has anti-diabetic potential by molecularly mimicking insulin, so it can increase the sensitivity of insulin receptors and maintain blood glucose levels within the normal range.

Cinnamon bark also contains cinnamaldehyde and procyanidin type-A polymers or proanthocyanidin which have antidiabetic activity. Based on research conducted by Purbowatingrum [(21)]et al, cinnamaldehyde was able to reduce blood glucose levels by 63.29% in streptozotocin-induced diabetic rats. This is in line with the opinion of P, Nor Basid A[(22)], stating that cinnamaldehyde contained in cinnamon bark extract has an antidiabetic mechanism by inhibiting the work of the α-glucosidase enzyme to break down carbohydrates into glucose. So, blood glucose levels can be controlled. In the results of our research, in the dose I and dose II groups, there was a decrease in the average blood glucose levels compared to the positive control group, namely rats induced by alloxan.

Our research results also found that in treatment group 3 with a dose of 300 mg/KgBW there was an increase in the average blood glucose level, namely 557.17 ± 24.87. Based on research conducted by Djadjat Tisnadjaja[(23)], stated that in high doses cinnamon bark extract has hepatotoxic side effects. This can trigger liver damage. This is in accordance with the opinion of Pitaro[(24)] et al, stating that cinnamon bark contains coumarin compounds which if consumed excessively can be toxic and damage the liver. Based on research by Fotland[(25)] et al, stated that cinnamon bark is safe for human consumption with a maximum consumption tolerance value of 5 mg/Kg of food. In addition, the increase in blood glucose levels at high doses suggests that cinnamon bark extract has a high concentration of antioxidants. This is in accordance with the opinion of Tyuryaeva & Lyublinskaya[(26)], which states that antioxidants in high concentrations can have biphasic properties which are able to stimulate and inhibit cellular activity so that they become toxic.

CONCLUSION

Based on research that has been conducted, cinnamon bark extract (*Cinnamomum burmannii*) has an effect on blood glucose levels. The best reduction in blood glucose levels is at a low dose, namely 100mg/kgBW.

Declaration by Authors

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