Effects of Black Turmeric Ethanol Extract (Curcuma Caesia Roxb) on Blood Glucose Levels, SGOT, SGPT, Histopathology Pancreas: A Preliminary Study

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KEYWORDS

Curcuma caesia Roxb, Blood Glucose Levels, Pancreatic Histopathology, Streptozotocin.

ABSTRACT

Diabetes mellitus (DM) is a condition that causes hyperglycemia and glucose intolerance. It can be caused by insulin deficiency, impaired insulin effectiveness, or both. Treatment of diabetes mellitus is long-term and certainly has unwanted side effects. The purpose of this study was to determine the effect of black turmeric extract on blood glucose, SGOT, SGPT values and pancreatic beta cell histopathology. This study used a Randomized Control Group Design on 30 white rats by giving a high-fat diet and induced streptozotocin 35 mg/kgbw intraperitoneally. Experimental animals were divided into 6 treatment groups, namely negative control, positive control, black turmeric extract doses of 250 mg/kgbw, 500 mg/kgbw, and 750 mg/kgbw. Assessment of the decrease in blood glucose levels is seen from the percentage of blood sugar reduction for 21 days, the value of SGOT, SGPT and histopathology of pancreatic beta cells. Data were analyzed using ANOVA test to see differences between groups. Based on the results obtained, that there is a significant difference in the administration of 750 mg/kgbw dose extract reduces blood sugar levels best by 57.71% compared to the negative control group where there is an increase in blood sugar by 9.94%. Based on the value of SGOT and SGPT levels, it was found that the 750 mg/kgbw dose of extract gave the best value compared to other treatment groups. Based on the parameters of the histopathological picture of pancreatic beta cells, it was found that the administration of black turmeric extract at a dose of 250 mg/kgbw experienced the mildest degeneration compared to other treatment groups. Ethanol extract of black turmeric (Curcuma caesia Roxb) is able to reduce blood sugar levels, SGOT, SGPT values and repair damage to pancreatic beta cells.

1. Introduction

According to WHO (World Health Organization) in 2018, the leading cause of death worldwide is noncommunicable diseases, which account for 71%. In addition, WHO also stated that the number of diabetics in adults increased by 8.5% or 422 million diabetics globally (Eka Dharma P.M, Muh. Farhant R, 2023). High levels of sugar in the blood can lead to diabetes, a long-term disease caused by the pancreas not producing enough insulin (a hormone that regulates blood sugar or glucose) or the body not being able to use the insulin it produces effectively. The International Diabetes Federation reports that in 2017, 8.8% of people in the world had diabetes, with the majority among those aged 20 to 79. An estimated seven people die every second from diabetes or its complications. About 2 million people, or 50% of them, are under 60 years old. And by 2045, it is estimated that this figure will increase to 9.9 percent (IDF, 2017).

In type 2 diabetes mellitus the body experiences pancreatic beta cell dysfunction (Nuralifah, 2022). Characteristic and progressive changes to the structure of pancreatic beta cells are characteristic of diabetes mellitus. These changes can occur quantitatively, such as a decrease in number and size, or qualitatively, such as necrosis and degeneration (E. Zubaidah and I. N. F, 2015).

Black turmeric (Curcuma caesia Roxb.) is an emerging variant in herbal medicine, especially in India, Pakistan, and Turkey. In Indonesia, it comes from the lesser-known curcuma species (Sudewo, 2012). Because it contains bioactive compounds such as flavonoids, phenols, and alkaloids, black turmeric (Curcuma caesia Roxb.) has potential as a medicinal plant (Fong, 2012).

Black turmeric rhizome contains abundant curcuminoids, oils, flavonoids, phenolics, amino acids, proteins, and alkaloids. This suggests that the medicinal use of Curcuma caesia Roxb is related to the presence of bioactive secondary metabolites. According to (Udayani, N. N. W., Ratnasari, N. L. A. M., & Nida, 2022), Flavonoids contained in black turmeric (Curcuma caesia Roxb.) have antioxidant properties, the ability to capture free radicals, and anti-inflammatory and anticarcinogenic. The curcumin contained has also long been known to have antioxidant properties. Flavonoids are divided into six subclasses: flavonols, flavones, isoflavones, flavanols, and anthocyanidins (Al-Ishaq RK, 2019). Anthocyanins can also improve tissue uptake and utilization of glucose in streptozotocin-induced diabetic rats and mice, and protect pancreatic cells against necrosis induced by

streptozotocin (Różańska D, 2018).

2. Methods

Tools

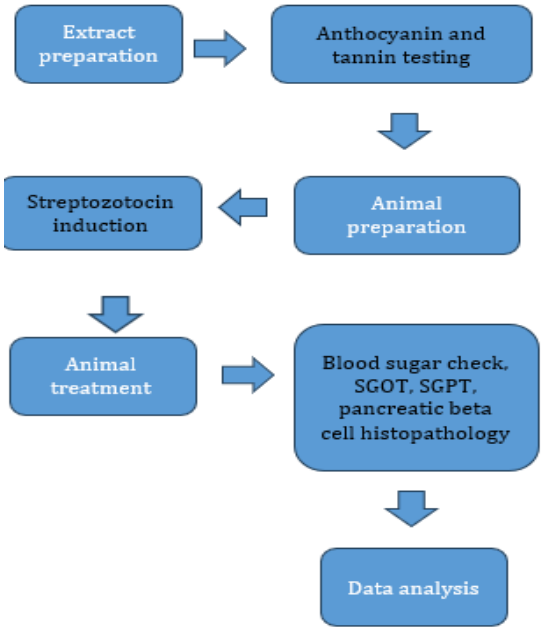
Digital analytical balance (Ohaus, USA), oven (Memmert), cabinet dryer, thermometer, freezer, blender (Philipp), 40 mesh sieve, rotary vacuum evaporator (Buchii), centrifugator (MSE Micro Centaur), glassware (pyrex), five cages, feeders, drinking water bottles, Easy Touch blood glucose meter, glucometer strip, syringe, gastric sonde, gloves, cotton, jar, measuring cup (pyrex), plastic basin, scale, blender, sieve, spatula, Buchner funnel, suction pump, rotary evaporator, separate flask, filter paper, spectrophotometer and refrigerator. For histopathology, we need optilab and Olympus microscope.

Material

The material used in this study was black turmeric obtained from Manikliyu Kintamani District, Bangli Regency. The materials used are pro-analysis quality such as 96% ethanol, streptozotocin (Sigma-Aldrich, USA), metformin (PT Phapros Tbk, Indonesia), CMC Na 0.5%, chicken feed, distilled water, drinking water, and husks for cage mats.

Testing

In this study, experimental animals were obtained from the Pharmacology Laboratory of the Faculty of Pharmacy, Mahasaraswati University, Denpasar. This research was also conducted at the Laboratory of the Faculty of Pharmacy, Mahasaraswati University with an ethics committee issued by the University of Surabaya with No: 82/KE/VI/2022.



Black turmeric was taken from Kintamani District, Bangli Regency, and then oven dried at 50°C. The simplisia was pulverized with a blender and sifted to produce a 40 mesh powder, 150 grams of simplisia was then dissolved in 1000 milliliters of 96% ethanol. Maceration is carried out until the macerate is colorless (clear), usually by remaceration and stirring. After the maceration process is complete, the filtrate is combined with a Rotary Evaporator until a thick extract is produced (Setyawaty, Aptuning B and Dewanto, 2020).

A 2-gram sample was taken, mixed with 0.5% HCL in 18 milliliters of ethanol, and kept for one hour for pigment extraction to determine anthocyanin content. Absorbance analysis at 520 nm was performed on the filtered mixture (Teng et al., 2020). In the determination of total tannins, the extract was analyzed using the Folin-Denis method. A total of 0.01 g of extract was diluted into 5 ml of phosphate citrate buffer. The diluted sample was pipetted as much as 0.25 ml and then added 0.25 ml of Folin-Denis reagent, then vortexed and added 2 ml of 5% Na2CO3. The solution was vortexed and then incubated for 30 minutes. The absorbance was measured using a spectrophotometer at a wavelength of 725 nm (Bizuayehu, Atlabachew and Ali, 2016).

Easy Touch glucometer was used to measure blood glucose levels in white rats (Rattus norvegicus). The

method of taking blood is to clean the tail with a cotton swab that is given water so that the attached dirt is gone, then clean again with 70% alcohol. The blood that comes out is then pumped into the glucometer strip. Before treatment and four days after streptozotocin administration, the blood glucose level of rats was measured, which was shown in mg/dL on the screen after ten seconds (Ramachandran, Rajasekaran and Manisenthilkumar, 2012).

The in vivo study was conducted on 30 male white rats of the wistar strain. They were divided into five treatment groups, with six white rats each. The experiment included negative and positive control groups, with doses of 250 mg/kgbw, 500 kg/kgbw, and 750 mg/kgbw, respectively. On the first day, all white rats had their blood glucose levels measured to ensure normal blood glucose levels. After that, streptozotocin was administered intraperitoneally to all white rats at a dose of 35 mg/kgbw. On the first day of treatment, streptozotocin was given once. Blood glucose levels were measured again after four days of streptozotocin administration to create a consistent rise in blood glucose. In the negative control group that experienced an increase in blood glucose, CMC Na 0.5% was given, and in the positive control group a dose of metformin was given at a dose of 45 mg/kg BW, while groups P1, P2, P3 were given black turmeric extract at a dose of 250 mg/kg BW, 500 mg/kg BW, 750 mg/kg BW. Measurement of blood sugar levels was measured until the 21st day. Blood was taken through the heart for SGOT and SGPT measurements, as well as organ harvesting for histopathology testing.

This study made histopathological preparations that included necropsy, sample isolation, fixation, dehydration, clearing, embedding, tissue cutting, staining, and observation with a light microscope (C. M. Hermawati, A. J. Sitasiswi, and S. N. Jannah, 2020). Anesthetized organs were removed with chloroform, then cleaned with 0.9% physiological sodium chloride, and then fixed with 10% neutral phosphate buffered formalin (BNF). During histopathology preparation, tissue fixation was performed by immersing it in 10% phosphate buffered formalin for 24 hours. After that, the tissues were sliced (trimming) with a thickness of ± 3 mm so that they could be inserted into the cassette for processing in the tissue machine. After using ethanol for two hours, the dehydration process was continued. Then, the tissue was cleared by inserting the cassette into xylol I, xylol II, and xylol III. Immersion (embedding) and printing (blocking) occurred when the tissue was put twice into liquid paraffin heated at 56 degrees Celsius for two hours. After that, the tissue is taken out with tweezers, and paraffin is used to block it. The cut was performed with a microtome with a thickness of 4-5 μm. The cut tissue appeared on the water bath and was captured by an object glass. It is then dried at room temperature and the preparations are ready to be stained with hematoxylin eosin (HE). This is done by immersing the preparations on a glass slide in xylol I, II, and III for five minutes. Next, the preparations were immersed in 96 percent, 80 percent, and 70 percent alcohol for five minutes each. Then washed with distilled water and immersed in hematoxilin meyer for seven minutes. For five minutes, washed with running water. Then, the preparations were dipped in Eosin for ten seconds. Then, the preparations were immersed in graded alcohol 70%, 80%, and 96% alcohol for five minutes each, and clarified in xylol I, II, and III for five minutes each. After that, the preparations were dried and mounted with a mount. Examine the preparations under a microscope for histopathologic changes (I. M. I. Swarayana, 2012). Histopathology preparations were examined under a microscope at five microscopic field of view each. Histopathologic changes were observed at 100 times and 400 times magnification. There was fatty degeneration and necrosis.

Data Analysis

Statistical analysis was performed with the SPSS for Windows 26 program with a 95% confidence level using the One Way Anova test along with LSD post hoc. Histopathology results were evaluated by descriptive method, presented in the form of images and shapes of pancreatic beta cells.

3. Results

The resulting extraction result is a thick blackish brown extract of 63 grams. The calculation is done using the following formula:

$$\text{Yield (\%)} = \frac{\text{Extract Weight}}{\text{Initial Simplisia Weight}} \text{ x } 100\%$$

$$= \frac{83 \text{ gram}}{800 \text{ gram}} \text{ x } 100\% = 10.37\%$$

Determination of black turmeric rhizome plants was carried out at the Indonesian Institute of Sciences (LIPI) which is located at UPT Balai Konvervasi Tumbuhan Kebun Raya Eka Karya Bali with number B-308/III/KS.01.03/I/2021. The results of the determination state that the type of plant used in this study is true

black turmeric rhizome (Curcuma caesia Roxb).

The chemical content found in black turmeric (Curcuma caesia Roxb) is alkaloid, flavonoid and tannin (Udayani, N. N. W., Ratnasari, N. L. A. M., & Nida, 2022). Other studies mention the content in black turmeric, namely steroids, terpenoids, alkaloids, glycosides, tannins, phenols, and so on (Pakkirisamy, Kalakandan and Ravichandran, 2014). Curcuma caesia Roxb contains curcuminoids, oil content, phenolics, and various amino acids, the presence of these bioactive secondary metabolites correlates with the medicinal use of Curcuma caesia Roxb.

Anthocyanin and Tannin Content

The assay results of anthocyanin content obtained a value of 4.05 g/100 g of extract. The medicinal benefits of flavonoids increase with their levels. Anthocyanins can be used to maintain health and cure chronic diseases such as diabetes mellitus when consuming 19.8 - 64.9 mg anthocyanins in women and 18.4 - 44.1 mg in men every day (Priska, 2018). Anthocyanins also improve tissue uptake and utilization of glucose in streptozotocin-induced diabetic rats and mice, and protect pancreatic cells against streptozotocin-induced necrosis (Różańska D, 2018).

The results of testing the total tannin content obtained a value of 155.31 mg/100 g of extract. Tannins function as antidiabetics by stopping glucose absorption in the intestine and stopping adipogenesis, which is potentially part of diabetes treatment. In addition, tannins function as free antiradicals and activate antioxidant enzymes that regenerate pancreatic cells (Fitri Febriani, 2023).

Hyperglycemia and abnormalities in carbohydrate, fat, and protein metabolism are signs of diabetes mellitus, caused by decreased insulin secretion or decreased insulin sensitivity (Andrie, 2014). Blood glucose, or blood sugar, levels that exceed normal are known as diabetes mellitus (DM), a chronic disease characterized by blood sugar levels equal to or greater than 200 mg/dl and fasting blood sugar levels greater than or equal to 126 mg/dl. Because diabetes mellitus often goes unnoticed by those who suffer from it and complications only occur when it is noticed, it is known as the silent killer. Diabetes mellitus can infect almost all systems of the human body (Petersmann et al., 2018).

One alternative treatment option that can be used is the use of traditional medicinal plants; black turmeric is one of them. Black turmeric rhizome, an herbal plant from the turmeric family, has been used by Asian people for its many health benefits. Curcumin, a polyphenol found in black turmeric rhizome, is one of its active compounds. Curcumin functions as an antioxidant, anti-inflammatory, antimutagenic, anticancer, and antimicrobial. In addition, curcumin functions as an antidiabetic in the same way as thiazolidinedione. The body's various molecular target mechanisms activated by curcumin may help prevent diabetic complications The content of curcumin, which has the potential to increase insulin secretion and reduce glucagon. Inhibiting poly ADP ribose polymerase (PARP) is an important mechanism of curcumin to control blood glucose levels. It also inhibits the expression of protein kinase C (PKC) and increases the activity of the enzyme glucose synthetase, which reduces oxidative stress on the cell (Qurrotul, Zakiyyah, 2023).

Blood Sugar Level Results

The results of the examination of blood sugar levels of rats with streptozotocin induction can be seen in Figure 1.

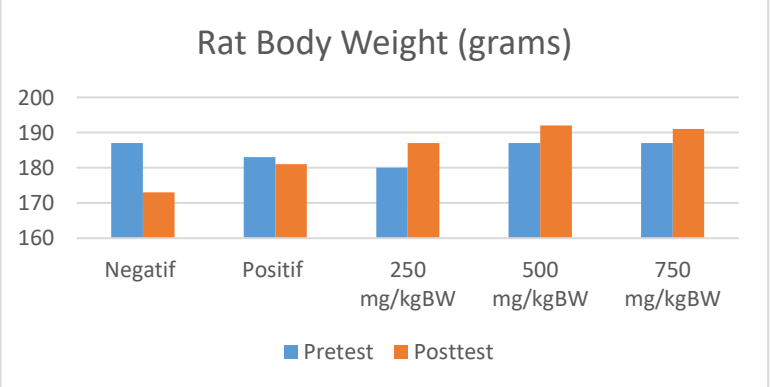


Figure 1. Average Body Weight of Experimental Animals by Group

Based on Figure 1, it is found that there is an increase in body weight in the normal control group and the treatment group from before treatment and after treatment. The highest increase in body weight was found in the treatment group that received a dose of black turmeric extract of 500 mg/kgbw, which was 5 grams.

According to research (Rias and Sutikno, 2017) there is a significant relationship between body weight and DM. Using the chi square test p>0.05, it was shown that there was a stronger relationship between overweight and increased blood sugar levels. This is due to the correlation between body weight and blood glucose levels. Insulin, which absorbs glucose through certain insulin-sensitive membranes, increases blood glucose levels due to delayed glucose uptake. In rats treated with 500mg/kgbw of black turmeric extract, weight gain may occur due to excessive nutrient intake; free fatty acids may circulate in the blood vessels throughout the body, causing lipotoxicity, an oxidative stress condition (Ghasemi and Jeddi, 2023). This effect is caused by the amount of free fatty acids released by triacylglycerols to compensate for the destruction of excess fat stores. This effect impacts both adipose and non-adipose tissues, as well as on the pathophysiology of diseases in several organs such as the liver and pancreas (Kottaisamy et al., 2021).

Thirty white rats were used in this study, and they were divided into six treatment groups. All white rats were given an intraperitoneal streptozotocin dose of 35 mg/kgbw before being divided into treatment groups. The results of blood glucose examination of rats induced by 35 mg/kgbw streptozotocin intraperitoneally showed that blood glucose increased far above the normal range. Easy Touch glucometer was used to check the blood glucose level. There are two categories of blood glucose examination: normal blood glucose/blood sugar levels below 126 mg/dL and high blood glucose/blood sugar levels above 126 mg/dL (Soviana and Maenasari, 2019).

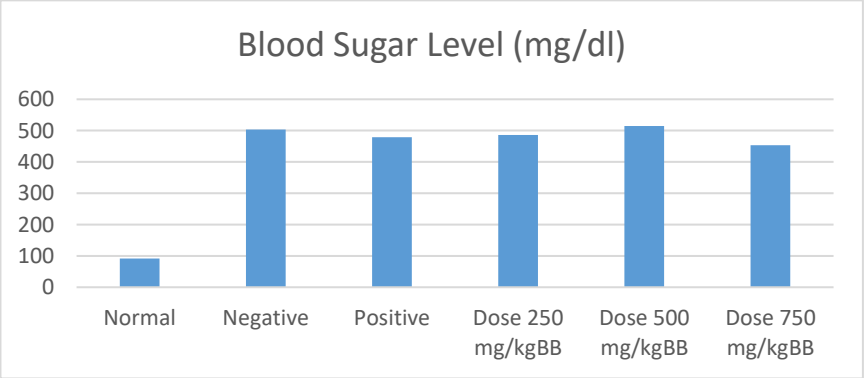


Figure 2. Graph of mean blood sugar levels after streptozotocin induction (Pretest)

Based on Figure 2 shows that the average blood sugar level of the negative control group after streptozotocin induction is 503 mg/dL; the average blood sugar level of the positive control group (metformin) after streptozotocin induction is 479 mg/dL; The mean blood sugar level of the 250 mg/kgbw dose group after streptozotocin induction is 486 mg/dL; the mean blood sugar level of the 500 mg/kgbw dose group after streptozotocin induction is 515 mg/dL; and the mean blood sugar level of the 750 mg/kgbw dose group after streptozotocin induction is 453 mg/dL. Based on the graph above, it can be seen that each group experienced a significant increase in blood sugar levels after being induced by streptozotocin.

One of the signs of diabetes mellitus is an increase in blood glucose or blood sugar levels above normal values (Nur Sahid and Murbawani, 2016). Streptozotocin increased blood sugar in all groups. Streptozotocin, a compound that has the ability to directly damage pancreatic beta cells and cause symptoms of diabetes mellitus, is one of the factors that can increase blood sugar levels. To induce type 1 and type 2 DM in experimental animals, streptozotocin or 2-deoxy-2-[3-(methyl-3-nitrosoureido)-D-gluco piranose] produced from Streptomyces achromogenes can be used. The intravenous dose for type 1 DM induction ranges between 40 and 60 mg/kg, while the intraperitoneal dose is more than 40 mg/kgBW (Nur Sahid and Murbawani, 2016).

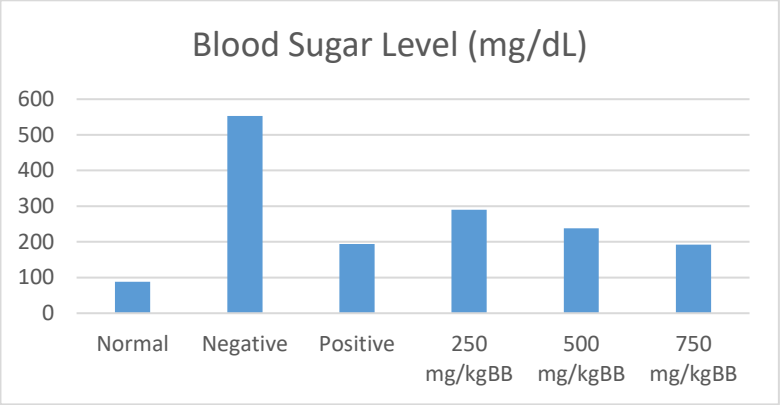


Figure 3. Graph of mean blood sugar levels after treatment (Posttest)

Based on the graph of the average blood sugar level after being given black turmeric extract above, it can be seen that the average blood sugar level of the negative control group (CMC) after being given black turmeric extract is 553 mg/dL; the average blood sugar level of the positive control group (metformin) after being given black turmeric extract is 194 mg/dL; The average blood sugar level of the 250 mg/kgbw dose group after being given black turmeric extract is 290 mg/dL; the average blood sugar level of the 500 mg/kgBW dose group after being given black turmeric extract is 238 mg/dL; and the average blood sugar level of the 750 mg/kgbw dose group after being given black turmeric extract is 192 mg/dL.

The average reduction in glucose levels during the 21-day treatment can be seen in Table 4.1

Table 4.1

	Pretest (mg/dL)	Posttest (mg/dL)	Decrease in blood sugar level (mg/dL)	Decrease in blood sugar level (%)
Normal control	92	88	4	4.54
Negative control	503	553	+50	9.94
Positive control	479	194	285	59.5
Dose of 250 mg/kgbw	486	290	196	40.33
Dose of 500 mg/kgbw	515	238	277	53.78
Dose of 750 mg/kgbw	454	192	262	57.71

Based on table 4.1, it was found that the highest decrease in blood sugar levels occurred in the extract group with a dose of 750 mg/kgbw, which was 57.71%. In the negative control, a group of diabetic animals that only received CMC, blood sugar levels increased by 50 mg/dL or 9.94%.

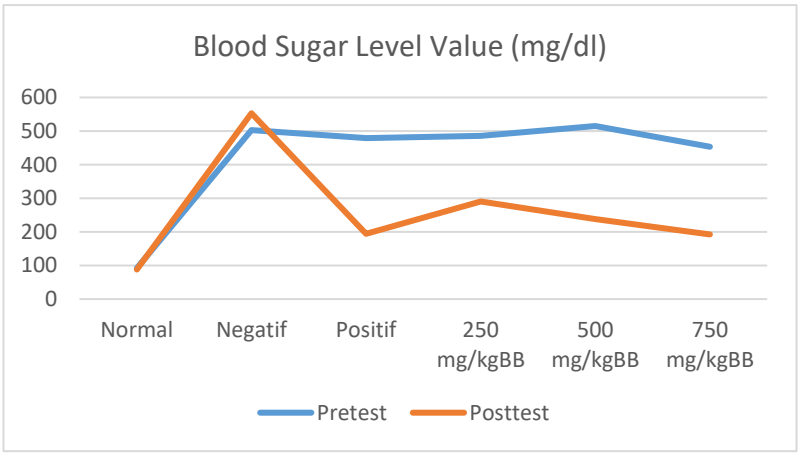


Figure 4. Pretest and Posttest Blood Sugar Values

Based on Figure 4, it was found that the 750 mg/kgbw dose group experienced the highest decrease after being given black turmeric extract, which was 57.71%. In contrast to the negative control group which experienced an increase in blood sugar levels by 10.34%. In the positive control, the decrease in blood sugar was 59.5%, this proves that metformin provides an effect as a diabetic drug in streptozotocin-induced rats.

Streptozotocin enters pancreatic β-cells via GLUT-2 and produces DNA alkylation, which can damage cell membranes, proteins, and DNA. If blood sugar levels increase, endocrine organs may secrete epinephrine. Ephinephrine is very effective in causing the process of glyconeogenesis in the liver, which will release a lot of glucose into the blood in a short time (Sharma K, 2022).

The data obtained were tested using SPSS One way ANOVA which previously conducted normality and homogeneity tests. The normality test results show the sig. P>0.05 so it can be concluded that the data is normally distributed. The homogeneity test value shows the sig. P>0.05 so it can be concluded that all combinations are homogeneous. Based on the ANOVA results, it was found that the sig value. 0.000<0.05, it can be concluded that the average of the five test groups is significantly different so that there is a difference in blood glucose levels of rats between the treatment group and the negative control group.

Giving extracts to experimental animals shows the activity of black turmeric in reducing blood sugar levels. The effect of reducing blood glucose levels given by black turmeric extract is due to the content of curcumin compounds, flavonoids, tannins and several other compounds that have an effect in reducing blood sugar levels. The content of curcumin compounds has activities related to stimulation of beta cell proliferation and insulin secretion which is important for the treatment and prevention of diabetes. Can improve glucose tolerance by stimulating the secretion of glucagon-like-peptide-1 (GLP-1) and also incretin from enteroendocrine cells L (GLUTag L). Where G-protein-coupled receptors (GPRs) are a group of free fatty acid receptors (FFAR) found on the surface of pancreatic beta cells, including GRP 40 and GRP 120 which are important for beta cells in mediating insulin secretion (Zhang and Kitts, 2021).

Flavonoids have antioxidant properties that protect the body against the effects of hyperglycemia by acting on biological targets such as α-glucosidase, glucose co-transporter, or aldose reductase. As antioxidants, flavonoids prevent the chain reaction of converting superoxide (LOO) to hydrogen superoxide by binding hydrogen atoms and electrons from the aromatic hydroxyl group to bind free radicals and convert them into reactive flavonoid radicals (LOOH), which protect pancreatic cells (Fang et al., 2019).

Tannins are potential antioxidants that can improve the pathological oxidative state of the diabetic situation. Tannins inhibit the action of the α-glucosidase enzyme in the intestine to convert disaccharides into glucose so that the rate of increase in blood sugar is not too high. The mechanism of action of tannins in reducing blood sugar levels is to reduce the absorption of nutrients by inhibiting the absorption of glucose in the intestine (Ardalani et al., 2021).

SGOT and SGPT results

The results of the examination of SGOT and SGPT levels in white rats after treatment are presented in table 4.2

Table 4.2

Group	Mean SGOT value (U/L)	Mean SGPT value (U/L)
Normal control	90.74±3.43	45.2±4.32
Negative control	126.25±4.37	74.8±3.42
Positive control	92±5.33	52±4.35
250 mg/kgbw dose	123±14.37	60.5±5.65
500 mg/kgbw dose	102.67±2.47	56±5.70
750 mg/kgbw dose	89±5.87	43.6±3.04

Description: SGOT and SGPT of diabetic white rats after being given black turmeric extract were declared normally distributed data with a significance value >0.05.

Based on the results of the above study, it was found that the administration of the extract can normalize the value of SGOT (Serum Glutamate Oxalacetate Transaminase) and SGPT (Serum Glutamate Pyruvate Transaminase) of diabetic white rats given streptozotocin induction. This can be seen in the administration of black turmeric extract at a dose of 750 mg / kgbw is able to provide SGOT and SGPT values close to the value of the normal group. Serum SGOT and SGPT are indicators of liver cell damage. Natural antioxidants that function as antioxidants are flavonoids. Sesquiterpene compounds can reduce insensitivity to insulin and improve glucose metabolism (Yuneldi, Saraswati and Yuniwarti, 2018).

Histopathology Results

Histopathology observation of rat pancreatic beta cells using hematoxylin eosin staining method. The results of pancreatic beta cell histopathology can be seen in Figure 5.

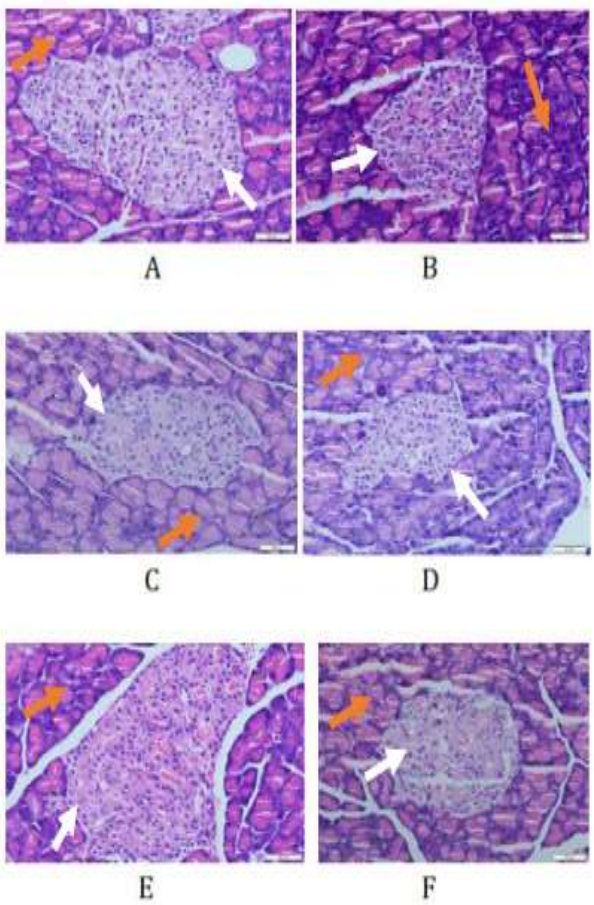


Figure 5 Microscopy of pancreatic beta cells with Hematoxylin-Eosin staining at 400x magnification.

(A) Overview of pancreatic beta cells in the normal control group; (B) Overview of pancreatic beta cells in the negative control group; (C) Overview of pancreatic beta cells in the positive control group; (D) Overview of pancreatic beta cells in the 250 mg/kgbw dose group; (E) Overview of pancreatic beta cells in the 500 mg/kgbw dose group; and (F) Overview of pancreatic beta cells in the 750 mg/kgbw dose group; (orange arrows) acinar cells; (white arrows) Langerhans Island.

Based on Figure 5, it was found that in all groups there was no necrosis and inflammation in pancreatic beta cells. In the treatment group, the 750 mg/kgbw dose of black turmeric extract had the least cell degeneration. Test animals diagnosed with diabetes mellitus have different histopathology from normal test animals. This can be seen from the number of endocrine cells that experience necrosis and cell degeneration as well as the shape of endocrine cells that experience degeneration and necrosis.

The area of the islets of Langerhans in diabetic rats was smaller compared to the normal control group. However, compared to the negative control, the three groups of animals that received black turmeric extract had a larger size of Langerhans islets. This is because STZ has a cytotoxic effect on cells, where the main cause of hyperglycemia conditions is beta cell damage (Metawea et al., 2023). In addition, the administration of Curcuma caesia Roxb can protect pancreatic beta cells from damage due to STZ toxicity.

According to research conducted by (Ibrahim et al., 2023), black turmeric was significantly able to reduce fasting blood glucose (FGB) and HbA1c. Black turmeric extract also showed strong glucose uptake activity in mast cells by promoting the facilitated diffusion process. Anthocyanins contained in black turmeric extract have activity in improving hyperglycemia conditions and insulin sensitivity through AMPK activation accompanied by increased GLUT4 regulation in skeletal muscle and decreased gluconeogenesis regulation which has been shown to reduce blood glucose levels and improve insulin sensitivity (Fang et al., 2019).

Dosing Curcuma caesia Roxb can provide therapeutic functions and microscopic changes in pancreatic beta cells that are different in STZ-induced rats. It can be seen that the 750 mg/kgbw dose group experienced the least degeneration compared to the 500 mg/kgbw dose group and the 250 mg/kgbw dose group. This is also in line with the decrease in blood sugar levels that occur in the 750 mg / kgbw dose group that provides the best

value after the administration of black turmeric extract.

4. Discussion

Based on the results obtained, it was found that the administration of black turmeric extract at a dose of 750 mg/kgbw reduced blood sugar levels best, the lowest SGOT and SGPT levels were 89 U/L and 43.6 U/L and experienced the lowest degeneration compared to other treatment groups. Further research needs to be done at several dose levels and different solvents.

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