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Original Research Article

Goroho Banana (*Musa acuminata* Sp) Flour: An Assessment for Type 1 Antidiabetic Solution

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ABSTRACT

This study assessed Goroho banana flour's functional capacities as a potential type 1 antidiabetic solution. The study incorporated an *in vivo* model of 25 male Sprague-Dawley rats aged 8-10 weeks. Fifteen rats were streptozotocin (STZ, 55mg/kg weight) induced as a type 1 diabetic model. Treatments were grouped: normal feed group (KN/K. Normal, Normal subject + standard rodent feed), a positive control group (K. Pos, Diabetic subject + standard rodent feed), the K3 group (Normal subject + Goroho flour feed), K4 group (Diabetic subject + Goroho flour feed), and K5 group (Diabetic subject + standard rodent feed + glibenclamide 5mg/kg weight). The test was conducted for 30 days intragastrical feed by oral gavage. Weight loss was observed in the modelled group, while weight gain was observed in the normal feed groups. Blood sugar in the K. Pos group appeared insignificantly different from K4. The Langerhans islets of K4 (161.07 µm) and K5 (162.05 µm) were insignificantly different from the K. Pos group (161.16 µm). Pancreatic β cells of K4 (70.4) and K. Pos (83.8) were insignificantly different. It was concluded that Goroho flour had no significant impact on type 1 diabetes models, and no blood sugar reduction was observed. Weight gain was observed on normal feed subjects without increased blood sugar levels.

Keywords: Antidiabetic, Assessment, Banana, Goroho flour, Type 1 Diabetes.

Introduction

Type 1 diabetes mellitus is an autoimmune disease that causes damage to the insulin-producing pancreatic β cells, thus leading to severe insulin deficiency. Cases of type 1 diabetes may occur in all ranges of age groups[1,2]. In these past years' cases of type 1 diabetes have risen considerably. Various studies have been conducted to overcome this disease, from the applications of exogenic insulin, pancreatic transplant, pharmacological therapies, and lifestyle management[3].

Carbohydrate consumption has a significant impact on blood sugar levels. In type 1 diabetic cases, understanding the amount of carbohydrate intake is very important to control the blood sugar levels[4]. Extensive research has been conducted on plant-based compounds and formulas that positively contribute to better diabetic regulating management. These plant-based agents were considered to have antioxidant and anti-hypoglycemic properties[5,6].

Bananas (*Musa acuminata*) were tested for their antidiabetic properties and were found to reduce blood sugar levels (21.9%) of albino mice[7]. Goroho bananas (*Musa acuminata* sp.) are endemic bananas of North Sulawesi known in North Sulawesi as an indigenous food supplement for people with diabetes due to secondary metabolites in the form of flavonoids, alkaloids, tannin, saponins and terpenoids, thus known for

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low glycaemic index[8]. Goroho banana fruit extract exhibited capabilities in inhibiting Maillard reactions and preventing the development of diabetes mellitus[9]. Another study was conducted on ethanol extracts of *Musa acuminata*, which was discovered to have antihyperglycemic properties and was noted for its properties in alleviating diabetes[10]. Functional food is consumed as a diet in the daily consumption pattern that positively influences well-being due to the nutritional contents and the bioactive compounds[11,12]. Active compounds in foods provide physiological effects and functional properties[13]. Goroho bananas are known to contain phenolic phytochemical compounds with strong antioxidant activities and thus have the potential to ward off free radicals[14]. Goroho banana flour formulated in food products influences starch absorption, nutrition composition and fibre, regulating the food's glycemic index and suppressing glucose absorption in the intestine[15]. The consumption of functional foods is essential in diabetic management and prevention. This study was carried out to understand the influence of Goroho banana flour on type 1 diabetic rat models.

Materials and Methods

Materials

Subjects were white male 8-10 weeks Sprague-Dawley rats with a body weight of 150-180 grams. Rats (25) were used for this study, where 15 were modelled type 1 diabetic. Type 1 diabetic modelling was performed by administering STZ (streptozotocin) injection (55mg/kg body weight) to the animals to induce diabetes. On Day 5, after induction, blood sugar was examined using an Accu check glucometer (Roche Diagnostics, USA). Modelling was successful when the blood glucose levels reached 180 mg/dL.

Goroho Banana Flour
Goroho bananas were obtained from Rasi village of Ratahan subdistrict, Southwestern Minahasa regency of North Sulawesi, Indonesia (1°02'19"N 124°46'40"E; Figure 1). Goroho bananas were peeled, cleaned and soaked in lukewarm water (approximately 40°C) to prevent enzymatic browning. Cleanly peeled bananas were thinly sliced into chips and sundried in stainless steel trays with 12-14% moisture content. The dried bananas were then grounded in a disc miller to a granular size of mesh 60 (Figure 2).

Experimental animals Care
In vivo testing in this research was approved by the Ethical Committee of Manado State University with number 521/UN41.9/TU/2024. The experimental animals (5 rats each) were placed in 625.5 cm^2 by 18.7 cm cages. The cages were equipped with an air handling unit set at an air speed of 60 ACH, where temperature and humidity are controlled by air conditioning at 22 ± 3°C and a relative humidity of 55-68%. The base utilises clean, dry rice husks, which were sanitised using UV (ultraviolet) lighting before being laid in the cage. The light source in the room was from artificial lights with a 12-hour light duration and a 12-hour dark duration. During the acclimatisation period, standard rodent feed with 18% crude protein and 5.7% fat was fed to the rats. The animals were allowed free access to clean drinking water, and special care was taken to prevent contamination. A week (7 days) before the acclimatisation period, the subjects were fed with standard rodent feed and standard drinking water in the current cage and room, as was the case throughout the study. The modelling process was conducted for 30 days with intragastrical feed and oral gavage[16]. Modelling of the 25 male rat subjects was treated as in Table 1.

Procedures
Blood samples were collected from the tail prick of the rats into EDTA bottles for blood glucose level measurement on days 7, 14, 21, and 30 using a one-touch glucometer (Accu Chek, Roche Diagnostics, USA). The animals were sacrificed under chloroform anaesthesia, and the pancreas was harvested and stained with H&E (Haemotoxylin and Eosin) for histopathological examination. The tissue sections were analysed under a trinocular research microscope (Olympus CX 41) fitted with an Olympus E420. Pancreatic histopathology analysis includes descriptive analysis of pancreatic damage and quantitative analysis of the Langerhans islet (number of islets, dimensions and proportions to β cells). The number of islets and the area of pancreatic tissue were counted at 40X magnification using the ocular grid. [17]

Blood Glucose Levels
Blood glucose levels were measured from the serum collected from the subject's blood for each treatment. The subjects previously fasted for 6 hours before the blood was collected from the *vena orbitalis* and collected (2 mL) in a plain *vacutube* where the serum was separated by centrifugation at 3000rpm for 10 minutes. The separated serum was then collected in a microtube and mixed with a Glory Diagnostic Glucose Reagent Kit (Linier Chemical, Spain). Each bloodwork was blended with 300 µL glucose reagent and 3 µL standard glucose reagent and further analysed calorimetrically using a spectrophotometer (Rayto RT-1200, China) at the 500 nm wavelength[16]. The data obtained was then tabulated and analysed using the R-Software ver. 3.6.1.

Pancreatic Histopathology
The pancreatic organs were harvested after the subjects were sacrificed and kept in 10% NBF (Neutral Buffered Formalin) solution for 3 days to fixate the tissues. Samples of the organs were taken, fitted to cassettes, and soaked again for 24 hours in 10% NBF solution before washing with distilled water for 30 minutes. The dehydration process was further conducted in 70%, 80%, 90% and 96% ethanol (2 hours each), followed by a final soaking of the samples in 100% ethanol for 2 hours. Samples were then soaked in xylol I, II and III (45 minutes each) before entering the tissue processing machine and stored chilled for 24 hours. Samples were cut using a microtome blade at 5 µm and placed on an object glass, ready for staining. The staining process begins with rehydration in Xylol I to V for 5 minutes (each), where the samples were then soaked in absolute ethanol 96%, 80% and 70%, respectively, for 5 minutes each. This was followed by a wash with running distilled water for 5 minutes and then soaking in Haemotoxylin for 5 minutes before washing the excess Heamotoxylin under running distilled water until the colour fades. The sample was then dipped in lithium dilution 10 times and washed under distilled water. This process was repeated with Eosin staining by soaking for 5 minutes and left on clean tissue for 2-3 minutes. The dehydration was finally done by dipping the stained samples (20 times) in 70%, 80%, and 96% absolute ethanol, soaked in Xylol I to V for 5 minutes each before closing the cover glass and sealed with etching glue. The samples are ready for the descriptive analysis of the pancreatic tissue and the Langerhans islet quantifications[16].

Data analysis
Statistical analysis normalises the data with the Shapiro-Wilk test and homogenises the data with the Levene test. A multiple comparison method on independent data was used to define the data normality, equality variance and the proper analysis required. All the analysis utilises R software ver. 3.6.1.

Results and Discussion

The weight gain in all the groups is shown in Figure 3. The observation indicates that on day 14, all the groups were not significantly different in weight. From day 21 until the 28th day, a decrease in body weight was observed on modelled subjects; on the contrary, weight gain was observed on the normal feed subjects. Throughout the study, it was observed that the type 1 diabetic model experienced significant weight loss, while the normal-fed subjects appeared to have experienced weight gain. Weight loss is a common indication of type 1 diabetes due to the hyperglycemic condition caused by insufficient insulin production[18]. In a diabetic condition, the blood sugar levels are high, but tissues and cells cannot gain glucose from the blood. Without glucose as the major energy source, tissues and cells consume lipids and muscle mass for energy replacements. Thyroid dysfunction is closely linked to diabetes mellitus. Thyroid autoimmune disruptions are the most common immunological conditions suffered by type 1 diabetic patients[19]. Hyperthyroidism (high concentrations of thyroid hormones) is most likely to be correlated to diabetes and weight loss. In hyperthyroidism, excessive hormone production leads to weight loss due to the increase in metabolic rate, which requires large amounts of energy to digest fat and muscle mass[20]. Weight gain shown in the K. Pos and K3 groups indicated that the nutritional content of the Goroho banana flour is adequate to fulfil the dietary requirements of the subjects. The proximate contents of the Goroho banana consist of 75.18% carbohydrate, 5.16% protein, 0.97% fat, 2% fibre, and 80.89% of the carbohydrate starch[21]. With the nutritional contents of the Goroho flour, although it was sufficient for the normal feed subjects (K. Pos and K3) to gain weight, Goroho flour could not assist the diabetic models to gain weight.
The blood glucose of all the subjects can be seen in Figure 4. The results indicated significant differences between the K. Pos (Positive Control) and other groups. The K3 group has an average blood glucose level close to the normal group. The K4 group, a diabetic-modelled group fed with Goroho banana flour, had an observable increase in glucose levels.

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Figure 1: The location of Rasi Village, Ratahan Subdistrict, Southwestern Minahasa Regency, North Sulawesi - Indonesia (1°02'19"N 124°46'40" E)

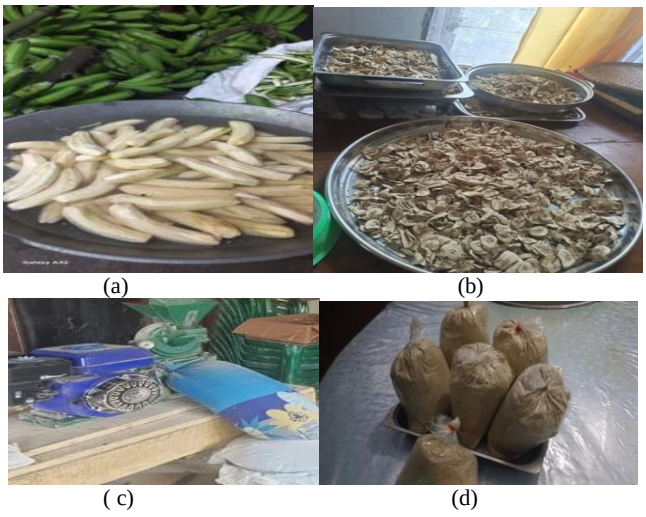

Figure 2: Goroho flour processing: (a) Goroho bananas, peeled and soaked in water. (b) Dried goroho banana chips. (c) Goroho banana milling process. (d) Goroho banana flour.

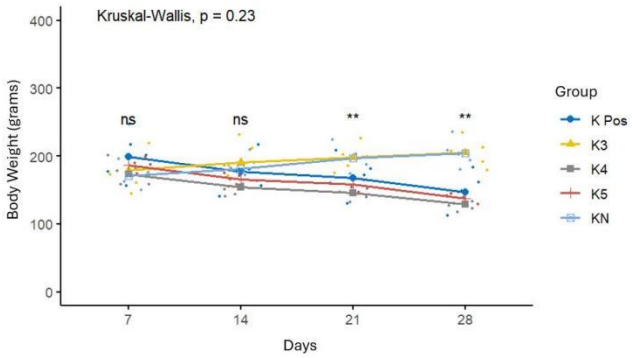

Figure 3: Weight gain (gram) of all the subjects. ns not significance; **Significance.

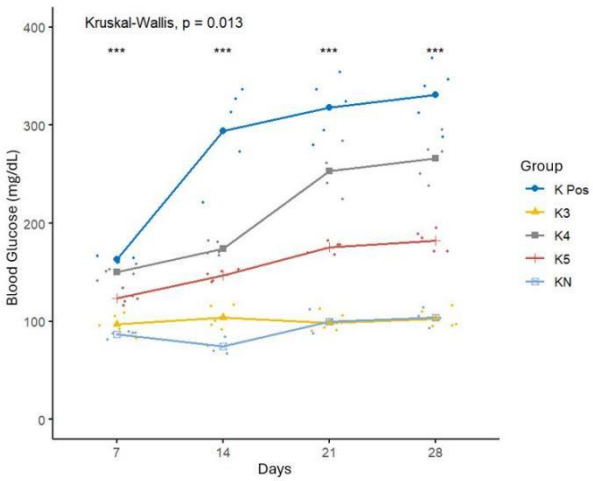

Figure 4: Blood glucose levels of the subjects in all model groups ***Significance

The diabetic-modelled group administered glibenclamide (K5) experienced increased blood glucose levels, but the level rise was insignificant. The increase in blood glucose levels of the K4 and K5 groups were insignificantly different. This study showed that administering Goroho banana flour to the type 1 diabetic-modelled subjects was inconclusive regarding antidiabetic activity. Although the blood glucose levels of the K4 and K5 groups were not significantly different, the trends still exhibited that the Goroho banana flour feed could reduce blood sugar levels in diabetic subjects. The administration of Goroho banana flour feed did not repair or relieve pancreatic damage or raise insulin excretions. This was observed from the increased blood sugar levels in the subjects throughout the study. The diabetic models administered with glibenclamide also indicated reduced blood glucose levels, though not as observed in the normal groups. Glibencamide is a pharmacological agent with the function of elevating the secretion of insulin from the pancreatic β cells. The mechanisms of glibenclamide work through closing the pathways of

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K+, which are ATP sensitive in the β cells, thus initiating membrane depolarisation that opens the Ca^{2+} pathway and increases intracellular Ca^{2+} and triggers insulin exocytosis[22,23].

Langerhans islets of all subjects of the groups can be seen in Figure 5. Measurement results of the islets indicated that K3 and KN were not significantly different, but there was a significant difference with the K. Pos group. Langerhans islets sizes of groups K4 and K5 were not

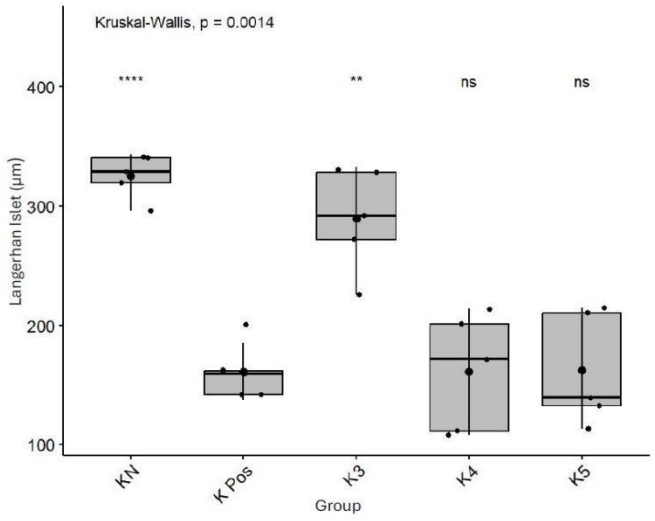

Figure 5. Langerhans islets (µm) of all groups. ns not significance ; **significance ; ***significance

significantly different from K. Pos group. Langerhans islets are a population of various endocrine cells scattered in the parenchyma of the pancreas. Each islet consists of 5 types of cells: the β cell (65-80%), the α cell (15-20%), the δ cell (3-10%), PP cell (1%), and ε cell[24]. Hormones produced by these cells are involved in various nutrient regulatory metabolism processes and blood sugar homeostasis[25]. In this study, all subjects modelled with the STZ (conditioned for type 1 diabetes) showed signs of decreasing sizes of Langerhans islets compared to the normal subjects. According to [26] Langerhans islet damage is closely linked to oxidative stress. Therefore, size reductions of the Langerhans islets in diabetic-induced subjects are due to cell death and tissue damage from oxidative stress. Insulin secretion disorders leading to diabetic conditions are linked to [Ca^{2+}] oscillatory activities of the islets and the functional connectivity between the β cells in the islet[27]. Langerhans islets are formed from cell replication and may be reduced by regulative apoptosis[28]. Thus, even though the Goroho banana flour has been recorded to have antioxidant activities[14], apparently, in this case, it was still not enough to inhibit the damage caused by oxidative stress in the diabetic models.

Effects on pancreatic beta cell count of K4, K5 and K. Pos were not significantly different. The highest cell count was seen in KN and K3. Pancreatic β cells of K4 were 70.4 while K. Pos was 83.8, and they were observed to be insignificantly different. The declining pancreatic beta cell count of the subjects was caused by damage caused by STZ induction. Streptozotocin (STZ) enters the β cell through glucose transporter (GLUT2) and releases toxic nitrate oxides that inhibit aconitase activity, damaging DNA. Consequences of STZ activity result in β cell necrosis[29]. STZ identifies the GLUT2 receptors abundant in the β cells membrane plasma, making the pancreatic β cells a specific STZ target[30]. β cell damages are strongly influenced by hyperglycemic insulin production. Low antioxidant activity is a mechanism that leads pancreatic β cells to be extremely sensitive towards reactive oxygen species (ROS), causing cell death[31]. Therefore, administering exogenous antioxidants exhibits a protection system for the pancreatic β cells[32]. The number of pancreatic β cells in the diabetic groups continuously decreased unless cell protection is sufficiently provided, such as by supplementing exogenous antioxidants. Elevation in blood sugar levels was apparent throughout the study period, while the declining insulin levels are coherent with the diminishing numbers of pancreatic β cells. Goroho banana flour in this study had not made an impact that would provide protective activities towards the pancreatic β cells of the diabetic subjects.

The pancreatic microanatomy of the groups (Figure. 7) depicts the Langerhans islets of the normal-fed subjects being visually larger than the diabetic models. Langerhans islets of the normal-fed subjects appeared histologically normal, with islet cells nearing the capillary (Figure 7, K Negative). The Langerhans islets of K4 were 161.07µm, and K5 (162.05µm) were not significantly different from the K.Pos

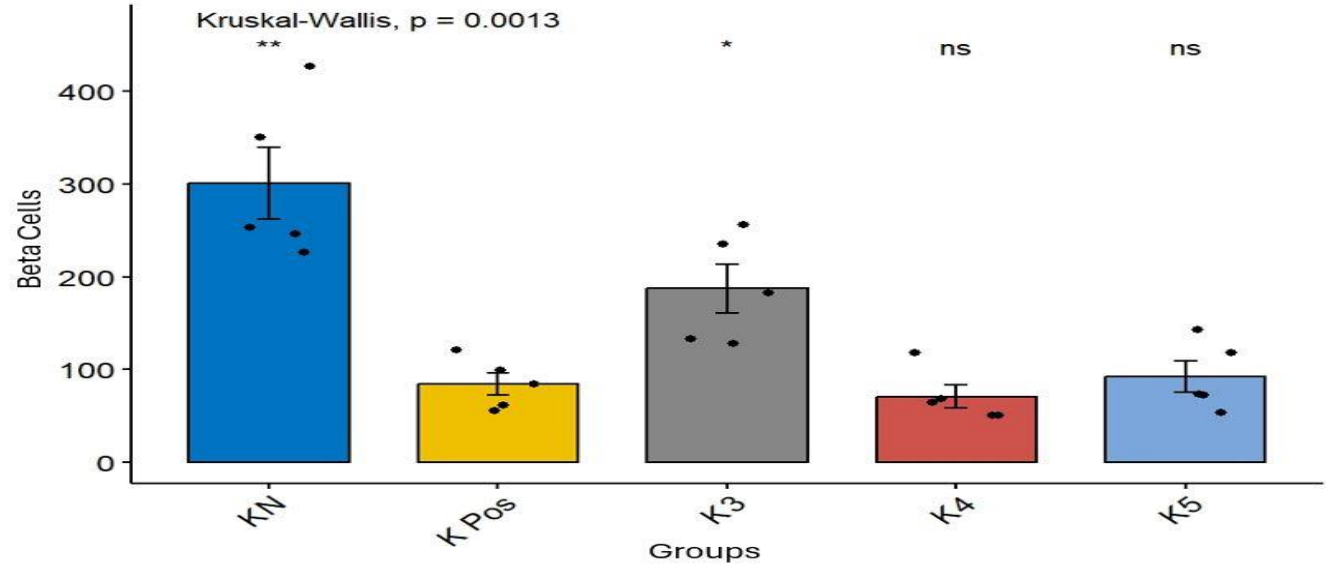

Figure 6: β cells of the groups. ns not significance; *significance; **significance

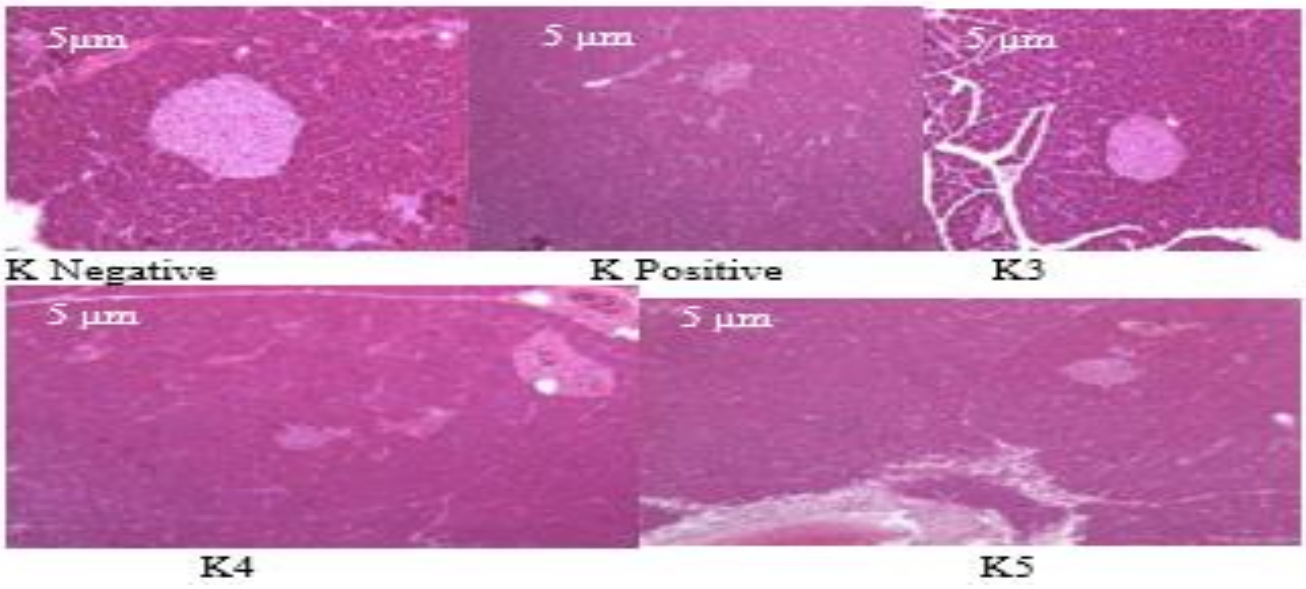

Figure 7: Histology micrographs of the subject's pancreas

Table 1: Group model of treatments

Group	Treatment	Modelling	Number of Animal
KN	Normal Healthy Rat + Standard Rodent Feed	-	5
KPos	Diabetic Rat + Standard Rodent Feed	√	5
K3	Normal Healthy Rat + Goroho Flour	-	5
K4	Diabetic Rat + Goroho Flour	√	5
K5	Diabetic Rat + Standard Rodent Feed + glibenclamide 5mg/kg body weight	√	5

KN Normal Healthy Rat + Standard Rodent Feed; KPos Diabetic Rat + Standard Rodent Feed; K3 Normal Healthy Rat + Goroho Flour; K4 Diabetic Rat + Goroho Flour; K5 Diabetic Rat + Standard Rodent Feed + glibenclamide 5mg/kg body weight

group (161.16 µm). The pancreas of the STZ-induced diabetic subjects appeared to show islets that are experiencing atrophy with mild degranulation, the disintegration of the β cells, and the endocrine cells that are separated by a void. A study conducted[33], indicated that the Langerhans islets of STZ-induced diabetic mice also experienced atrophy and β cell degradations, followed by the forming of hyaline sediments and congestion in the artery. Similar results were observed[34] where STZ-induced subjects notably had smaller Langerhans islets. Histological graphs showed that both groups treated with the Goroho banana flour and glibenclamide on STZ-induced diabetic subjects were not sufficient to repair the endocrine cells of the Langerhans islets.

Goroho banana flour alone had no significant impact on type 1 diabetes. Goroho banana neither repaired nor relieved pancreatic cell damage nor regulated the insulin in the subjects, and despite the insignificant effects of Goroho banana flour towards type 1 diabetes-induced subjects, the Goroho banana flour, however, towards normal subjects (non-diabetic induced groups) had a positive impact of maintaining a stable blood glucose level while providing sustenance with ample nutrition to achieve a stable increase of weight gain. As a functional food or nutraceutical function, the Goroho banana did not impact the subjects in a rehabilitative or recuperative state. Still, it is notably considered to have a preventive function. Further research on this function and its mechanism should be investigated, while potential fortifications to enhance its functionality are also an option to be explored. Explorations towards potential combinations with various antidiabetic or antioxidant compounds such as *Gnetum gnemon L.* seed protein[35,] which potentially would provide free radical scavenging and antidiabetic activities to the end product, or curcumin[36] would be beneficial for its pro-inflammatory, hepatoprotective and kidney protective features. Astaxanthin compound would also be a good fortification material because of its anti-inflammatory, antioxidant, and positive impacts on diabetes and other cardiovascular diseases [36,38].

Conclusion

Goroho bananas in this study are local endemic banana species from North Sulawesi. Goroho bananas, according to folk indigenous knowledge, were known to have medicinal effects on diabetics. This study concludes that the Goroho banana flour had no significant impact on the experimental animals (subjects) suffering from diabetes mellitus. Goroho banana flour in this study did not repair and relieve pancreatic damage or raise insulin excretions. Goroho banana flour and glibenclamide on STZ-induced diabetic subjects were insufficient to restore the Langerhan islets' endocrine cells. Meanwhile, Goroho banana flour fed on healthy subjects displayed good weight gain without significant elevations in blood sugar levels, indicating that the Goroho banana flour contains sufficient nutrients as a staple but does not induce diabetes mellitus. Therefore, Goroho bananas are good functional staples that maintain a stable blood sugar level. In order to upgrade the Goroho banana flour to an active functional food status, it is recommended to be fortified with other compounds with strong antioxidative activities.

Conflict of Interest

The authors declare no conflict of interest

Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

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