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Antihyperglycemic Activity of Ethanol Extract of Robusta Coffee Beans (Coffea canephora) in Mice Induced by Streptozotocin-Nicotinamide

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A B S T R A C T

Diabetes mellitus is a disease that occurs due to damage to pancreatic beta cells, which cells that are responsible for producing the hormone insulin greatly affects the metabolism of glucose in the body. Coffee robusta beans are known to have chlorogenic acid, which is a derivative of a class of flavonoid compounds which have antioxidant activity that can be used as an antihyperglycemic. to find out whether robusta coffee beans have antihyperglycemic activity. The study was conducted using the antihyperglycemic method in mice induced by streptozotocin-nicotinamide. The streptozotocy-nicotinamide-induced mice were divided into 4 categories consisting of 3 male mice each, group 1 (negative control) was only given CMC 1%, category 2 (positive control) was given glibenclamide 0.65 mg/kg, category 3 was given an ethanol extract of coffee robusta beans 200 mg/kg, category 4 they were given ethanol extract of coffee robusta beans 400 mg/kg. Blood glucose was measured on days 7, 14 and 21 after induction. The results obtained from the Robusta coffee bean extract at a dose of 200mg/kg and 400mg/kg has activity in reducing blood glucose levels in male mice that have been induced by STZ-Na.

INTRODUCTION

Diabetes mellitus is a disease that occurs due to damage to pancreatic beta cells, a group of cells responsible for producing a group of cells that produce the hormone insulin, which greatly influences glucose metabolism in the body and functions as a reducer of glucose levels in the blood (Suarsana et al. 2012). The insulin hormone experiences impaired insulin secretion in beta Langerhans cells or reduced insulin sensitivity to receptors or both, resulting in hyperglycemia accompanied by impaired carbohydrate, fat, and protein metabolites that can cause DM and its complications (Dipiro, 2015). Hyperglycemia is indicated by blood glucose levels above 126 mg/dL in fasting conditions and blood glucose levels 2 hours after eating that are above 200 mg/dL. If blood pressure has reached the limit, it can cause hyperglycemia (American Association of Diabetes, 2021). One plant that can be used is robusta coffee beans (Coffea canephora), which have antioxidant content derived from high chlorogenic acid compounds and can be used to reduce type 2 DM (Lin et al., 2011).

Coffee plants have many benefits. One part of the coffee plant that can be used is the Robusta coffee bean. It is known to contain flavonoids, alkaloids, tannins, and saponins, which have health benefits (Patay et al., 2016). Chlorogenic acid is a derivative of the flavonoid group of compounds, which are themselves polyphenols. Chlorogenic acid, found in coffee beans, accounts for 90% of the total phenols in coffee beans (Yusmarini 2013). Chlorogenic acid has strong antioxidant activity, thus having an antihyperglycemic effect.

LITERATURE REVIEW

Several studies have reported that Robusta coffee beans can lower blood glucose levels at a dose of 200mg/kgBW in mice induced by glucose, and that coffee infusion can lower blood sugar levels in mice induced by streptozotocin.

Coffee is a very popular beverage, but it is still rarely used as a treatment. Therefore, researchers wanted to determine its effectiveness in lowering blood glucose levels in mice induced by streptozotocin-nicotinamide.

METHODOLOGY

Tools and materials

The materials used in this study were robusta green coffee beans, ethanol 70% glibenclamide, CMC Na%, tools used in the oven, rotary evaporator.

Research Methology

Robusta Coffee Bean Extraction

Robusta coffee (Coffea canephora) bean samples were extracted using the maceration method, using ethanol as a solvent. The resulting ethanol extract was collected and evaporated using a vacuum rotary evaporator to obtain a thick Robusta coffee bean extract. This was then evaporated in an oven at 50°C to obtain a ready-to-use ethanol extract of Robusta coffee beans.

Animal Treatment

The test animals used were 12 healthy male mice (Mus musculus) weighing approximately 15-25 g, divided into four groups of three animals each. The test animals were fasted for ± 10 hours then their fasting blood glucose levels were measured as the initial glucose levels (T0) then all test animals were induced

with streptozotocin-nicotinamide with a dose of streptozotocin 5.6 mg/kg BW of mice and nicotinamide 15.4 mg/kg BW of mice intraperitoneally then on the third day the blood sugar levels of the test animals were checked (T1). All groups were induced then after the mice experienced an increase in blood glucose levels >200 mg/dL in the negative control group (K-1) only given 1% cmc solution, the positive group (K-2) given glibenclamide 0.65 mg/kg BW, in group 3 given ethanol extract of Robusta coffee beans 200mg/kg BW, and in group 4 given ethanol extract of Robusta coffee beans at a dose of 400mg/kg BW. Then blood glucose measurements were carried out through the animal's tail. Measurement tests were carried out on the 7th, 14th and 21st days after drug administration. Data on the decrease in blood glucose and the percentage decrease in blood glucose levels were processed statistically using the ANOVA method.

RESULTS AND DISCUSSION

Diabetes is a chronic disease that occurs when the pancreas is no longer able to produce insulin according to the body's needs. Blood glucose levels are considered elevated when they exceed 200 mg/dL (Ministry of Health, 2020) . The data obtained shows that at T0, all groups of test animals remained in normal condition and did not experience an increase in blood glucose levels. This is because the test animals had not been induced.

This study used robusta coffee bean samples (*Coffea canephora*) and measurements were taken on the test animals before and after induction. A study conducted by Szkudelski (2001) found that STZ at a dose of 40-60 mg/kg body weight, administered intravenously or intraperitorially, can induce diabetes mellitus in test mice.

Measurements were taken on the 3rd day after induction (T1) all groups of test animals experienced an increase in blood glucose levels, then the test animals in the K- group were only given 1% CMC so that at T2, T3 and T4 there was no decrease, in the K+ group, the 200 mg/kg BW coffee bean extract group and the 400 mg/kg BW coffee bean extract group experienced a decrease at T2, T3, and T4. The decrease in blood glucose levels of mice can be seen in Table 1.

However, in the positive control group with 400mg/kg BW extract, the mice were in the same subset, meaning that the two groups did not show any differences.

Table 1. Results of measurements of average blood glucose levels before induction, after induction and after therapy

Group	Blood Glucose levels (Mean±SD)					
	Mean fasting blood glucose levels of mice (Mean±SD)					
	T0 Day 0	T1 Day 3	T2 Day 7	T3 Day 14	T4 Day 21	% decrease
K -	105,7 ±5,1	325,7 ±12,9	363,3 ± 15,3[b]	371,3 ±15,5[b]	375,0 ±15,1[b]	-15,2
K +	110,0 ±8,7	302,7 ±7,4	196,7 ± 34,1[a]	125,0 ±26,0[a]	91,3 ±4,9[a]	69,8
K 200 mg/kgBW	115,7 ±5,1	313,7 ±6,4	240,3 ±34,4[a]	179.0 ±1,0[ab]	148,0 ±7,6[ab]	52,7
K400 mg/kgBW	114,7 ±4,5	317,7 ±6,1	216,0 ±9,5[a]	140,0 ±7,0[a]	111,0 ±9,0[a]	65,0

Information:
a : Significantly different from the negative group
b : Significantly different from the positive group

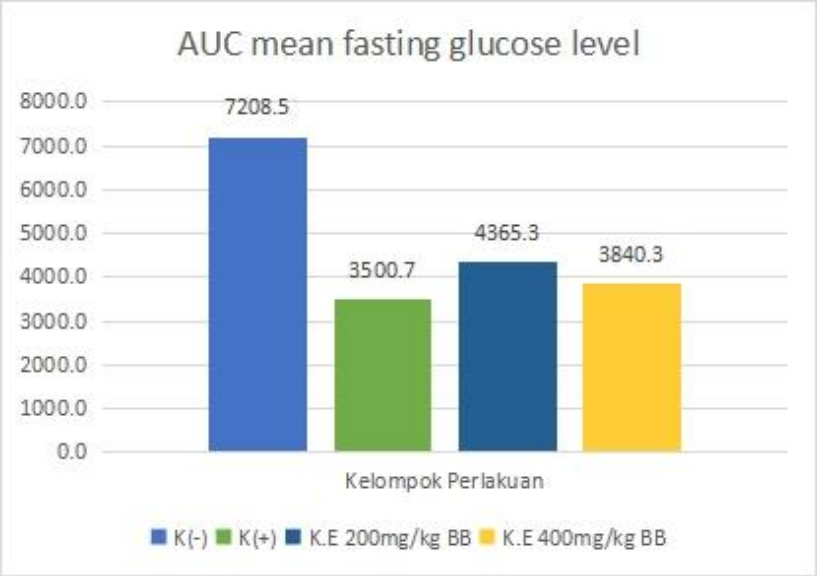

Figure 1. AUC Blood Glucose Levels

Figure 1 shows that the highest AUC value was in the negative group, which was only given STZ-Na induction without the administration of the test solution. STZ-Na can reduce insulin receptor sensitivity, resulting in increased blood glucose levels. The increase in blood glucose levels at T1 in the test animals was caused by STZ induction administered intraperitorially. Administration of Na before STZ administration serves to reduce STZ cytotoxicity. Na also prevents damage to all pancreatic cells and can protect some pancreatic cells (Ghasemi et al., 2014) .

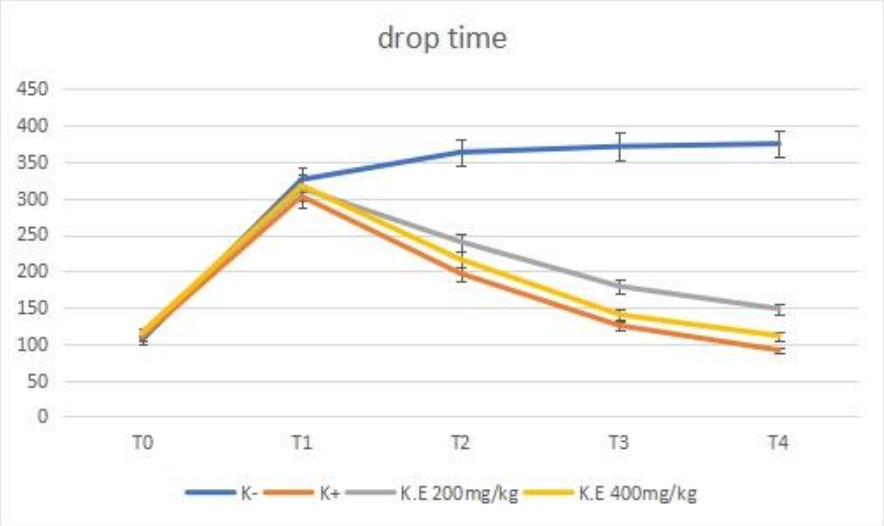

Figure 2 Graph of decreasing blood glucose levels

Figure 2 describes the relationship between average blood glucose and time of day for each treatment. Based on the graph in Figure 2, it is known that on the 3rd day there was an increase in blood glucose levels in each group compared to day 0, after experiencing an increase in blood glucose levels, a test was then carried out using a test preparation to see whether there would be a decrease after being given the test solution.

From the results of the reduction in blood glucose levels by the test extract group and the positive control glibenclamide, the one that provided the most effect was the positive control with a percentage reduction of 68.4%. This is because glibenclamide is an oral hypoglycemic drug and has been proven to have good efficacy in overcoming hyperglycemic conditions. Its hypoglycemic mechanism is based on the K-ATP channel inhibition pathway on the beta cell membrane, thereby preventing the release of K ions. As a result, beta cell depolarization occurs and triggers the opening of Ca^{2+} channels . The opening of these channels causes the entry of Ca^{2+} ions into beta cells and increases the level of Ca^{2+} ions which triggers the release of insulin out of the cell (Katzung *et al* ., 20015).

Furthermore, if we look at the results of the decrease in glucose levels in each group, it was found that the robusta coffee bean extract with a dose of 400 mg/kg BW experienced the same decrease as the positive control which was equivalent to T0 of the test animals before being given induction.

CONCLUSION

Robusta coffee bean extract at a dose of 200mg/kg of mouse body weight and 400mg/kg of mouse body weight has activity in reducing blood glucose levels in male mice that have been induced by STZ-Na, has the result of reducing blood glucose levels that are almost the same as the decrease in blood glucose in the test animals in the positive control group, this indicates that robusta coffee beans can be used as an antihyperglycemic**.**

FURTHER STUDY

This research still has limitations so further research on this topic is still needed "Antihyperglycemic Activity of Ethanol Extract of Robusta Coffee Beans (Coffea canephora) in Mice Induced by Streptozotocin-Nicotinamide"

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