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Effect of Catechins *Uncaria gambir* Roxb. on Blood Sugar Levels of *Mus musculus* L. Hyperglycemia

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Abstract: Sugar is one of the main energies for the body, but do not consume it in excess, because it causes blood sugar levels to increase, this condition is called hyperglycemia. Gambir contains beneficial antioxidants such as catechins. Catechins are polyphenolic compounds belonging to the flavonoid group. The purpose of this study was to determine the effect of gambier catechins on blood sugar levels in hyperglycemic mice. This study is an experimental study with a completely randomized design using 25 samples of male mice for 42 days with two control groups and three treatment groups, namely the negative control was not treated, and the positive control was given glibenclamide after sucrose induction, P1, P2, and P3 were taken with catechins different concentrations after sucrose induction. Checking blood sugar levels using a glucometer (Easy Touch). Data were analyzed by one-way of variance (ANOVA) followed by a DMRT follow-up test at a 5% level. The results showed that gambier catechins had an effect ($p<0.05$) on blood sugar levels in hyperglycemic mice. The most effective gambier catechin administration was at P2 (80% catechin concentration).

Keywords: Catechins; Gambir; Hyperglicemia

Introduction

Sugar is one of the main sources of energy for our bodies (Chen et al., 2019; Ohayon et al., 2020). The largest source of sugar commonly consumed by people comes from carbohydrates (Sheehy et al., 2019). One food that is rich in carbohydrates is rice. However, it should not be consumed in excess, this will have an impact on health and metabolism in the body. The habit of frequently consuming foods containing uncontrolled sugar that occurs repeatedly and continuously causes the sugar levels consumed to increase and exceed the normal limits of sugar consumption in the body (Pang et al., 2021).

According to the Indonesian Ministry of Health, sugar consumption per day is 10% of the total 200 kcal energy, equivalent to 4 tablespoons per day equivalent to 50 grams. WHO recommends consuming no more than 5 teaspoons of sugar per day. According to (Pangribowo, 2020) normal adult blood levels are <140 mg/dl, a person can be said to be hyperglycemic if their blood sugar levels are around 140-199 mg/dl and are said to be diabetic if their blood sugar levels are above 200 mg/dl. Normal mice's blood sugar levels are 62.8 mg/dl-176 mg/dl (Pangribowo, 2020; Santika, 2012). Mice are said to be hyperglycemic if their blood sugar levels are >180 mg/dl (Iskandar, 2019). More than 346 million people in the world are affected by diabetes mellitus in 2020, which means there will be an increase of 56, 2% from 2015 to 2040 and Indonesia is the country with the sixth highest number of diabetes mellitus sufferers in the world (Pangribowo, 2020). Where the common age range affected by diabetes mellitus is 20 to 79 years (Aziz, 2010). Based on 2018 R&D data, the number of people with diabetes in West Sumatra is 46,000 people.

Hyperglycemia is a condition where there is a decrease in the function of the hormone insulin (Costa et al., 2020) which causes the sugar consumed cannot to be digested properly, resulting in an increase in blood sugar levels in the body (Mukhtar et al., 2020; Rahman et al., 2021). Hyperglycemia causes a buildup of blood glucose in cells and tissues (Dewi, 2020) which causes extensive damage to the body. This is caused by the

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disruption of glucose metabolism, protein, and so on due to the effects of insulin secretion. Hyperglycemia is triggered by excessive glucose consumption which is not matched by sufficient insulin secretion (Yuniarti, 2018).

Hyperglycemia that occurs along with excessive sugar consumption continuously results in diabetes mellitus (Papachristoforou et al., 2020). Usually, conditions such as hyperglycemia occur in people with diabetes mellitus which indicates blood sugar levels increase above normal limits. Diabetes mellitus is a chronic metabolic disorder caused by insufficient insulin production (Yenni et al., 2019). There is no effective use of insulin so blood sugar absorption is not perfect (Etriyanti et al., 2018). According to Nasution (2018), "diabetes mellitus is a hyperglycemic state and is accompanied by other disorders". Diabetes mellitus is caused by a decrease in the function of pancreatic beta cells which results in chronic hyperglycemia (Dekroli, 2019).

Indonesia is a country with a tropical climate that is very rich in natural resources and has more than a thousand medicinal plants. The use of medicinal plants is increasing, due to the many side effects of synthetic chemical drugs. West Sumatra to be precise, Muarapati, Fifty Cities is one of the plantation areas with the largest export commodity, namely gambier (*Uncaria gambir* Roxb.) (Isnawati et al., 2012). Gambir is a plant that belongs to the Rubiaceae family and reproduces generatively or by seed and harvesting can be done two to four times a year. Gambir can grow well in places with an altitude of 100-500 meters above sea level.

Gambir contains flavonoids, quinic acid, and quercetin (Hilmi et al., 2018) with the main content of catechins 7-33% (Muchtar, 2014). Catechins are the main bioactive compounds in gambier (Anggraini, 2011) and act as antioxidants (Fahruddin, 2015) because they have two phenolic groups known as polyphenols. The content of catechins in gambier is a characteristic that determines the level of quality of gambier because catechins are the main substituent of gambier which is most widely used (Yeni, 2017).

Method

This research is experimental. This research was conducted at the Animal Physiology Laboratory and Animal House, Department of Biology, Faculty of Mathematics and Natural Sciences, Universitas Negeri Padang.

The tools used in this study were rat cages, cables, fans, rat feeding containers, drinking bottles, analytical scales, measuring cups, beakers, stirring rods, solution bottles, 1 ml sonde, easy-touch glucometer, strips, and medical scissors. The materials used in this study were gambier catechins, male mice aged 8-10 weeks weighing 30-35 grams, pellets, drinking water, rice husks, sucrose, aquades, alcohol swabs, and red medicine. The research work steps can be seen in Figure 1.

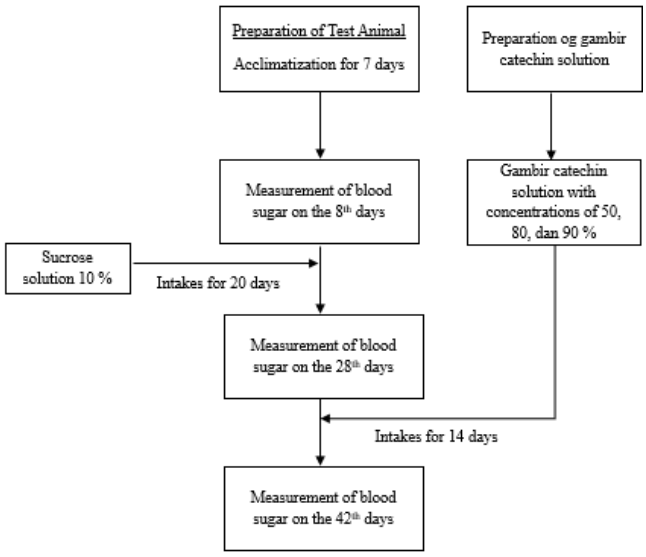

Figure 1. Research flow

This study is an experimental study with a Completely Randomized Design (CRD), with two control groups and three treatment groups consisting of positive control given glibenclamide, negative control, P1, P2, using 25 samples of mice with a duration of 42 days. The measurement of sugar content was carried out 3 times, namely on the 8th day, 28th day, and 42nd day. Measurement of blood sugar levels in mice was done by taking blood from the tails of mice and measuring using a glucometer (easy touch). Data were analyzed by ANOVA followed by a 5% DMRT follow-up test.

Result and Discussion

The results of research on the effect of giving gambier catechins on blood sugar levels of hyperglycemic mice showed the following results.

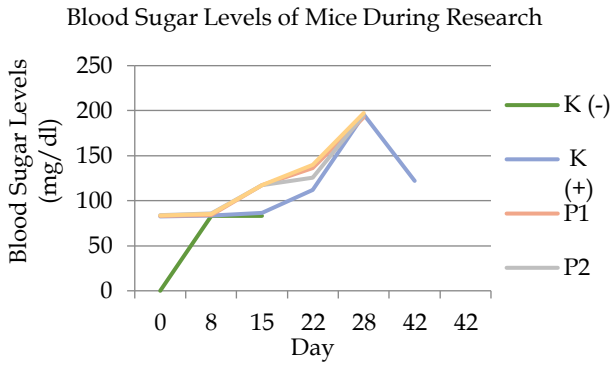

Figure 2. Blood sugar levels of mice during the study

Based on Figure 2. It shows the blood sugar levels of mice from the beginning of the study, namely normal conditions, and then taken with sucrose for 20 days to make the mice hyperglycemic. Where the changes from normal to hyperglycemia can be seen clearly in the table above.

Table 1. Average Blood Sugar Levels of Mice Under Hyperglycemic Conditions and After Administration of Gambir Catechins

Treatment (%)	Before Mean±SD	After Mean±SD
K-	83.22 ± 0.84	89.60 ± 1.52
K+	195.80 ± 6.02	121.80 ± 6.26
P1 50	192.60 ± 7.09	128.60 ± 0.96
P2 80	195.20 ± 5.85	107.80 ± 15.9
P3 90	197.40 ± 5.37	119.80 ± 2.17

Based on Table 1 shows the average blood sugar levels of mice during hyperglycemia (after a sucrose diet) and after treatment with gambir catechin intake at various concentrations with the same dose according to the experimental design which showed an increase and decrease. in blood sugar levels in mice.

Table 2. Percentage of Decrease in Blood Sugar Levels in Mice

Treatment (%)	Blood Sugar Levels After Treatment (mg/dl)
K-	89.60 [a]
K+	121.80 [c]
P1 50	128.60 [c]
P2 80	107.80 [b]
P3 90	119.80 [c]

Table 2 shows the blood sugar levels of mice after giving gambier catechins, where the table shows the blood sugar levels of mice in normal conditions, which are still in the range of 62.8-176 mg/dl, normal is best in negative controls. at 89.6 mg/dl and P2 of 107.8 mg/dl, blood sugar levels were quite good at P1 at 128.6, in positive control at 121.6 mg/dl, and at P3 at 119.8 mg/dl.

This research has been successfully carried out by obtaining data on blood sugar levels of mice after treatment with gambir catechins with various concentrations used with the same dose, the results showed that gambir catechins affected blood sugar levels in hyperglycemic mice.

Mice become hyperglycemic after being given a sucrose diet, this is due to the absorption of glucose in the body, consequently, glucose enters the blood due to excessive glucose consumption which causes mice to become hyperglycemic so that the cells cannot work optimally.

Insulin plays a role in pushing glucose into cells to be metabolized, but because these cells are damaged, glucose cannot be metabolized, so it accumulates in the blood, resulting in an increase in blood sugar levels in mice to hyperglycemia (Sayed et al., 2022). The high blood sugar level in hyperglycemic mice is caused by increased enzyme activity in the gluconeogenesis pathway, thereby accelerating the glycogenolytic and lipolytic pathways, so that metabolism in the body of mice is disrupted, because enzyme activity in the glycolytic and pentose phosphate pathways decreases and blood sugar levels increase (Punita, 2005). According to Yuniarti (2017), high glucose triggers an increase in free radicals that damage pancreatic beta cells so that insulin secretion decreases.

After hyperglycemic mice, glibenclamide was taken to reduce the blood sugar levels of mice in the positive control group, the average blood sugar level of mice was 120.75 mg/dl. Glibenclamide is a synthetic drug for hyperglycemia that has a therapeutic effect in lowering blood sugar levels, so it is often chosen as a comparison material in research.

In addition to glibenclamide intake, hyperglycemic mice consumed gambir catechins with various combinations of different concentrations and doses for each treatment group, where the concentrations used were concentrations of 50%, 80%, and 90% for 14 days (Rekha et al., 2019; Zhu et al., 2021). The purpose of using the difference in concentration and dose is to see the concentration and dose of catechins that can reduce blood sugar levels in hyperglycemic mice optimally. From the results obtained, there was a decrease in blood sugar levels in hyperglycemic mice after giving gambier catechins.

Based on the one-way ANOVA test, catechins have an effect on blood sugar levels in hyperglycemic mice. From hyperglycemic mice to mice with normal blood sugar levels. This is because the calculated f value is greater than the f table and $p < 0.05$. Based on the data and based on analysis with Ducan, it was found that catechins with a concentration of 80% had an optimal effect in lowering blood sugar levels in hyperglycemic rats to normal again.

Catechins are one of the main constituents of gambier (Monica & Husna, 2022; Syukri, 2023). Catechins are flavonoid compounds found in green tea, black gambier tea, wine, and cocoa. Catechins contain antioxidants which are flavonoids and are included in phenolic compounds that can neutralize free radicals (Fahruddin, 2015; Ahmad & Ghosh, 2022; Ahmed et al., 2021). Gambier catechins can reduce blood sugar levels of hyperglycemic mice because catechins are tannin derivatives in the form of flavonoids which are very good as antioxidants and are used as antidiabetics.

Catechins have antioxidant activity that can prevent the oxidation of glucose in the blood (Muniroh, 2020). Catechins can reduce the enzyme aldose reductase and alpha-glucosidase enzymes, thereby helping the regeneration of pancreatic cells and increasing insulin secretion. So, the presence of insulin can regulate blood sugar levels to be metabolized into energy and stored in cells and muscles, so blood sugar levels decrease. In addition, with their antioxidant properties, catechins can protect pancreatic cells from damage and can stimulate glucose and fat metabolism, so that accumulation in the blood can be avoided and can increase hypoglycemic activity by increasing glycogenesis (Araujo et al., 2021).

According to Yuniarti et al. (2019), the flavonoid group is an antioxidant that binds to hydroxyl radicals that damage pancreatic cells so that insulin production increases. Catechins have antioxidant activity that can prevent the oxidation of glucose in the blood. Capturing free radicals and preventing the formation of ROS that trigger pancreatic cell repair. Catechins can reduce aldose reductase and alpha-glucosidase enzymes, thereby helping the regeneration of pancreatic cells and increasing insulin secretion (Yuniarti, 2018). According to Indah (2014), gambier affects blood sugar levels in male mice induced by alloxan, gambier can reduce blood sugar levels in mice after alloxan is induced but the decrease is not too significant, this study is different from research conducted because of its beauty.

Pure gambier catechins, as well as in Indah's study, rats were taken with alloxan which made rats diabetic and caused more damage to the pancreas than sucrose intake, whereas in this study rats were made hyperglycemic with a sucrose diet.

Conclusion

Gambier catechins (*Uncaria gambir* Roxb.) affect blood sugar levels in hyperglycemic mice (*Mus musculus* L.). Gambier catechins (*Uncaria gambir* Roxb.) with a concentration of 80% affect reducing blood sugar levels of hyperglycemic mice (*Mus musculus*. L.).

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For research articles with several authors, a short paragraph specifying their individual contributions must be provided. The following statements should be used "Conceptualization, methodology, and data analysis, Sari Ramadhani and Elsa Yuniarti.; writing—original draft preparation, Sari Ramadhani.; resources, writing—review and editing, funding acquisition, Elsa Yuniarti. All authors have read and agreed to the published version of the manuscript."

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The authors declare no conflict of interest

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