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Antidiabetic Effect of Functional Foods Containing *Ipomoea batatas* and *Cinnamomum burmanii* In Alloxan Induced Diabetic Rats

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KEYWORDS

Biscuits, Cinnamomum burmanii, Diabetes Melitus, Functional Food, Ipomoea batatas

ABSTRACT:

Introduction: Diabetes Mellitus (DM) is a heterogeneous disease with signs of chronic hyperglycemia. Patients with DM must continue to consume sufficient food so that their nutritional needs are met. In this study, a functional food product was made in the form of biscuits made from purple sweet potato and cinnamon, which have been widely proven to contain anthocyanins and polyphenols that can affect blood glucose levels.

Objectives: This research used 25 Sprague Dawlay rats aged 2-3 months which were then divided into 5 test groups and then intervened based on group division for 21 days

Methods: The treatment dose 1,5 g/kg BW and 3,0 g/kg BW was carried out for 21 days calculated from 3 days after the induction of alloxan 150 mg/kg BW single dose, then the examination of blood sugar levels was carried out on day 12. After entering day 21, rats were taken blood for measurement parameters

Results: The results of the histological picture on pancreas organs of diabetic rats given both experimental doses also regenerate cells in the islets of Langerhans. Functional food in the form of biscuits containing of purple sweet potato and cinnamon, can have a significant effect in reducing blood glucose, cholesterol, triglycerides, creatinine, SGOT and SGPT levels and can repair damage to the pancreas of diabetic rats.

Conclusions: Giving biscuit functional food preparations from *Cinnamomum burmanii* and *Ipomoea batatas* at a dose of 3.0 g / kg BW has a better effect on reducing blood glucose levels, improving lipid profiles, improving liver function, improving kidney function and can improve the histology of pancreatic islet cells of Langerhans diabetic rats.

1. Introduction

Diabetes mellitus (DM) is a group of metabolic diseases characterized by hyperglycemia due to abnormal insulin secretion, abnormal insulin action, or both (Kumari et al., 2013). Currently, the discovery of antidiabetic drugs has shifted its focus to natural plant sources that have minimal side effects). Research has shown purple sweet potato (*Ipomoea batatas*) extract as a potential antidiabetic (Kumari et al., 2013). Purple sweet potato contains 255.8 mg/100 g anthocyanins (Zaddana et al., 2021). Anthocyanins play a high role as antioxidants because of their ability to capture free radicals and inhibit fat peroxidation, the main cause of cell damage associated with aging and degenerative diseases. This agent inhibits digestive tract glucose absorption through alpha-glucosidase inhibition, thus anthocyanins have a hypoglycemic effect (Mahendra et al.,2013). Research conducted by Alsoodeeri *et al*., (2020) used purple sweet potato extract at a dose of 200 mg / kg BW in DM rats induced by alloxan can reduce blood glucose levels and hepatic MDA of hyperglycemic rats. In addition, research conducted by Sulistyani et al., (2023) on the formulation of bangle rhizome and purple sweet potato biscuits can provide antioxidant activity in increasing the activity of GPx and catalase enzymes in rats induced by a high-fat diet.

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In vivo and in vitro studies prove that cinnamon (*Cinnammomum burmannii*) contains polyphenol active substances that work by increasing insulin receptor proteins in cells, so as to increase insulin sensitivity and reduce blood glucose levels close to normal (Rats *et al*,. 2019). One of the polyphenol components is Cinnamaldehida with a mechanism of action as anti-inflammatory, antioxidant, antihyperglycemic and antihyperlipidemic. Cinnamon has been shown to have insulin potential through upregulation of glucose uptake in cultured adipocytes (Singh et al., 2020). Research conducted by Fathi et al, (2015) proves that the administration of cinnamon extract at a dose of 200 mg / kgBB in STZ-induced rats can reduce blood glucose levels and reduce body weight in DM rats, this is possible due to the synergistic effect of polyphenols that can increase glucose metabolism and reduce adipocyte insulin resistance, and increase insulin secretion from pancreatic islet Langerhans cells. Cinnamon has phenolic components that act as antioxidant compounds but also help inhibit the formation of glycation process end products associated with its ability to trap reactive oxygen species (ROS) compounds and capture reactive carbonyl species (RCS) (Kasim et al., 2014).

The development of functional food products made from local raw materials such as purple sweet potato flour and cinnamon is also an effort to reduce the use of imported ingredients 3 such as wheat in Indonesia. (Zaddana et al., 2021). Purple sweet potato and cinnamon biscuits as functional food are expected to have health benefits such as high protein, rich fiber, and low glucose so that these biscuits are good for consumption by the community, especially people with DM. (Officinale & Verum, 2017)

2. Objectives

The materials used were biscuits made from purple sweet potato and cinnamon. Alloxan (Sigma Aldrich catalog A7413-25G), Glibenclamid (Kan Ying, India), test subjects were Sprague-Dawley white rats with 2-3 months of age as many as 25 heads with a body weight of 150-200 grams found from the Pharmacology Laboratory of the Faculty of Pharmacy, Muhammadiyah University of Yogyakarta.

3. Methods

A. Preparation Of Animals Test

Twenty-five Sprague-Dawley white rats were placed in individual cages for acclimatization for 7 days before treatment. The cage temperature was maintained at 24°C and the room lighting cycle was 12 hours dark-light. Mice were fed standard AD2 diet and drank distilled water ad libitum. All animal treatments were approved by the Ahmad Dahlan University Research Ethics Committee with no. 012212190.

B. Grouping of Animals Test

Treatment of test animals by dividing into 5 groups, namely the normal group of rats given standard feed. The negative control group of rats injected alloxan dose 150 mg/kg BW once intraperitoneally and given normal feed. The positive control group of rats was given a dose of glibenclamide 0.09 mg/kg BW and given normal food. Group 4, rats were treated with biscuits orally at a dose of 1.5 g/kg BW. Group 5, rats were treated with biscuits orally at a dose of 3.0 g/kg BW. The treatment was carried out for 21 days starting after the administration of alloxan.

C. Induction Of Diabetes Using Alloxan

The dose of alloxan used refers to research (Putra *et al*., 2020) using alloxan monohydrate dose of 150 mg/kg BW which has been dissolved in 0.9 g NaCl and distilled water was added to a volume of 100 mL. Physiological saline is injected into rats intraperitoneally. After 3 days post-induction, rats were fasted for 12 hours and then blood glucose levels were measured and body weight was weighed. Rats are characterized to be diabetic if blood glucose levels are > 200 mg/dL (Samsuri *et al*., 2020).

D. Experimental Design

Observation Of Diabetes Parameters

Blood glucose level was examined before alloxan injection, 3 days after alloxan induction taken at the tail to analyze blood glucose before treatment (pre test) and day 21 before surgery. On day 21, rat blood was taken from the retro orbitalis plexus using a capillary tube through the eppendorf wall. After 30 minutes, the blood was centrifuged for 20 minutes at 8000 rpm at 25°C to obtain blood serum (Kintoko et al., 2017). Determination of blood glucose levels, lipid profiles, SGOT, SGPT and creatinine based on blood sugar levels determination kit (Glucose Oxidase-Peroxidase (GOD-PAP)) Dyasys®, lipid profiles triglycerides (GPO-PAP) (Glycerol Phosphate Oxidase-Para Aminophenazone) Diasys® and cholesterol (Glycerol Phosphate Oxidase (GPO)) Dyasys®, SGOT (ASAT (GOT) FS (Aspartate Aminotranserase)) Dyasys®, SGPT (ALAT (GOT) FS (Alanine Aminotransferse)) Dyasys®, and creatinine (creatinine FS) Dyasys® what is done according to the instructions. After that, the test animals were sacrificed, and the pancreas organs were taken for histopathologic examination.

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After that, the test animals were sacrificed and the pancreas was taken for histopathologic examination. The design for measuring blood glucose levels (BGL) in rats is presented in figure 1.

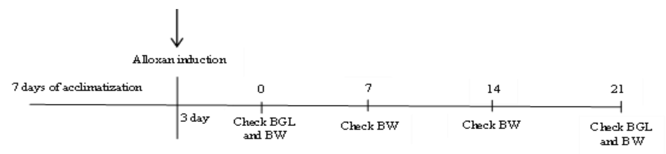

Figure 1: 7 days post-acclimatisation, followed by alloxan induction, after 3 days calculated by day 0: check BGL and BW, day 7: check BW, day 14: check BW, day 21: check BGL and BW.

Histopathologic Examination Of The Pancreas

On day 21, after blood sampling, the test animals were anesthetized using CO_2 gas, then the rats were dissected in the abdomen. Pancreatic organs were
taken and washed with 0.9% NaCl. Then histopathological preparations were made with thin sections (1 mm x 1 mm x 1 mm), then paraffin was added using standard techniques and stained with hematoxylin eosin (HE), then pancreatic organs were carefully examined under a microscope using 400x magnification.

E. Data Analysis

The data obtained were statistically analysed using SPSS IBM 25 with One Way Anova test with confidence level (P=95%). Measurement of the diameter of the islets of Langerhans was calculated based on the sum of the mean diameter of all islets of Langerhans of the rat group observed with a microscope which was then followed by the IBM SPSS 25 test

Results

A. Rat Body Weight Measurement

Body weight weighing of rats was carried out to see the effect of giving purple sweet potato (*Ipomoea batatas*) and cinnamon (*Cinnamomum burmanii*) biscuit functional food preparations in the antihyperglycemic test on weight loss. Pre-induction day showed no significant difference (p>0.05) in all test groups Table 1. After alloxan induction, body weight weighing on day 0 has not shown any significant difference in body weight change (p>0.05) in all groups.

Table 1. Effect of purple sweet potato and cinnamon combination biscuits on body weight in alloxan induced diabetic model rats.

Group	Mean ± SD			
	Day 0	Day 7	Day 14	Day 21
Normal Control	199.44±0.45	197.38±3.38*	198.18±3.01*	199.24±3.31*
Negative Control	199 ± 0.95	178.24 ±0.95$^{\#}$	161.24 ±4.17$^{\#}$	156.52 ±6.00$^{\#}$
Positive Control	198.76 ± 1.52	183.34±2.90$^{*\#}$	194.3 ± 1.75*	196.62 ±1.79*
Dose of 1.5 g/kg BW	199±0.56	177.96 ±0.56$^{\#}$	179.36±5.56$^{*\#}$	187.38 ±4.48$^{*\#}$
Dose of 3.0 g/kg BW	199.42 ± 0.14	180.28±0.14$^{\#}$	185 ±3.90$^{*\#}$	192.32±1.54$^{*\#}$

Notes: *= significantly different from negative control (p<0.05)
#= significantly different from normal control (p<0.05)

B. Test Parameters Blood Glucose Level

Purple sweet potato has a high anthocyanin content of about 467.99 ppm which is antidiabetic. Purple sweet potato (*Ipomoea batatas*) has a high anthocyanin content ranging from 110 mg-210 mg/100 g. Anthocyanins are flavonoid phytopigments, are water-soluble, have antioxidant properties. Anthocyanins have a C6-C3-C6 structure and are positively charged. The types of anthocyanins contained in purple sweet potatoes are cyanidin, peonidin, and pelargonidin (I'tishom et al., 2021).

Measurement of blood glucose levels after the rats were fed for 24 hours using a *glucometer*. The results of checking blood glucose levels after acclimatization, after alloxan induction and before decapitation are presented in Table 2.

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Table 2. Mean blood sugar levels after acclimatization, after alloxan induction and before decapitation Group

	Mean ± SD		
	Post aclimat (H-7)	Post alloxan-induction (H-11)	21 Day Post (H-21)
Normal Control	97.8 ± 16.84	101.6 ± 13.14*	113 ± 5.09*
Negative Control	112 ± 14.98	324 ± 64.26$^{\#}$	292.2 ± 15.6$^{\#}$
Positive Control	96.6 ± 21.84	252.80 ± 47.44$^{*\#}$	124 ± 5.09*
Dose of 1.5 g/kg BW	97.4 ± 9.18	272 ± 46.95$^{\#}$	144 ± 9.40$^{*\#}$
Dose of 3.0 g/kg BW	98.6 ± 8.29	288.2 ± 24.44$^{\#}$	135 ± 6.40$^{*\#}$

Notes: *= significantly different from negative control ($p<0.05$)
#= significantly different from normal control ($p<0.05$)

C. Lipid Profile Level Test Parameters

Dyslipidemia is characterized by increased total cholesterol levels, increased LDL (Low Density Lipoprotein), increased triglyceride levels, and decreased HDL (High Density Lipoprotein) levels in the blood (Ariyanti & Besral, 2019).

Measurement of cholesterol and triglyceride levels is used to determine lipid function parameters in test animals that have been induced by alloxan and given BKMU with 2 dose variants shown in Table 3.

Table 3. Results of measurement of cholesterol parameters of diabetic rats on the administration of cinnamon and purple sweet potato combination biscuits.

Treatment	Cholesterol (mg/dL) ± SD	Triglycerides (mg/dL) ± SD
Normal Control	98.74 ± 17.01*	95.97 ± 16.18*
Negative Control	159.02 ± 15.13$^{\#}$	170.34 ± 8.10$^{\#}$
Positive Control	113.29 ± 21.32*	115.59 ± 11.89$^{*\#}$
Dose of 1.5 g/kg BW	128.11 ± 9.09$^{*\#}$	131.71 ± 9.89$^{*\#}$
Dose of 3.0 g/kg BW	122.38 ± 5.37$^{*\#}$	128.67 ± 6.52$^{*\#}$

Notes: *= significantly different from negative control ($p<0.05$)
#= significantly different from normal control ($p<0.05$)

Test Parameters SGOT and SGPT Levels

Measurement of SGOT and SGPT levels to see liver function parameters in test animals that have been induced by alloxan and given functional food with 2 dose variants can be seen in Table 4.

Table 4. Measurement results of SGOT and SGPT parameters of diabetic rats on the administration of cinnamon and purple sweet potato combination biscuits.

Treatment	SGOT (U/L) ± SD	SGPT (U/L) ± SD
Normal Control	14.35 ± 2.82*	19.57 ± 1.11*
Negative Control	30.50 ± 2.28$^{\#}$	29.73 ± 2.44$^{\#}$
Positive Control	16.15 ± 4.46*	20.33 ± 1.67*
Dose of 1.5 g/kg BW	18.42 ± 0.48*	24.51 ± 2.56$^{*\#}$
Dose of 3.0 g/kg BW	17.99 ± 4.20*	22.39± 4.24*

Notes: *= significantly different from negative control ($p<0.05$)
#= significantly different from normal control ($p<0.05$)

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D. Test Parameters Serum creatinine levels

The measurement results of serum creatinine parameters in test animals that have been induced by alloxan and given BKMU with 2 dose variants can be seen in Table 5.

Table 5. Measurement results of serum creatinine parameters of diabetic rats on the administration of cinnamon and purple sweet potato combination biscuits

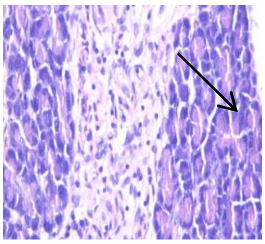
Treatment	Creatinine (U/L) ± SD
Normal Control	0.87 ± 0.182*
Negative Control	3.07 ± 0.198#
Positive Control	0.97 ± 0.172*
Dose of 1.5 g/kg BW	1.20 ± 0.200*#
Dose of 3.0 g/kg BW	1.03 ± 0.217*

Notes: *= significantly different from negative control (p<0.05)

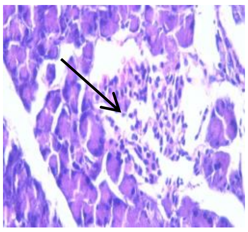
#= significantly different from normal control (p<0.05)

E. Histopathologic Profile of Diabetic Rat Pancreas

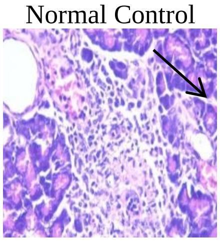
Histological observations on pancreatic tissue pieces from all treatment groups were observed on the morphological shape of pancreatic tissue cells stained with hematoxylin-eosin (HE) staining. Qualitative parameters assessed are whether there are changes in the state of pancreatic tissue histologically such as fibrosis or inflammation after the test animals were induced by alloxan and given BKMU for 21 days which can be seen under a light microscope. presented in Figure 2.



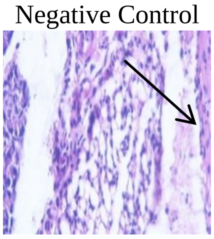
Normal Control



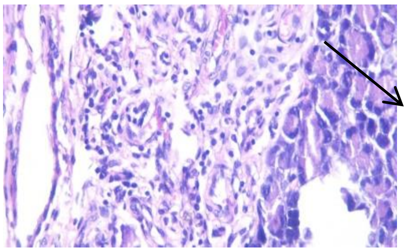
Negative Control



Positive Control



Dose of 1.5 g/kg BW



Dose of 3.0 g/kg BW

Figure 2. Histology results of pancreatic organs with HE staining (magnification 400x) in normal control: no inflammation, negative control: inflammation occurs, positive control: inflammation occurs, dose control 1.5 g / kg BW: inflammation occurs, dose control 3.0 g / kg BW: inflammation occurs. black arrow indicates inflammation

Inflammation is the immune system's natural response to injury, infection or stress and is a complex process involving the release of chemicals from immune cells, blood vessels and other tissues that help fight harmful substances and repair damaged tissue. These immune cells include lymphocytes, histiocytes, and neutrophils (Atlas of pathology., 2023). In addition, the ratio of inflammation in the pancreas of each group of rats treated with cinnamon and purple sweet potato combination biscuits is shown in Table 6.

Table 6. Inflammation ratio in the pancreas of each group of rats treated with cinnamon and purple sweet potato combination biscuits.

Treatment group	Inflammation Ratio
Normal Control	0/3
Negative Control	3/3
Positive Control	1/3
Dose of 1.5 g/kg BW	2/3
Dose of 3.0 g/kg BW	1/3

Description: The number 3 indicates the number of test samples per group Ratio: incidence of inflammation number of rats per group

In addition to histological assessment and the ratio of pancreatic inflammation, the average diameter of the islets of Langerhans of each group of rats treated with cinnamon and purple sweet potato combination biscuits is presented in Table 7.

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Table 7. The results of measuring the mean diameter of the islets of Langerhans in each group of rats treated with cinnamon and purple sweet potato combination biscuits.

Group	Mean (µm) ± SD
Normal Control	506.22 ± 26.15*
Negative Control	321.64 ± 54.10#
Positive Control	443.96 ± 12.27*
Dose of 1.5 g/kg BW	418.20 ± 65.04*#
Dose of 3.0 g/kg BW	428.01 ± 34.37*

Notes: *= significantly different from negative control ($p<0.05$)
#= significantly different from normal control ($p<0.05$)

In addition to looking at inflammatory parameters, the diameter of the islets of Langerhans in the pancreas of each representative group of diabetic rats was also measured, which is presented in Figure 3.

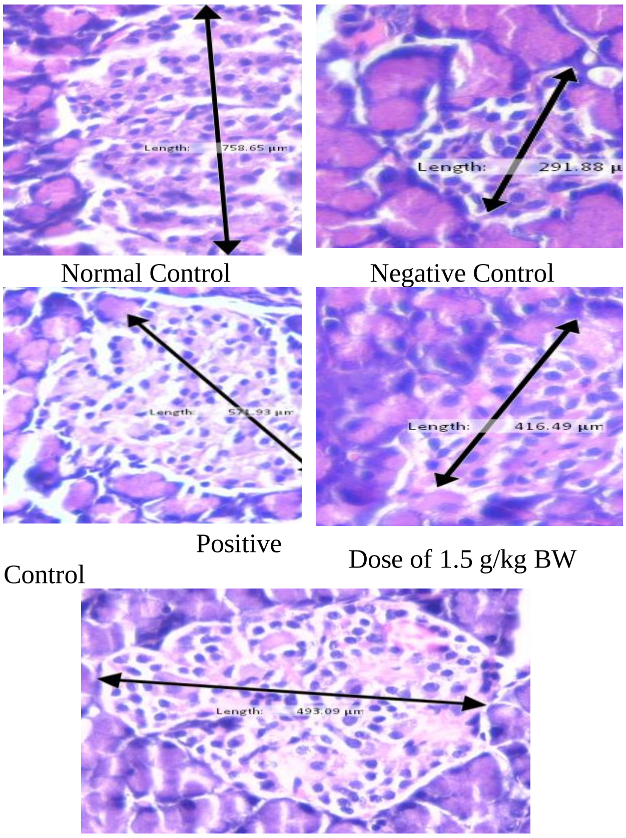

Figure 3: The results of histopathologic observation of the diameter of the islets of Langerhans with HE painting observed at 400x magnification microscope for each representative group of rats. Normal control was 758.65 µm, negative control was 291.88 µm, positive control was 571.93 µm, dose control 1.5 g/kg BW was 416.49 µm, dose control 3.0 g/kg BW was 493.09 µm. black arrow indicates the diameter of the islets of Langerhans

Discussion

A. Rat Body Weight Measurement

Body weight on day 7 has not shown any significant difference in weight change ($p>0.05$) in all groups. Body weight on day 21 showed that the weight of the negative control group decreased in weight when compared to the normal group, this indicates that the administration of alloxan dose of 150 mg/kg BW effectively reduces the body weight of rats after the onset of diabetes. In the body weight of the dose group of 1.5 g/kg BW and 3.0 g/kg BW compared with the negative control also obtained significantly different results ($p<0.05$). In the positive control body weight, there was an increase in body weight which showed that there was no significant difference with the normal group ($p>0.05$).

The decrease in body weight in the group of rats suffering from hyperglycemia is due to the condition of rats that are unable to use glucose as an energy source due to insulin deficiency. Although the measurement of the hormone insulin was not done, but in theory it can be ascertained that rats induced by alloxan experienced a decrease in insulin due to damage to pancreatic beta cells that produce the hormone insulin (Li *et al*., 2019). Changes in body weight in the group of rats given Functional food biscuit formulation of cinnamon and purple sweet potato with a biscuit dose of 1.5 g/kg BW and biscuit dose 2 of 3.0 g/kg BW per day showed an increase in body weight compared to the negative control ($p<0.05$). This occurs because purple sweet potato contains carbohydrates, protein, and vitamins. Protein is needed for growth so it is possible to improve the nutritional status of diabetic rats (Akhtar *et al*., 2018)

B. Test Parameters Blood Glucose Level

Observing Table 2, it is known that all groups of rats after acclimatization did not show an increase in blood glucose, indicating that blood glucose levels in rats are normal. Furthermore, the post alloxan induction group H-11, showed that in all treatment groups there was a significant increase in blood glucose levels when compared to the normal group ($p<0.05$). This indicates that the administration of alloxan dose of 150 mg/kg BW effectively raises blood glucose levels in rats. The 21-day post-treatment showed that the negative control group experienced an increase in blood glucose levels when compared to the normal group. In the dose group of 1.5 g/kg BW and dose of 3.0 g/kg BW compared to the negative control did not experience a significant decrease in blood

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glucose levels (p>0.05). In the 1.5 g/kg BW dose group (144 ± 9.40) compared to the 3.0 g/kg BW dose (138 ± 6.40) the spss test data showed results that were not significantly different (p>0.05). Comparison between these doses shows that the dose of 1.5 g/kg BW given to rats can already show the effectiveness of blood glucose reduction. In the 3.0 g/kg BW dose group compared with the positive control showed results that were not significantly different (p>0.05). This shows the effectiveness of reducing blood glucose levels is the same between the dose of 3.0 g/kg BW with the administration of oral diabetes drugs, namely glibenclamide. In the positive control group, there was also a decrease in blood glucose levels that was not significantly different when compared to the normal group (p>0.05). This indicates that the administration of glibenclamide can reduce blood glucose levels in diabetic rats.

This decrease is thought to be the result of a combination of active compounds of cinnamon (Cinnamaldehyde) which has a role as an enhancer of insulin sensitivity and production (Guo *et al*., 2017), inhibition of alpha-glucosidase enzyme activity so that the absorption of glucose from food can be reduced. Blood sugar rise can be controlled (Ernawati *et al*., 2017), antioxidant and anti-inflammatory properties that can protect body cells from oxidative damage and diabetes-related inflammation (Sena *et al*., 2023). Cinnamon has a procyanidin compound that can act like insulin because it increases glucose uptake (Kumar *et al*., 2012). The content of active substances in purple sweet potatoes, namely anthocyanins, antioxidants, and high total polyphenol content (Li *et al*., 2019) plays a role in inhibiting carbohydrate absorption (Nurdjanah *et al*., 2022)

C. Lipid Profile Level Test Parameters

Based on the data in Table 3, it can be seen that the negative control group experienced an increase in cholesterol levels when compared to the normal group (p<0.05). In the dose group of 1.5 g/kg BW and dose of 3.0 g/kg BW compared to the negative control had a significantly different cholesterol level decrease (p<0.05). In the 1.5 g/kg BW dose group (128.11 ± 9.09) compared to the 3.0 g/kg BW dose (122.38 ± 5.37) the spss test data showed results that were not significantly different (p>0.05). In the 1.5 g/kg BW dose group (128.11 ± 9.09) and the 3.0 g/kg BW dose (122.38 ± 5.37) compared to the positive control showed no significant difference (p>0.05). This indicates that the treatment of cinnamon biscuits with purple sweet potato at a dose of 1.5 g/kg BW and a dose of 3.0 g/kg BW has the same effectiveness in reducing choleterol levels compared to the administration of glibenclamide. In the positive control group, there was also a decrease in cholesterol levels that was not significantly different when compared to the normal group (p>0.05).

Examination of triglyceride levels in the negative control group increased triglyceride levels when compared to the normal group (p<0.05). In the 1.5 g/kg BW dose group and the 3.0 g/kg BW dose compared to the negative control group, there was a significant decrease in triglyceride levels (p<0.05). In the 1.5 g/kg BW dose group (131.71 ± 9.89) compared to the 3.0 g/kg BW dose (128.67 ± 6.52) the spss test data showed results that were not significantly different (p>0.05). In the 3.0 g/kg BW dose group compared with the positive control showed results that were not significantly different (p>0.05). From the test results, then BKMU dose 2, which is 3.0 g / kg BW (128.67 ± 6.52) is a better dose in reducing cholesterol levels in diabetic rats when compared to a dose of 1.5 g / kg BW.

The decrease in cholesterol levels and triglyceride levels is possible due to the content of polyphenolic compounds in the form of flavonoids in both active substances purple sweet potato and cinnamon which have antihypercholesterolemia activity and can bind apolipoprotein B. Flavonoids reduce cholesterol levels in the blood by inhibiting the work of the HMG Co-A reductase enzyme. The function of the HMG Co-A reductase enzyme is to convert HMG Co-A into mevalonate. So, if HMG Co-A reductase is inhibited, mevalonate is not formed. (Vasconcelos et al., 2017)

D. Test Parameters SGOT and SGPT Levels

The examination of SGOT levels can be seen that the negative control group experienced an increase in SGOT levels when compared to the normal group (p<0.05). In the dose group 1.5 g / kg BW and dose 3.0 g / kg BW compared to the negative control had a significant decrease in SGOT levels (p<0.05). In the 1.5 g/kg BW dose group (18.42 ± 0.48) compared to the 3.0 g/kg BW dose (17.99 ± 4.20) the spss test data showed results that were not significantly different (p>0.05). This indicates that the treatment of cinnamon biscuits with purple sweet potato at a dose of 1.5 g / kg BW and a dose of 3.0 g / kg BW has the same effectiveness in reducing SGOT levels compared to glibenclamide administration. From the test results, BKMU dose 2, which is 3.0 g / kg BW (17.99 ± 4.20) is a better dose in reducing the SGOT levels of diabetic rats when compared to the dose of 1.5 g / kg BW.

SGOT and SGPT examinations are used to detect liver function abnormalities (Rahayu, 2017). Hyperglycemia damages hepatocytes, causing GPT and GOT enzymes to enter the blood circulation and consequently increase SGOT and SGPT in the blood. Cinnamon bark is known to contain glutathion and lipid conjugated dienes that can stimulate antioxidant enzyme activity, besides containing the enzyme GST (Glutation S Transferase) which can increase serum and liver glutathione (Husen *et al*., 2019).

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Purple sweet potatoes contain polyphenols that can prevent tissue damage due to free radicals by reducing or eliminating reactive oxygen so that regeneration of injured liver cells can occur. (Su et al., 2020) Antioxidants in the liver are able to combat oxidative stress so as to protect the liver from fat accumulation (Li *et al.*, 2015).

Cinnamon can reduce the risk of hyperglycemia and inflammation by slowing the process of gastric emptying, reducing the activity of the enzyme α-glucosidase, restraining glucose absorption and increasing glycogen synthesis. (Sham, 2011). Cinnamon polyphenols also increase SOD (Super Oxide Dismutase) and GSH-Px (Glutathione Peroxidase) activities and decrease malondialdehyde (MDA) in pancreatic gland liver of diabetic rats. (Liang et al., 2019). The mechanism of this decrease is because cinnamon can inhibit liver damage through Peroxisome Proliferator Activated Receptor-Gamma (PPARγ). Inactivation of PPARγ in hepatocytes is associated with increased body and liver weight, as well as decreased serum AST levels. In addition, PPARγ activation is associated with other beneficial effects such as down-regulation of the expression of pro-inflammatory cytokines, such as tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and C-reactive protein (CRP), which are involved in the pathogenesis of NAFLD (Medagama, 2015).

E. Test Parameters Serum creatinine levels

The examination of serum creatinine levels can be seen that the negative control group experienced an increase in creatinine levels when compared to the normal group ($p<0.05$). In the 1.5 g/kg BW dose group and the 3.0 g/kg BW dose compared to the negative control group, there was a significant decrease in creatinine levels ($p<0.05$). In the 1.5 g/kg BW dose group (1.20 ± 0.200) compared to the 3.0 g/kg BW dose (1.03 ± 0.217) the spss test data showed results that were not significantly different ($p>0.05$). Comparison between these doses shows that the dose of 1.5 g/kg BW given to rats can already show the effectiveness of reducing blood serum creatinine levels of diabetic rats. In the dose group of 1.5 g/kg BW and dose of 3.0 g/kg BW showed results that were not significantly different compared to the positive control ($p>0.05$), this indicates that the treatment of cinnamon biscuits with purple sweet potato at a dose of 1.5 g/kg BW and a dose of 3.0 g/kg BW has the same effectiveness in reducing serum creatinine levels compared to the administration of glibenclamide. These results are in line with research conducted by Shen *et al*., (2010) showed that the administration of cinnamon extract in diabetic rats can affect kidney function and glycemic effects. This is possible due to the active compounds of polyphenols from cinnamon which act as antioxidants and anti-inflammatory in reducing serum creatinine levels with the mechanism of suppressing oxidative stress from various oxidative reactions that occur in the kidneys (Bellassoued *et al*, 2019). In addition to the content of cinnamon compounds, according to research conducted by (Ervika *et al*, 2020) , the administration of purple sweet potato extract at a dose of 100 mg / kg BW for 35 days can reduce blood MDA levels, reduce serum glutamic oxalacetate transaminase (SGOT) and serum glutamic pyruvate transaminase (SGPT) in the liver and improve the kidney system, anthocyanin compound extracts in purple sweet potatoes can reduce ureum and creatinine levels by protecting cell mitochondrial function.

F. Histopathologic Profile of Diabetic Rat Pancreas

In the normal group showed that no damage occurred, this is possible because there is no influence of toxic substances into the body, because in normal rats there is no special treatment. In the glibenclamide group, the biscuit dose of 1.5 g/kg BW and the biscuit dose of 3.0 g/kg BW also experienced inflammation but the picture showed cell regeneration with changes in pancreatic pathophysiology and a reduced damage ratio when compared to the negative control. This is in line with research conducted by Lairin Djala et al., (2016), which showed that cinnamon was able to repair the pancreatic structure of Balb-C strain male mice after exposure to alloxan. The ability to regenerate pancreatic beta cells depends on the regulation of normal blood glucose levels, and in cinnamon there are double-linked procyanidin type-4 polymerase compounds that have insulin-like activity that can play a role in regulating blood glucose levels. In research conducted by Darwis *et al*, (2021) also proved that the administration of cinnamon ethanol extract can reduce blood glucose levels, and cinnamon extract shows effective similarities with glibenclamide in lowering glucose. This is due to the content of antioxidant compounds in cinnamon. Stress conditions on the endoplasmic reticulum (RE) and destabilization of lysosomes stimulate necrosis and inflammation in cells (Ghorbani *et al*., 2019). Elevated glucose levels cause metabolic disturbances and produce free radicals. These free radicals can damage cells in our body such as the liver and kidneys (Azemi *et al*., 2012).

Based on the histopathological picture of pancreatic damage and diameter of islets of Langerhans, there are differences in each group presented in Table 7. In the normal group, the average diameter of the islets of Langerhans was 506.22 µm, these results indicate normal histological conditions in the study, so the normal control is used as a reference for normal conditions to describe the description of the average diameter of other groups.

The negative control group showed a high percentage of severe histopathological damage when compared to the normal control. Alloxan itself has a diabetogenic effect on beta cells that can destroy cells, cells will undergo necrosis-apoptosis so that cell histopathology will change and the number of cells will decrease then cause the islets of Langerhans to atrophy or shrink. This is in accordance with the observations in the alloxan control which shows the average diameter of the islets of Langerhans which is 321.64 µm. Therefore, the negative control group is used as a reference for abnormal conditions to describe the histopathology picture and the average of other groups. The positive control (glibenclamide), showed a histopathological picture close to normal control. The average diameter of the positive control langerhans islands is 443.96 µm, the diameter is classified as normal and wider when compared to the negative control diameter of 321.64 µm. Based on these results, the biscuit dose group of 1.5 g/kg BW and the biscuit dose of 3.0 g/kg BW can reduce the level of damage to the islets of Langerhans, although it has not fully returned to normal conditions.

Purple sweet potato and cinnamon contain antioxidants that can reduce the level of cell damage by providing an opportunity for cells to regenerate and increase the size of the diameter of the islets of Langerhans (Pruteanu *et al*., 2023).

The results of HE staining of pancreatic tissue are in accordance with the average results of in vivo tests of blood glucose, cholesterol, triglycerides, creatinine, SGOT and SGPT levels that have been carried out, namely at a dose of 1.5 g/kg BW biscuits can already have an effect on the repair of pancreatic islets of diabetic rats induced by alloxan and at a dose of 3.0 biscuits is an effective dose in repairing the pancreas of diabetic rats.

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