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The Effect of Cinnamon Bark Extract *(Cinnamomum burmanii)* on Blood Malondialdehyde (MDA) Levels in Hyperglycemia Rats

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ABSTRACT

Hyperglycemia is a condition where blood glucose levels increase beyond normal limits. Hyperglycemia can induce oxidative stress conditions caused by an increase in free radicals and a reduction in endogenous antioxidant defenses, characterized by an increase in blood malondialdehyde levels. Oxidative stress causes malondialdehyde levels to increase and endogenous antioxidants to decrease, therefore the body needs exogenous antioxidants. One plant that is rich in antioxidants is cinnamon bark, where cinnamon bark can increase antioxidant capacity. This study aims to examine the effect of cinnamon bark extract (Cinnamomum burmanii) on reducing blood malondialdehyde levels in hyperglycemic rats. This research is experimental research using the Post Test-Only Control Group design. Male Wistar rats were divided into 5 groups (n=6), negative control (K-), positive control (K+), P1 (dose 100 mg/kgBW), P2 (dose 200 mg/kgBW), P3 (dose 300 mg/kgBW). The normality test was carried out using the Shapiro-Wilk test followed by One Way Anova and Kruskal Wallis. The results showed that cinnamon bark (Cinnamomum burmanii) was proven to be able to reduce blood malondialdehyde levels, where the optimal dose was P1 (dose 100mg/kgBW) whereas in the P1 group, the average malondialdehyde levels were found to be the lowest compared to other treatment groups.

Keywords: Hyperglycemia; cinnamon bark; malondialdehyde; oxidative stress

INTRODUCTION

Diabetes mellitus (DM) is a chronic disease that occurs due to the pancreas not producing enough insulin or the body being unable to use the insulin produced effectively(1) . diabetes mellitus is a chronic disease characterized by metabolic disorders resulting in increased blood glucose levels. The incidence of diabetes mellitus in the world has reached 537 million people, aged 20 - 79 years. The probability of death due to diabetes mellitus statistically reaches 6.7 million people or one person every five seconds. The increase in prevalence is due to changes in lifestyle starting with diet. Type of food consumed and lack of physical activity, obesity, hypertension, and genetic factors (2).

Indonesia is ranked 7th in the world with the most diabetes mellitus sufferers out of 10 countries, after China, India, the United States, Pakistan, Brazil, and Mexico, reaching 10.7 million people who suffer from diabetes mellitus (2). Diabetes mellitus is generally divided into two types, namely Type 1 DM and Type 2 DM (3). Type 1 DM

is an autoimmune disease that can damage pancreatic beta cells, causing insulin deficiency. If there is no insulin hormone, glucose cannot be taken up by the tissues so glucose levels in the blood increase, this condition is called hyperglycemia(4).

Hyperglycemia can induce oxidative stress. Oxidative stress occurs due to an increase in free radicals or reduced antioxidant defence activity, this condition is often known as reactive oxygen species (ROS) and reactive nitrogen species (RNS). Oxidative stress is a condition where there is an imbalance between oxidants (free radicals) and antioxidants in the body. So it can cause cell damage(5). Oxidative stress can be indicated by MDA levels in serum and tissue(6). MDA levels are formed from conditions of increased ROS in the body which causes lipid peroxidation in cell membranes, namely in free radical reactions with polyunsaturated acids (PUFA). If there is an increase in MDA levels, this will indicate a process of lipid peroxidation and oxidative stress(7).

Tissue damage resulting from hyperglycemia is caused by four ROS mechanisms, namely activation of protein kinase C (PKC), increase in the hexosamine pathway, increase in glycation end products (AGE), and increase in the polyol pathway(3). Oxidative stress in diabetes mellitus sufferers can be determined by measuring markers of oxidative stress, namely MDA levels in serum or blood plasma. MDA levels are one of the end products of lipid damage in the polyunsaturated acid (PUFA) group in cell membranes. Oxidative stress conditions will cause damage to various body cell components such as proteins, lipids, and Deoxyribonucleic Acid (DNA)(7).

The body has natural endogenous antioxidants in the body such as superoxide dismutase (SOD), catalase, and glutathione peroxidase (GPx) which will reduce free radicals naturally in the body. If free radicals continue to increase in the body, it can cause a decrease in antioxidant enzyme activity(8). High levels of reactive oxygen species trigger oxidative stress conditions so that natural antioxidants in the body decrease because they require antioxidants that come from outside the body (exogenous antioxidants). One example of exogenous antioxidants is those from fruits, vegetables, spices, and herbal plants(9). Indonesia is a country rich in spices. This spice can be used as a natural exogenous antioxidant to reduce free radicals in the body. One of the spices that is widely available in Indonesia is cinnamon bark.

Cinnamon bark is rich in antioxidants and other compounds, namely compounds such as eugenol, safrole, cinnamaldehyde, and tannin. Cinnamon bark extract can produce 68.65% metaldehyde compounds as a source of antioxidants to ward off free radicals. The cinnamaldehyde compound is included in the phenylpropanoid group, which is a phenol derivative compound that plays an important role in antioxidant activity(10). Based on this, researchers are interested in examining the effect of cinnamon bark extract (Cinnamomum burmannii) on blood Malondialdehyde 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; 96% ethanol; Sterilized water dor injection; Aquades (Aquabidest); 70% alcohol; Handschoen; blood; TBA Reagent; TCA 5% Reagent; MDA standards; Cinnamon bark ethanol extract; Rat (Rattus norvegicus)

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 alloxan induction process in white mice begins with food restriction for 30 hours before injection. The mice were not given food but only given water. After the fasting period is complete, the rat will be manually restrained and receive an intraperitoneal injection of 100 mg/kg BW alloxan in the lower right abdomen(11). Next, the mice were placed back in their cages and given standard food and water. After 7 days, the mice that were induced with alloxan had their blood glucose levels checked to determine the hyperglycemic effect before being given treatment.

b. Making cinnamon bark extract

Cinnamon bark extract is made using the maceration method with a mixture of 96% ethanol. The cinnamon bark is first dried and ground, then 1,000 g of cinnamon bark powder is soaked in 96% ethanol with a volume of 1,000 ml for 72 hours at room temperature until it settles. After three days the soaking results were put into an evaporation flask. The evaporation flask is installed on the evaporator and fill the water bath with water until it is full. All series of equipment are installed including the rotary evaporator, water bath heater (set to a temperature of 60°C), connected to electricity. Then wait until the ethanol solution separates from the active substance that is already in the evaporation flask, then leave it until the ethanol flow stops dripping into the collection flask (± 1.5 to 2 hours for one flask). The extraction results are put into a glass bottle and stored in the refrigerator or freezer (12).

c. examination of blood malondialdehyde levels

Malondialdehyde levels were measured using the colorimeter method by measuring the TBA (thiobarbituric acid) reaction. This method is easy to carry out and obtain and has quite high accuracy and precision, and the reagents used are relatively cheap. Procedure for checking malondialdehyde levels: Put 500 ul of serum into a test tube using a micropipette; Add 2.5 ml TCA 5%; Then homogenize using a vortex mixer; Then centrifuged at a speed of 10,000 rpm for 15 minutes; Pipette 1 ml of filtrate; Add 1 ml of TBA reagent; Incubate in a water bath for 30 minutes at 100 °C; chill; Then the MDA levels were measured using a spectrophotometer with a wavelength of 530 nm.

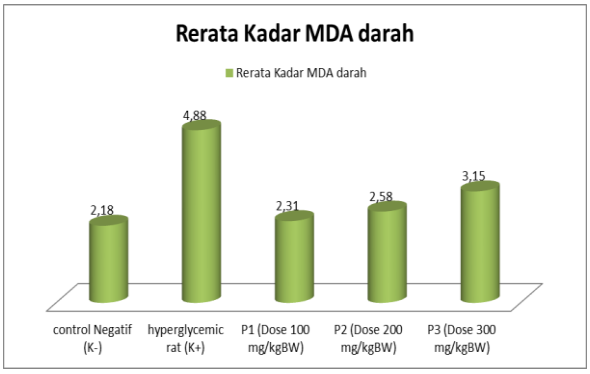
STATISTICAL ANALYSIS

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

Effect of Cinnamon Bark Extract (Cinnamomum burmanii) on Blood Malondialdehyde (MDA) Levels

The results of measuring MDA levels in hyperglycemic rats given cinnamon bark extract (Cinnamomum burmanii) can be seen in the following bar diagram.



Based on the diagram above, it can be seen that the average blood MDA level given cinnamon bark extract was the lowest in treatment group 1 (dose 100 mg/kgBW),

namely 2.31 (0.18) nmol/ml compared to treatment group 2 (dose 200 mg /KgBW) and treatment 3 (Dose 300 mg/KgBW). The results of statistical tests can be said that there is an influence of cinnamon bark extract on blood levels of malondialdehyde (MDA) ($p<0.05$).

Next, a follow-up test was carried out to find out at what dose the effect began to be meaningful or significant (Bonferroni Post-Hoct test).

Bonferroni Post-Hoc Test Results on the Effect of Cinnamon Bark Extract on Blood Malondialdehyde Levels nmol/ml.

	Group	**Group**	**p*Value***
MDA Level	Control (+)	P1(Dose 100mg/kgBW)	0,000
		P2(Dose 200mg/kgBW)	0,000
		P3(Dose 300mg/kgBW)	0,000

Based on the table above, there was a significant difference between the hyperglycemia group (control+) and the group given cinnamon bark extract at graded doses.

DISCUSSION

The results of this study showed that there were significant differences in blood MDA levels between the five groups of rats using the one-way ANOVA test ($P < 0.05$). The results of the research showed that blood MDA levels in hyperglycemic rats in the positive control group of mice showed an increase in the average blood MDA level, namely 4.88 nmol/ml, where in this group the highest MDA levels were obtained among the 5 treatment groups. The positive control group of rats was induced with alloxan intraperitoneally at a dose of 100 mg/kgBW. The increase in MDA levels in the positive control group was caused by the administration of alloxan which caused damage to pancreatic beta cells so that insulin secretion decreased as a result of which hyperglycemia occurred[(13)]. Hyperglycemia causes an increase in ROS resulting in an imbalance between oxidants and antioxidants or oxidative stress conditions[(14)]. Oxidative stress conditions trigger lipid peroxidation in cell membranes which is characterized by an increase in MDA levels[(7)].

The group of mice given cinnamon bark extract at a dose of 100 mg/kgBW (P1) obtained a mean blood MDA level of 2.31 nmol/ml, a decrease compared to the positive control group and was the lowest MDA level of all treatment groups. The group given cinnamon bark extract at a dose of 200 mg/kgBW (P2) obtained a mean MDA level of 2.58 nmol/ml where the MDA level was higher than in the P1 group but lower than in the K(+) group. The group given cinnamon bark extract at a dose of 300 mg/kgBW (P3) obtained a mean MDA level of 3.15 nmol/ml which was higher than the P2 group and still lower than the positive control group (K+).

Cinnamon bark contains several antioxidants such as polyphenols, flavonoids, vitamins A, B, C, and E as well as proanthocyanidins which are able to neutralize the lipid peroxidation process by reducing free radicals due to increased ROS so that MDA levels decrease [(15)]. The antioxidants contained in cinnamon bark work to protect cells from oxidative damage caused by an increase in free radicals. These results are in line with previous research where there was a decrease in serum MDA levels in mice given cinnamon bark extract [(16)]. The mechanism for reducing blood MDA levels in the group given cinnamon bark extract involves the ability of antioxidants to counter the oxidative effects that cause MDA production. Antioxidants work by inhibiting oxidant enzymes (NOS, NOX, COX, MPO) resulting in a decrease

in ROS, interacting with redox signaling pathways resulting in the activation of nuclear factor E2 – related factor 2 (NRF-2), and inhibiting NF-KB which will activate the response antioxidant enzymes (CAT, SOD, GPX) in preventing oxidative damage. Then by reacting directly with ROS/RNS to form less reactive compounds [(17)].

MDA levels in treatment group 3 (dose 300 mg/kgBW) were higher compared to treatment groups 1 (dose 100 mg/kgBW) and 2 (dose 200 mg/kgBW) this was because the higher dose of cinnamon bark extract could provide toxic effects. The toxic compound in cinnamon bark is the compound coumarin, and the liver is the main target organ for coumarin. Coumarin first enters the blood vessels and then circulates throughout the body. When the blood passes through the organs, the coumarin diffuses into the organs, and most of the blood enters the liver, causing hepatotoxicity in the liver[(18)]. The liver has an important role in blood glucose regulation, in addition to its important role in energy storage, namely glycogen and triglycerides. Hepatotoxic conditions cause glucose to not be stored in the liver so that blood glucose levels are high in the blood and hyperglycemia remains[(19)]. Hyperglycemia conditions trigger an increase in ROS in the body and lipid peroxidation occurs, characterized by high MDA levels, therefore MDA levels at high doses are still high compared to the administration of cinnamon bark extract at low doses [(20)].

CONCLUSION

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

Declaration by Authors

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