RUMPHIUS PATTIMURA BIOLOGICAL JOURNAL
Volume 6, Issue 1 (2024), 001-005
E-ISSN: 2684-804X
DOI: https://doi.org/10.30598/rumphiusv6i1p001-005

Potential of Hotong Flour (*Setaria italica* (L.) Beauv) from Buru Island in Reducing Blood Cholesterol Levels in Wistar Rats with Diabetes Mellitus

Windi Mose [1*], Syahran Wael [2], Mimi Salmawati [3], Didik Wahyudi [4], & Pudji Astuti [5]

[1] Department of Biology, Faculty of Mathematics and Natural Sciences, Universitas Pattimura. Jl. Ir. M. Putuhena, Ambon 97233, Indonesia
[2] Biology Education Study Program, Faculty of Education and Teacher Training, Universitas Pattimura, Jl. Ir. M. Putuhena, Ambon 97233, Indonesia
[3] Department of Chemistry, Faculty of Mathematics and Natural Sciences, Universitas Pattimura. Jl. Ir. M. Putuhena, Ambon 97233, Indonesia
[4] Sekolah Tinggi Ilmu Kesehatan Nasional Surakarta. Jl. Raya Solo, Sukoharjo, Jawa Tengah. 57552, Indonesia
[5] Department of Physiology, Faculty of Veterinary Medicine, Universitas Gadjah Mada. Jl. Fauna, Yogyakarta 55281, Indonesia

**Corresponding Author e-Mail*: windimose@gmail.com

Check for updates

Article History:
Submitted:
January 1st, 2024
Accepted:
January 25th, 2024
Published:
March 20th, 2024

Keywords:
hotong flour; cholesterol; diabetes

ABSTRACT

Hotong flour (*Setaria italica*) can be used as a functional food as therapy in the treatment of diabetes mellitus by reduce cholesterol levels in the blood. Hotong is a rice-like food crop that is usually consumed by the people of Buru Island. Hotong seeds have quite high nutritional content, namely containing 11.18% protein, 2.36% fat, 73.36% carbohydrates, 11.78% water, and 1.32% ash. The energy produced per 100 grams of hotong seeds is 359 calories. Hotong plants can be used as an alternative commodity in a carbohydrate-producing food diversification program. This study aims to determine the potential dose of hotong flour in treating diabetes mellitus by reducing cholesterol levels in the blood of rat. This research used 24 wistar rats animals which were divided into 6 groups which were given hotong flour for 21 days and the cholesterol levels were evaluated on the 7th, 14th, and 21st day. Determination of rat blood cholesterol levels using the enzymatic method. Hotong flour can reduce blood sugar levels at doses of 1 g/kg bw and 1.5 g/kg bw in rat that have been made diabetic by examination on days 7, 14 and 21 days.

How to cite this article:
Mose, W., Wael, S., Salmawati, M., Wahyudi, D., & Astuti, P. (2024). Potential of Hotong Flour (*Setaria italica* (L.) Beauv) from Buru Island in Reducing Blood Cholesterol Levels in Wistar Rats with Diabetes Mellitus. *Rumphius Pattimura Biological Journal, 6*(1), 001-005. https://doi.org/10.30598/rumphiusv6i1p001-005

Journal Homepage: https://ojs3.unpatti.ac.id/index.php/rumphius
Journal E-mail: rumphiusbiojournal@gmail.com ; rumphius.journal@mail.unpatti.ac.id
Research Article: Open Access

INTRODUCTION

Diabetes mellitus or diabetes is a chronic disease that can last a lifetime. Diabetes mellitus (DM) is caused by metabolic disorders that occur in the pancreas organ which is characterized by increased blood sugar or often referred to as hyperglycemia which is caused by a decrease in the amount of insulin from the pancreas. Diabetes can cause cardiovascular disorders, which are quite serious diseases if treatment is not given immediately, which can increase hypertension (Narayan, 2003). Diabetes has 2 types, namely type 1 diabetes mellitus which is the result of an autoimmune reaction against pancreatic cell proteins, while type 2 diabetes is caused by a combination of genetic factors related to impaired insulin secretion, insulin resistance and environmental factors such as obesity, overeating, undereating, exercise and stress, and aging. Diabetes mellitus can arise due to exocrine pancreatic disease when damage occurs to the majority of the islets of the pancreas. Insulin resistance in muscles is the earliest disorder detected in type 1 diabetes (Kong, 2024). The causes of insulin resistance are: obesity/overweight, excess glucorticoids (Cushing's syndrome or steroid therapy), excess growth hormone (acromegaly), pregnancy, gestational diabetes, polycystic ovary disease, lipodystrophy (acquired or genetic, associated with lipid accumulation in the liver), autoantibodies to the insulin receptor, insulin receptor mutations, peroxisome proliferator activator receptor (PPARγ) mutations, mutations causing genetic obesity (e.g.: melanocortin receptor mutations), and hemochromatosis (a hereditary disease that causes tissue iron accumulation). In type 1 diabetes, pancreatic beta cells have been destroyed by an autoimmune process, so insulin cannot be produced (Unnikrishnan, 2024).

Fasting hyperglycemia occurs due to glucose production that cannot be measured by the liver. Although glucose in food remains in the blood and causes postprandial hyperglycemia (after eating), glucose cannot be stored in the liver. If the glucose concentration in the blood is high enough, the kidneys will not be able to reabsorb all the glucose that has been filtered (Mittendorfer *et al.,* 2024). Therefore the kidneys cannot absorb all the filtered glucose. As a result, it appears in the urine (diabetes). When excess glucose is excreted in the urine, this waste will be accompanied by excessive electrolytes. This condition is called osmotic diuresis. Excessive fluid loss can cause increased urination (polyuria) and thirst (polydipsia). Insulin deficiency can also disrupt protein and fat metabolism, leading to weight loss. If there is a lack of insulin, the excess protein in the circulating blood will not be stored in the tissues. In the absence of insulin, all aspects of fat metabolism are greatly increased. Usually this occurs between meals, when insulin secretion is minimal, but when insulin secretion approaches, fat metabolism in diabetes will increase significantly (Su *et al.,* 2024). To overcome insulin resistance and prevent the formation of glucose in the blood, it is necessary to increase the amount of insulin secreted by pancreatic beta cells. In sufferers of impaired glucose tolerance, this condition occurs due to excessive insulin secretion, and glucose levels will remain at normal levels or increase slightly. However, if the pancreatic beta cells cannot meet the increased demand for insulin, then glucose levels will increase and type II diabetes will develop (Fan *et al.,* 2024).

Diabetes is often caused by genetic factors and a person's behavior or lifestyle. Apart from that, social environmental factors and the use of health services also cause diabetes and its complications. Diabetes can affect various organ systems in the human body over a certain period of time, which are called complications. Diabetes complications can be divided into microvascular and macrovascular (Sari *et al.,* 2024). Microvascular complications include nervous system damage (neuropathy), kidney system damage (nephropathy) and eye damage (retinopathy). Risk factors for type 2 diabetes mellitus include age, physical activity, smoke exposure, body mass index, blood pressure, stress, lifestyle, family history, cholesterol, triglycerides, history of glucose abnormalities and other disorders (Jalali *et al.,* 2024). Tests for diabetes mellitus that can be carried out include random blood sugar checks, fasting blood sugar checks, 2-hour prandial blood sugar checks, hBa1c checks, and oral glucose tolerance checks. Diagnosis of checking blood sugar levels such as fasting blood sugar > 126 mg/dL, 2 hour blood sugar > 200 mg/dL, random blood sugar > 200 mg/dL. This reference applies throughout the world. Another way of diagnosis is by measuring HbA1c > 6.5%. Prediabetes is a patient with fasting blood glucose levels between 100 mg/dL to 125 mg/dL; or 2 hours of fasting between 140 mg/dL to 199 mg/dL, or A1C levels between 5.7–6.4% (Rothberg, 2024). Treatment that can be done for diabetes mellitus sufferers is insulin therapy, taking diabetes medication, trying alternative treatments, undergoing surgery and improving life style (Yadav *et al.,* 2024).

Diabetes mellitus can be treated by several synthetic drugs such as insulin and oral hypoglycemic agents. However, they have some side effects at higher doses, and oral medications are not suitable for use during pregnancy. Thus, one effort to manage diabetes mellitus is through non-pharmacological therapy, namely by consuming functional foods. Functional food is categorized as food that contains active compounds that have health benefits (Elkhalifa *et al.,* 2024). Functional foods come from natural ingredients that improve the immune system, prevent disease, help to recover from certain disease conditions, control physical and mental disorders, and prevent aging. Currently, there are many food products circulating in Indonesia that have certain physiological benefits, such as lowering blood sugar, lowering cholesterol levels, increasing calcium absorption, lowering blood pressure, and others that come from various groups of compounds such as fiber, oligosaccharides, isoflavones, polyphenols, peptides, unsaturated fatty acids, lactic acid bacteria or others (Kumar *et al.,* 2024). In Maluku, a potential source of ingredients that can be used as a natural functional food source to treat diabetes mellitus is the hotong plant. Hotong is a plant originating from the island of Buru, Maluku province, consumed by local people as a substitute for rice. The use of hotong seeds as an alternative food to lower cholesterol levels is not yet widely known by the public. This is because there is no scientific evidence regarding the truth of its efficacy in reducing blood cholesterol levels. For this reason, it is necessary to carry out research on gived hotong flour to reduce cholesterol levels in rat.

MATERIALS AND METHOD

This research was an experimental study using 3 month old male Sprague dawley rats divided into 6 groups. Group 1 as a control was given water. Group 2 as a negative control was only given the hyperuricemia inductor potassium oxonate 250 mg/kg bw. Group 3 as a positive control was gived allopurinol 5 mg/kg bw. Group 4 was gived hotong flour 1 gram/kg bw. Group 5 hotong flour 1.5 grams/kg bw. Group 6 was gived hotong flour 2.5 grams/kg bw. The dose of potassium oxonate that can cause hyperuricemia in test animals is 250 mg/kg bw. The dose of Allopurinol used in the treatment of rat with hyperuricemia was 5 mg/kg bw rat. Induction of hyperuricemia was carried out by dissolving 250 mg/kg bw of potassium oxonate in 0.5% CMC-Na, administered via the intraperitoneal route to each test animal treatment, two hours after administration of hotong flour on days 0, 7, 14, 21 days. Hotong flour is gived twice a day. Blood samples were taken from rat, carried out 2 hours after potassium oxonate induction.

Data analysis was carried out by processing the recorded absorbance data and calculating it into blood cholesterol levels in mg/dL units. The tools used were: rat cage, rat drinker, glucometer, syringe plunger, analytical scale, gloves, blender, flour sieve, syringe, measuring cup, rotary evaporator, and 500 mL beaker glass. The materials used were 3 month old male rats weighing around 250 g, cotton, physiological NaCl, hotong seeds, sterile distilled water, absolute ethanol, technical glucose, and glucose strips.

RESULTS AND DISCUSSION

Hotong flour uses as raw material 5 kg of ground hotong seeds taken from Waeperang Village, Buru Island, Maluku, Indonesia. Determination of rat blood cholesterol levels used the enzymatic photometric test method, namely cholesterol oxidase phenol aminoantipyrone, is cholesterol in blood plasma reacting with cholesterol esterase to produce free cholesterol which then reacts with phenol, 4-aminoantipyrine with a peroxidase catalyst to form quinoneimine which is red in color. Quinoneimine is what absorbance is measured. The blood cholesterol levels of diabetic rat can be seen in **Table 1**.

Table 1. Average value and standard deviation of rat blood cholesterol levels.

Group	Days			
	0	7	14	21
Control	58.38 ± 11	56.24 ± 55	57.62 ± 35	54.08 ± 19
Control negative	76.33 ± 47	72.61 ± 52	79.70 ± 27	76.11 ± 39
Control positive	60.41 ± 16	44.49 ± 39	67.30 ± 46	71.74 ± 15
Hotong flour 1 g/kg bw	65.33 ± 27	40.46 ± 36	43.97 ± 84	68.77 ± 32
Hotong flour 1.5 g/kg bw	77.21 ± 8	65.78 ± 26	56.90 ± 75	52.96 ± 39
Hotong flour 2.5 g/kg bw	75.49 ± 30	76.50 ± 64	78.61 ± 31	73.57 ± 41

In this study, rats were given hotong flour twice a day for 21 days and induced with the hyperuricemia inducer potassium oxonate and blood samples were taken two hours later. Blood samples were taken on day number 0, 7th, 14th and 21st. The blood was then centrifuged for 10 minutes at a speed of 8000 rpm. The blood plasma that has been separated from the centrifugation results is transferred into a tube and reacted with CHOD-PAP reagent, then after the operating time (OT) the absorbance of the solution at the wavelength obtained is read (Zhang *et al.,* 2024). Absorption data obtained from sampling day 0, 7th, 14th and 21st was then converted into blood cholesterol level data. The results of the conversion of data on blood cholesterol levels from each group showed changes from normal levels. Cholesterol levels in the treatment and control groups experienced irregular fluctuations, possibly due to the rats' hormones being uncontrolled. Blood cholesterol levels that occurred on 7th day in the positive control group (44.49 ± 39), hotong group 1 g/kg bw (40.46 ± 36), hotong group 1.5 g/kg bw (65.78 ± 26), lower than the negative control (72.61 ± 52) while the 2.5 g/kg bw hotong group (76.5 ± 64) was higher. On the 14th day, blood cholesterol in the positive control group (67.30 ± 46), hotong group 1 g/kg bw (43.97 ± 84), hotong group 1.5 g/kg bw (56.90 ± 75), group hotong 2.5 g/kg bw (78.61 ± 31), lower than the negative control (79.70 ± 27). On the 21st day, blood cholesterol in the positive control group was (71.74 ± 15), the hotong group was 1 g/kg bw (68.77 ± 32), the hotong group was 1.5 g/kg bw (52.96 ± 39), the hotong 2.5 g/kg bw (73.57 ± 41), lower than the negative control (76.11 ± 39).

Dietary fiber by consume foods in fiber experienced a significant reduction in the prevalence of hypertension, blood cholesterol levels and blood triglyceride levels. Intake of foods containing high levels of fiber can influence changes in blood cholesterol levels. The antioxidant activity contained in hotong is also one of the factors that influence changes in rat blood cholesterol (Yang *et al.,* 2024). The antioxidant activity can reduce cholesterol levels by the mechanism of antioxidant activity from the active compounds contained in hotong flour, increasing the metabolism of cholesterol into bile acids, and increasing excretion, bile acids through feces. Hotong flour can be used as the main raw material in the production of foods containing soluble dietary fiber, which can be a new additional ingredient for research and development of functional foods. Hotong flour can be a functional food that can reduce blood cholesterol levels for diabetes sufferers. Hotong flour generally has a higher protein content than sweet potato flour, but lower than wheat flour, corn flour and cassava, but the carbohydrate content is higher (Citarrella *et al.,* 2024). Hotong has a starch content of 90% and amylose 31.3-38.9%. Starch is of two types: amylose, a straight-chain polyglucan consisting of about 1000 α-D (1→4) glucose; and amylopectin, a branched glucan consisting of approximately 4000 glucose units with many branches with α-D (1→6) bonds. Inside the granule. This molecular structure makes flour difficult for digestive enzymes such as amylase to access. The amylose and amylopectin contained in hotong flour are thought to play a role in reducing cholesterol levels in this study. The final result of amylose metabolism in the body is glucose, with the help of the amyloglucosidase and amylase enzymes glucose can be formed.

CONCLUSION

Hotong flour can be a functional food that can reduce blood cholesterol levels for diabetes sufferers. Intake of foods containing high levels of fiber can influence changes in blood cholesterol levels, increase the metabolism of cholesterol into bile acids, and increase the excretion of bile acids through feces. Cholesterol levels in the treatment group give hotong flour and the control experienced irregular fluctuations, possibly due to the hormones of the mice which could not be controlled. The blood cholesterol levels that occurred on the 7th day in the positive control group, the hotong group was 1 g/kg bw, and the hotong group was 1.5 g/kg bw lower than the negative control, while the hotong group was 2.5 g/kg bw is higher. On the 14th day, blood cholesterol in the positive control group, the hotong group was 1 g/kg bw, the hotong group was 1.5 g/kg bw, the hotong group was 2.5 g/kg bw lower than the negative control. On the 21st day, blood cholesterol in the positive control group, the hotong group was 1 g/kg bw, the hotong group was 1.5 g/kg bw, the hotong group was 2.5 g/kg bw lower than the negative control.

AUTHORS CONTRIBUTION

S. Wael designed and conducted the study, analyzed and interpreted the data, and wrote a draft of the manuscript. W. Mose and D. Wahyudi analyzed and interpreted the data. M. Salmawati & P. Astuti reviewed the draft manuscript, and supervised the entire process.

ACKNOWLEDGMENTS

Financial support for this research and development provided by the Industrial Research and Technology Agency, Pattimura University, PNBP Program No: 248/UN13.3/LT/LPPM/2023.

CONFLICT OF INTEREST

The authors declare no conflicts of interest, and will take full responsibility for the content of the article, including implications of AI-generated art.

REFERENCES

Citarrella, R., Chianetta, R., Amodeo, S., Mirarchi, L., Licata, A., Soresi, M., & Giannitrapani, L. (2024). Effectiveness of a Food Supplement Based on Glucomannan, D-Chiro-Inositol, Cinnamomum zeylanicum Blume and Inulin in Patients with Metabolic Syndrome. *Nutrients*, *16*(2), 249. https://doi.org/10.3390/nu16020249

Elkhalifa, A. M., Nazar, M., Ali, S. I., Khursheed, I., Taifa, S., Ahmad Mir, M., & Nabi, S. U. (2024). Novel Therapeutic Agents for Management of Diabetes Mellitus: A Hope for Drug Designing against Diabetes Mellitus. *Life*, *14*(1), 99. https://doi.org/10.3390/life14010099

Fan, G., Zhang, B., Wang, J., Wang, N., Qin, S., Zhao, W., & Zhang, J. (2024). Accurate construction of NIR probe for visualizing HClO fluctuations in type I, type II diabetes and diabetic liver disease assisted by theoretical calculation. *Talanta*, *268*, 125298. https://doi.org/10.1016/j.talanta.2023.125298

Jalali, M., Bahadoran, Z., Mirmiran, P., Azizi, F., & Hosseinpanah, F. (2024). Severity of adipose tissue dysfunction is associated with progression of pre-diabetes to type 2 diabetes: the Tehran Lipid and Glucose Study. *BMC Public Health*, *24*(1), 1-9. https://doi.org/10.1186/s12889-023-17381-1

Kumar, P., Rai, S., & Joshi, A. (2024). Role of functional foods and nutraceuticals for depression, post-traumatic stress disorder, and suicidal behaviors. In *Nutraceutical Fruits and Foods for Neurodegenerative Disorders* (pp. 101-122). Academic Press. https://doi.org/10.1016/B978-0-443-18951-7.00006-2

Kong, A. P., Chow, E. Y., Luk, A. O., & Chan, J. C. (2024). Other Disorders with Type 1 Diabetes and Atypical Phenotypes. *Textbook of Diabetes*, 216-224. https://doi.org/10.1002/9781119697473.ch15

Mittendorfer, B., van Vliet, S., Smith, G. I., Petersen, M. C., Patterson, B. W., & Klein, S. (2024). Impaired plasma glucose clearance is a key determinant of fasting hyperglycemia in people with obesity. *Obesity*. https://doi.org/10.1002/oby.23963

Narayan, K. V., Boyle, J. P., Thompson, T. J., Sorensen, S. W., & Williamson, D. F. (2003). Lifetime risk for diabetes mellitus in the United States. *Jama*, *290*(14), 1884-1890. https://doi.org/10.1001/jama.290.14.1884

Rothberg, A., Lean, M., & Laferrère, B. (2024). Remission of type 2 diabetes: always more questions, but enough answers for action. *Diabetologia*, 1-9. https://doi.org/10.1007/s00125-023-06069-1

Sari, D. V., Ediyono, S., & Fatmawati, F. (2024). The relationship between smoking behavior and the fulfillment of nutritional needs in the community based on the health belief model theory on blood sugar levels in patients with diabetes mellitus. In *Proceedings of Malikussaleh International Conference on Education Social Humanities and Innovation (Miceshi)* (Vol. 1, No. 01, pp. 0002-0002).

Su, T., He, Y., Huang, Y., Ye, M., Guo, Q., Xiao, Y., & Luo, X. (2024). Myeloid-derived grancalcin instigates obesity-induced insulin resistance and metabolic inflammation in male mice. *Nature Communications*, *15*(1), 97. https://doi.org/10.1038/s41467-023-43787-x

Unnikrishnan, R., & Mohan, V. (2024). Pancreatic Disease and Diabetes. *Textbook of diabetes*, 319-329. https://doi.org/10.1002/9781119697473.ch23

Yang, D., Shen, J., Tang, C., Lu, Z., Lu, F., Bie, X., & Zhao, H. (2024). Prevention of high-fat-diet-induced obesity in mice by soluble dietary fiber from fermented and unfermented millet bran. *Food Research International*, 113974. https://doi.org/10.1016/j.foodres.2024.113974

Yadav, J. P., Singh, A. K., Grishina, M., Pathak, P., Verma, A., Kumar, V., & Patel, D. K. (2024). Insights into the mechanisms of diabetic wounds: pathophysiology, molecular targets, and treatment strategies through conventional and alternative therapies. *Inflammopharmacology*, 1-80. https://doi.org/10.1007/s10787-023-01407-6

Zhang, H., Sun, Y., Zou, Y., Chen, C., & Wang, S. (2024). Stigmasterol and gastrodin, two major components of banxia-baizhu-tianma decoction, alleviated the excessive phlegm-dampness hypertension by reducing lipid accumulation. *Journal of Ethnopharmacology*, *319*, 117193. https://doi.org/10.1016/j.jep.2023.117193