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Sorghum flour's effect on improving plasma lipid profile and atherogenic index in diabetic rats

Pengaruh tepung sorgum dalam memperbaiki profil lipid plasma dan indeks aterogenik pada tikus diabetes

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Abstract

Dyslipidemia increases the risk of coronary heart disease in people with diabetes. Increased consumption of foods substantial in fiber and antioxidants, such as sorghum, can help people with diabetes manage their lipid profiles and improve insulin sensitivity. The study aimed to evaluate how sorghum flour affected diabetic rats' plasma atherosclerosis index (IAP) score and blood lipid profile. A randomized control design was used for the research's experimental methodology. In 2019, the study was carried out at P3G Laboratory UGM. 18 male Wistar rats served as the subjects and were separated into three groups: treatment (P) (5 g/mouse/day for 28 days), positive control (K+), and negative control of sorghum flour (K-). By administering nicotinamide and streptozotocin (STZ), the DM rat model was created (NA). The GPO-PAP method was used to measure TG levels. Total cholesterol, low-density lipoprotein, and high-density lipoprotein were all measured using CHOD-PAP. The log (TG/HDL) ratio (IAP) calculated the plasma atherosclerosis index. Paired T-tests, Wilcoxon, Anova, and Kruskal-Wallis, were used to evaluate the data. According to the findings, there were significant changes in the groups' baseline and post-intervention levels of total cholesterol (p=0,003), triglycerides (p=0,002), low-density lipoprotein (p=0,003), high-density lipoprotein (p=0,002), and IAP (p=0,001). In conclusion, feeding DM rats sorghum flour altered their blood lipid levels and plasma atherosclerosis index (IAP). Their LDL, triglycerides, and total cholesterol can all be reduced with a daily intake of 5 g per person.

Keywords: Diabetes mellitus, lipid profile, sorghum flour

Abstrak

Penderita diabetes berisiko terhadap penyakit jantung koroner karena faktor dislipidemia. Profil lipid penderita diabetes dapat dikontrol dengan meningkatkan asupan makanan tinggi serat dan antioksidan berupa sorgum, yaitu meningkatkan sensitivitas insulin dan memperbaiki profil lipid. Tujuan dari penelitian adalah untuk mengukur pengaruh pemberian tepung sorgum terhadap profil lipid darah dan nilai indeks aterosklerosis plasma (IAP) pada tikus diabetes. Desain penelitian yaitu eksperimental melalui rancangan kontrol acak. Penelitian telah dilakukan di Laboratorium P3G UGM, 2019. Subjek merupakan 18 ekor tikus wistar jantan dibagi menjadi 3 kelompok, kontrol negatif tepung sorgum (K-), kontrol positif (K+), dan perlakuan (P) (5 g/tikus/hari selama 28 hari). Model tikus DM diperoleh dengan menginduksi streptozotocin (STZ) dan nicotinamide (NA). Kadar trigliserida (TG) diukur dengan metode GPO-PAP. Kolesterol total, low-density lipoprotein dan high-density lipoprotein diukur dengan metode CHOD-PAP. Sementara itu, indeks aterosklerosis plasma (IAP) dihitung dari log (TG/HDL). Analisis data menggunakan uji T berpasangan, Wilcoxon, Anova, dan Kruskal-Wallis. Hasil penelitian menunjukkan bahwa terdapat perbedaan yang bermakna kadar kolesterol total (p=0,003), trigliserida (p=0,002), low-density lipoprotein (p=0,003), high-density lipoprotein (p=0,002) dan IAP antara kelompok sebelum dan sesudah nilai intervensi (p=0,001). Kesimpulannya, pemberian tepung sorgum berpengaruh terhadap lipid darah dan indeks aterosklerosis plasma (IAP) pada tikus DM, dan dosis 5 g/ekor/hari dapat menurunkan LDL, trigliserida, kolesterol total.

Kata Kunci: Diabetes mellitus, profil lipid, tepung sorgum

Introduction

Diabetes mellitus (DM) is a metabolic disorder characterized by hyperglycemia, impaired insulin action, or both (Punthakee et al., 2018). According to the International Diabetes Federation (IDF), in 2021, as many as 537 million people worldwide will suffer from DM. It is estimated to continue to increase until 2030 to 643 million people and 783 million people in 2045 (International Diabetes Federation, 2021). In Indonesia in 2019, 10,7 million cases were found. This number makes Indonesia the only Southeast Asian country out of 10 with the highest number of diabetes cases worldwide (Kemenkes RI, 2020).

DM patients have substantial risk factors for cardiovascular disease. Dyslipidemia in DM has a risk of 2 to 4 times higher than non-DM. Diabetes is characterized by increased triglycerides (TG), a drop in HDL, and a rise in LDL (LDL). Lipid damage in diabetes accelerates atherosclerosis (Balikai et al., 2020; Pinakesty & Azizah, 2020). Index atherogenic plasma (IAP) characteristics derived from triglyceride (TG) and high-density lipoprotein (HDL) profiles can be used to determine atherosclerosis risk. IAP is a mathematical relationship between TG and HDL in the form of logs (TG/HDL), from which three risk classes are derived, namely (1) low risk with an IAP value of <0,11; (2) moderate risk if the IAP value is between >0,12 and <0,21; (3) high risk if the IAP value is >0,21 (Karunia et al., 2021). Dietary regulation is needed to reduce DM risk factors by increasing the consumption of fresh vegetables and fruits, whole grains, lean milk, fish, and nuts (Amanda et al., 2021; Basiak-Rasała et al., 2019).

One of the local foods that contain high antioxidants and fiber, and low IG is sorghum (*Sorghum bicolor L. Moench*), the five most essential kinds of cereal in the world after wheat, rice, corn, and barley (Jyothsna et al., 2015). In addition, sorghum can also be an alternative to functional food because it contains anthocyanins and dietary fiber that are beneficial for health (Monikasari et al., 2023; Yustina et al., 2021).

A study on the effect of sorghum extract on lipid profiles in rats fed a high-fat diet showed that 5% of sorghum extract reduced total cholesterol, LDL, and triglyceride levels (Park et al., 2012). Several studies have demonstrated that sorghum extract can reduce blood glucose levels and enhance insulin sensitivity in rats on a high-fat diet. Additionally, phenolic sorghum extract can reduce serum insulin levels in diabetic rats (Chung, 2011).

The manufacture of sorghum flour will encourage the emergence of processed sorghum products that are more diverse and practical to support the diversification program of food consumption. Sorghum can be processed into intermediate or semi-finished products like rice seeds and flour. Processing into flour and extending shelf life can also increase swellability and is more soluble in water so sorghum flour can be made into various dry and wet foods (Sutrisna, 2012).

Sorghum flour has a protein content of 10,11%; fat 3,65%; crude fiber 2,74%; ash 2,24%; and 80,43% starch. The starch content of sorghum flour is higher than that of corn and wheat flour. Sorghum flour's fiber and fat content are also higher than wheat flour. Research on the administration of sorghum in flour in diabetic rats associated with lipid profile and index atherogenic plasma is still limited. Based on this description, it is necessary to conduct a study that examines the effect of giving sorghum flour (Sorghum bicolor L. Moench) on lipid profiles and index atherogenic plasma in diabetic rats. The study aimed to determine the effect of sorghum flour on lipid profile and index atherogenic plasma in Wistar rats (Rattus norvegicus) with diabetes mellitus.

Methods

The research is a true experimental study with pre-and post-tests and a control group design. The research was conducted in January and February 2019 at the Central Laboratory of Food and Nutrition Studies, Gadjah Mada University (UGM), Yogyakarta. The Health Research Ethics Committee (KEPK) of the Faculty of Medicine at

Diponegoro University approved the study, with code of ethics number 03/EC/H/FK - UNDIP/I/2019, on January 7, 2019.

The research subjects used 18 male rats of the Wistar strain (Rattus norvegicus) obtained from the Experimental Animal Development Unit (UPHP) Universitas Gadjah Mada, with initial body weight 180 - 200 g, aged 8-12 weeks, healthy (not disabled) and had GDP > 250 mg/dl. Sampling was done by simple random sampling method into three groups, and each group consisted of 6 tails, namely the negative control group, healthy rats fed standard feed (K-). The positive control group, DM rats, was fed a standard diet (K+). Moreover, the treatment group, DM rats, were given intervention feed in 5 g/rat/day sorghum flour homogenized with standard feed (P).

All subjects were acclimatized in individual cages, given standard Comfeed AD II feed of 20 g/day, and drank ad libitum for seven days. Comfeed AD II contains 51% carbohydrates, 15% protein, 7% fat, and 7% fiber. The rats were kept in a well-ventilated room, with 12 hours of the light cycle (06.00-18.00), cage temperature 25-28°C, and cage cleaning every day. The rest of the feed was weighed every day. Furthermore, the body weight of the rats was weighed every three days during the study. After acclimatization, the positive control and treatment group rats were injected intraperitoneally with STZ 45 mg/kg/W and NA 110 mg/kg/W. Furthermore, the rats fasted for 8-10 hours three days after injection. Then blood was taken through the retro-orbital plexus to determine the GDP, total cholesterol, LDL, HDL, triglycerides levels, and IAP (pre-test). Rats have diabetes when the GDP is >250 mg/dl (Ghasemi et al., 2014).

The intervention feed was grinding the dried whole sorghum seeds using a grinder with a sieve size of 70 mesh. Sorghum seeds are obtained from Pracimantoro, Wonogiri. The finished sorghum flour was then homogenized with Comfeed AD II standard feed with 5 g of sorghum flour and 15 g of standard feed. After the sorghum flour was mixed with standard feed, it was molded into pellets using an extruder and dried at a low temperature of ±40°C for 8 hours using a cabin dryer. Sorghum flour contains 73,06% carbohydrates, 8,91% protein, 4,14% fat, and 8,83% fiber. Making intervention feed is conducted at the Laboratory of the Center for Food and Nutrition Studies (PSPG), UGM.

The intervention was carried out for 28 days. During the intervention period, group (P) rats were given intervention feed in the form of 5 g of sorghum flour, which had been homogenized with 15 g of AD II standard feed and drinking water ad libitum, while the (K-) and (K+) groups were only given AD standard feed II as much as 20 g and drinking water ad libitum. After the intervention, the rats were fasted for 8-10 hours and then anesthetized using ketamine 60 mg/kg BB rats. Then 3 ml of rat blood was taken through the retro-orbital plexus to check the triglycerides, total cholesterol, LDL, and HDL levels and get the IAP (post-test) value. Triglyceride levels were determined by the Glycerol 3 Phosphate Oxidase-Phenol Amino Phenazone (GPO-PAP) method and total cholesterol, LDL, and HDL using Cholesterol Oxidase-Peroxidase Aminoantipyrine Phenol (CHOD-PAP) with the principle of enzymatic spectrophotometry. Meanwhile, Plasma Atherogenic Index (IAP) was calculated from log (TG/HDL). Rat blood serum was analyzed in the Center for Food and Nutrition Studies Laboratory, Gadjah Mada University, Yogyakarta.

The normality of the data was tested with Shapiro-Wilk. All variables consisting of triglycerides, HDL, LDL, and IAP values were normally distributed, so the statistical test was Paired T-Test. Differences in the effect between groups were analyzed by ANOVA parametric statistical test on normally distributed data, followed by Duncan's Post Hoc test. Not normally distributed data were tested by Kruskal Wallis non-parametric statistics and continued with the Mann-Whitney Test to see the difference in influence between groups.

Result and Discussion

Subject Condition After Injection of Streptozotocin (STZ) and Nicotinamide (NA)

Based on Table 1, the negative control group (K-) has an average GDP in the normal range. There was no significant difference in the average body weight of rats between groups (p>0,05). Mice with normal lipid profile category were seen based on cholesterol < 200 md/dL, HDL 35 mg/dL, LDL 7-27.2 mg, and triglycerides 26-145 mg/dL (Mahdi et al., 2020; Sa'adah et al., 2017).

Table 1. Results of conditioning for DM Rats

Groups	n	GDP Average ± SD (mg/dl)	p-value
Negative control (K-)	6	67,97 ± 1,83^{a}	0,001^{1**}
Positive control (K+)	6	267,06 ± 3,31*^{b}	
Treat (P)	6	267,06 ± 3,26*^{b}	

*Meet the criteria for diabetes mellitus, ^{1}One Way Anova test, ^{a,b}Different notations in the same column indicate a significant difference in Duncan's test, **Significant (*p*<0,05)

Conditioning DM rats after injection of streptozotocin (STZ) and nicotinamide (NA) showed that positive control (K+) and treatment (P) rats had diabetes with fasting blood glucose (GDP) >250 mg/dl (Ghasemi et al., 2014). DM occurs due to STZ acting directly on pancreatic cells β, with a cytotoxic action mediated by reactive oxygen species (ROS). STZ enters pancreatic cells β via the glucose transporter (GLUT2) and causes decreased excretion of GLUT2. It results in a decrease in peripheral insulin receptor sensitivity that has an impact on increasing insulin resistance and increasing blood glucose levels (Firdaus et al., 2016). Administration of NA serves to maintain the sensitivity of pancreatic cells so as not to cause excess toxicity caused by STZ (Fukaya et al., 2014).

This study's results align with research on the effect of Biophytum sensitivity in diabetic rats induced by STZ-NA. This study also aligns with research on the antioxidant role of coumarin in STZ-NA-induced diabetic rats. These two studies showed that the injection of STZ in as much as 45 mg/kg BB rats and NA in as much as 110 mg/kg BB rats could increase the GDP levels of rats to >250 mg/dl (Abd El-Twab et al., 2016; Ananda et al., 2012).

Subject's Weight During Research

The group (K+) significantly increased mean weight during acclimatization to DM conditioning, but there was a significant decrease during the DM conditioning period to intervention (Table 2).

Table 2. Average body weight of Rats during the study (n= 6)

Groups	Mean ± SD (mg/dl)			p^{1}	p^{2}
	Acclimatization	Conditioning DM	Intervention		
Negative control (K-)	185,00 ± 6,63	191,50 ± 6,83	215,83 ± 5,74^{a}	0,001^{2*}	0,001^{2*}
Positive control (K+)	187,17 ± 2,99	193,67 ± 3,33	178,17 ± 3,19^{b}	0,001^{2*}	0,001^{2*}
Treat (P)	185,83 ± 5,34	192,50 ± 5,65*	206,17 ± 5,19^{c}	0,001^{2*}	0,001^{2*}
p	0,772^{1}	0,793^{1}	0,001^{1*}		

^{1}One Way Anova test, ^{2}Paired T-Test, $^{a, b, c}$Different notations in the same column indicate a significant difference in Duncan's test, p1 Acclimatization-DM conditioning, p2 DM-intervention conditioning, *Significant (p<0,05)

Based on the One Way Anova test results, there was no significant difference in mean weight between groups during the acclimatization period (p=0,772) and DM conditioning (p=0,793). However, there was a significant difference during the intervention period (p<0,05). Duncan's Post Hoc test showed significant differences in triglyceride levels after the intervention between all groups.

The decrease in mean weight during the intervention in the (K+) group was due to this group's insulin resistance and not receiving nutritional therapy. Insulin resistance causes the body to be unable to absorb glucose in the blood optimally and disrupts the glycolysis process, triggering the glycogenolysis process (Savych & Marchyshyn., 2017). The process of glycogenolysis that occurs continuously can cause weight loss. Group (P) mice experienced increased body weight during the intervention because this group received nutritional therapy through feed with a low glycemic index, high fiber and antioxidants, and sorghum flour. This feed can increase insulin sensitivity so the body can absorb glucose in the blood and stop glycogenolysis (Kim & Park, 2012).

Rat Feed Consumption During Intervention

During the intervention period, there was a significant difference in the average feed consumption between groups (K-), (K+), and (P) based on the results of the One Way Anova test with p=0,001 (Table 3). In Duncan's Post Hoc test, it was found that the difference in the average feed was found in the (K+) group with the (K-) and (P) groups, but there was no difference in the average feed consumption among (K-) with a (P).

Table 3. Average feed consumption of rats during the intervention

Groups	n	Average ± SD (mg/dl)	p-value
Negative control (K-)	6	16,97 ± 0,28^{a}	0,001^{1*}
Positive control (K+)	6	18,66 ± 0,14^{b}	
Treat (P)	6	17,08 ± 0,24^{a}	

[1]One way Anova test, $^{a,\ b}$Different notations in the same column indicate a significant difference in Duncan's test, *Significant (p<0,05)

The highest average feed consumption was in the (K+) group, but there was a decrease in body weight in this group. Because the (K+) group experienced insulin resistance which caused the glycogenolysis process (Savych & Marchyshyn, 2017), the situation will cause leptin's performance in controlling appetite in the hypothalamus and brain stem from being disrupted because the body's cells do not receive glucose by insulin performance, so the body will assume that it still needs energy and continues to feel hungry. The body then produces energy by burning fat and muscle. This condition causes weight loss (Lee, 2010).

Total Cholesterol, Triglyceride, HDL, and LDL Levels Before and After Giving Sorghum Flour

Table 4 shows significant variations between the total cholesterol levels of each group before and after the intervention (p< 0,05). In addition, there were significant differences between groups in total cholesterol levels before and after the intervention and delta changes (p< 0,05). The high levels of total cholesterol in the (K+) and (P) groups before the intervention occurred because insulin resistance conditions increased gluconeogenesis which caused excess free fatty acids (Nuraini, Sulchan and Dieny, 2017). The group (K-) also experienced hypercholesterolemia, presumably due to an increase in the subject's body weight during the acclimatization period to DM conditioning.

Groups (K+) and (P) experienced hypertriglyceridemia with triglyceride levels >114 mg/dl after being conditioned to have DM. Significant differences also occurred in triglyceride levels before and after the intervention in each group and between groups (p<0.05) (Table 4). (Puspitasari, Widodo and Prayitno, 2018). Insulin resistance causes a decrease in the functional activity of cells so that in conditions of insulin resistance or insulin deficiency, it can interfere with the glycolysis process due to a decrease in the work of the enzymes glucokinase, phosphofructokinase, and pyruvate kinase. (Lenzen, 2014; Savych and Marchyshyn., 2017) Insulin resistance causes Hormone Sensitive Lipase (HSL) to be active, thereby increasing the lipolysis of triglycerides in adipose tissue to meet energy needs through gluconeogenesis. This situation causes excess free fatty acids, used as raw materials for formation (Nuraini et al., 2017).

Group (P) experienced a decrease in triglyceride levels by 46,68 mg/dl. The decrease in triglyceride and total cholesterol levels in the (P) group occurred because they were given feed containing high fiber and antioxidants in sorghum flour. Dietary fiber can reduce circulating cholesterol levels in blood plasma by binding bile salts, thereby preventing cholesterol absorption in the intestine and increasing the conversion of cholesterol into bile acids excreted with feces (Mancia et al., 2013).

Several studies have shown that fiber can significantly lower blood cholesterol and triglyceride levels (Khogare, 2012; Piraloo et al., 2014;). Sorghum has antioxidants in the form of anthocyanins. Anthocyanins play a role in reducing resistance and increasing insulin sensitivity, thereby inhibiting Hormone Sensitive Lipase (HSL), which prevents lipolysis and increases fatty acids. This study's results align with a study in Beijing 2013 regarding feeding high-starch-resistant sorghum to 60 overweight and obese rats. Overweight and obese mice fed a diet high in sorghum-resistant starch had positive changes in lipid levels (Shen et al., 2015). The same study also found that giving sorghum-glucan extract to rats in Pakistan in 2016 raised their plasma cholesterol levels. It is called hypercholesterolemia. Giving sorghum-glucan feed (SGF) containing soluble -glucan extract can reduce total plasma cholesterol, VLDL, LDL, and triglycerides and increase HDL (Hamid et al., 2017).

Table 4. Levels of total cholesterol, triglycerides, HDL, LDL, and IAP rats before and after intervention

Variable	Groups	Before Mean ± SD (mg/dl)	After Mean ± SD (mg/dl)	Δ Mean ± SD (mg/dl)	p^2
Total cholesterol	Negative control (K-)	78,22 ± 3,21^a	80,03 ± 2,92^a	1,80 ± 1,09^a	0,010^{2*}
	Positive control (K+)	185,17 ± 9,76^a	188,73 ± 3,91^b	3,57 ± 6,49^a	0,046^{4*}
	Treat (P)	191,24 ± 3,78^b	111,52 ± 3,94^c	-79,72 ± 6,19^b	0,001^{2*}
	p^1	0,002^{3*}	0,001^{1*}	0,003^{3*}	
Triglycerides	Negative control (K-)	69,8 ± 2,49^a	70,9 ± 3,08^a	1,1 ± 0,62^a	0,007^{2*}
	Positive control (K+)	142,4 ± 4,34^b	144,3 ± 4,42^b	1,9 ± 0,88^a	0,003^{2*}
	Treat (P)	147,0 ± 5,41^b	100,3 ± 1,69^c	-46,6 ± 5,78^b	0,0284^{4*}
	p^1	0,002^{3*}	0,002^{1*}	0,002^{3*}	
HDL	Negative control (K-)	82,1 ± 1,79^c	80,0 ± 1,55^c	2,1 ± 0,70^a	0,0012*
	Positive control (K+)	25,5 ± 1,41^a	22,3 ± 2,34^a	3,1 ± 1,71^a	0,0062*
	Treat (P)	28,4 ± 1,45^b	55,2 ± 2,64^b	26,77 ± 2,38^b	0,0012*
	p^1	0,001^{1*}	0,001^{1*}	0,002^{3*}	
LDL	Negative control (K-)	24,68 ± 2,08^a	25,79 ± 1,93^a	2,14 ± 0,70	0,001^{2*}
	Positive control (K+)	77,39 ± 3,37^b	79,50 ± 3,08^b	3.19 ± 1,71	0,027^{2*}
	Treat (P)	77,27 ± 4,54^b	43,81 ± 2,14^c	26,77 ± 2,38	0,001^{2*}
	p^1	0,001^{1*}	0,001^{1*}	0,003^{3,5*}	
IAP	Negative control (K-)	-0,07 ± 0,018^a	-0,05 ± 0,021^a	0,02 ± 0,008^a	0,001^{2*}
	Positive control (K+)	0,74 ± 0,017^c	0,81 ± 0,036^c	0,06 ± 0,033^b	0,001^{2*}
	Treat (P)	0,71 ± 0,022^b	0,26 ± 0,022^b	-0,45 ± 0,028^c	0,001^{2*}
	p^1	0,001^{1*}	0,001^{1*}	0,001^{3*}	

^{1}One Way Anova test, ^{2}Paired t-test, ^{3}Kruskal Wallis test, ^{4}Wilcoxon test, ^{5}Mann Whitney test, ^{a,b,c}Different notations showed a significant difference in the follow-up test *significant ($p<0,05$)

Dietary fiber functions to bind bile acids and form micelles that will be excreted through the feces, thereby reducing blood cholesterol levels (Ramadhani and Probosari, 2014). Soluble fiber can slow gastric emptying time and increase the thickness of the intestinal lining, slows the passage of food through the intestines so that it can reduce blood cholesterol and triglyceride levels (Yu et al., 2014; Hannon et al., 2019). The results of this study are also in line with a study in Seoul in 2012 regarding the effect of sorghum extract on lipid profiles in rats fed a high-fat diet. Giving as much as 5% of sorghum extract can reduce total cholesterol, LDL, and triglyceride levels (Salimi, 2012).

The results of research on antioxidant activity in sorghum showed that the antioxidant activity in sorghum was 89.,2% (Isdamayani & Panunggal, 2015). One of the antioxidants contained in sorghum is anthocyanins. Anthocyanins play a role in reducing insulin resistance and increasing insulin sensitivity so that they can inhibit HSL to prevent lipolysis and increase free fatty acids (Rózańska and Regulska-Ilow, 2018; Morigny et al., 2019). The mechanism of anthocyanins in lowering triglyceride levels is by inhibiting cholesterol synthesis. Anthocyanins activate adenosine monophosphate-activated protein kinase (AMPK), which plays a role in energy homeostasis. AMPK inhibits HMG-CoA reductase, which plays a role in cholesterol synthesis, so activating AMPK will reduce cholesterol synthesis. AMPK also contributes to reducing the activation of Acetyl Co-A carboxylase, thereby increasing fatty acid oxidation and decreasing fatty acid synthesis resulting in a decrease in cholesterol levels.

Based on the paired T-test results, there were differences in HDL cholesterol levels before and after the intervention was given in each group (Table 4). Changes in HDL levels occurred significantly in the (K-), (K+), and (P) groups, but the (K-) group was still within normal limits. In group K- there was a change in HDL levels where HDL levels decreased after the intervention. It allegedly occurred due to an increase in the subject's body weight during the acclimatization period to DM conditioning.

The decrease in HDL levels in the (K+) group was due to insulin resistance in the DM condition, which could trigger an increase in lipolysis in adipose cells. Insulin directly degrades apo B, the main protein of VLDL, and insulin also increases the secretion of apo B and VLDL (Dixit et al., 2014). As a result, there is an increase in fatty acid transport into the liver, so VLDL cholesterol levels increase. Increased glucose levels in DM rats can also decrease the activity of mitochondrial genes such as Peroxisome proliferator-activated receptor gamma (PPAR) and PPAR coactivator 1-α (PGC-1α), resulting in an increase in free fatty acids in the blood and an increase in cellular lipid accumulation. As a result, HDL levels decrease (Iqbal et al., 2017; Setyawati, 2014).

Rises cause a continuous increase in glucose (glucotoxicity), and the amount of fat in the blood increases/abnormally (lipotoxicity). LDL levels before and after the intervention in each group ($p<0.05$) showed a significant difference (Table 4). The increase in LDL levels in a group (K-) may be due to the subjects' weight gain during the study. The increase in LDL levels in the (K+) group is due to insulin resistance in DM conditions which can cause changes in the production and disposal of plasma lipoproteins. In adipose tissue, there is a decrease in the effect of insulin so that the lipogenesis process (fatty acid formation in the liver) decreases and lipolysis (fat breakdown).

After the intervention, there was a decrease in LDL and an increase in HDL in the (P) group. Increasing adequate high-fiber foods will help prevent clinical complications of DM. Dietary fiber functions to slow down digestion in the intestines, provide a more prolonged feeling of fullness and slow the appearance of blood glucose. Wresdiyati et al. reported that dietary fiber could bind LDL cholesterol directly, bind bile acids, and inhibit the enterohepatic circulation of bile acids. This mechanism will spur the loss of LDL cholesterol by increasing the expenditure of LDL cholesterol through feces (Wresdiyati et al., 2012). This study's results align with research on the effect of giving sorghum extract on lipid profiles in rats fed a high-fat diet. Giving as much as 5% of sorghum extract can reduce LDL levels (Park et al., 2012).). Usually, an increase in HDL is also associated with a decrease in LDL. The activity of the liver lipase enzyme can cause it. Liver lipase enzymes play a role in the process of catabolism or the reshuffle of HDL. When LDL levels decrease, lipase enzyme activity also decreases because the catabolism process decreases, it causes HDL to rise (Giammanco et al., 2021).

Plasma Atherogenic Index Before and After Sorghum Flour Feeding

Plasma atherogenic index (IAP) in the (K-) group was included in the low-risk category for coronary heart disease. There was a significant difference in plasma atherogenic index (IAP) values before and after the intervention ($p<0,05$) in each group. The (K-) and (K+) groups experienced an increase in the IAP value, while in the (P) group, there was a decrease in the IAP value. The K-group experienced increased IAP due to increased triglyceride levels and decreased HDL cholesterol levels, although they were within normal limits.

That is because group (K-) rats do not have diabetes mellitus (healthy). Increased triglyceride levels and decreased HDL levels in the blood (Table 4) in the rat group (K+) caused the IAP value of the group to increase. They were included in the high risk of coronary heart disease (CHD) category. The same thing happened to the group (K-) but still within normal limits and included in the low-risk coronary heart disease category because the mice were not diabetic (healthy). In the rats in the treatment group (P), there was no increase in IAP despite having diabetes, presumably due to the influence of the intervention of sorghum flour. Sorghum flour has a low glycemic index value of 36. Feed-containing carbohydrates with a low glycemic index can improve blood glucose levels in rats. The total dietary fiber content in sorghum flour is 8.83 g/100 g consisting of 6.44 g insoluble fiber and 2.39 g soluble fiber. The fiber in sorghum flour exceeds the fiber content in the standard feed of 6 g/100 g (Salimi, 2012).

Soluble dietary fiber can absorb fluids and form a gel in the stomach. The gel will slow down the peristaltic motion of the small intestine wall towards the absorption area, decreasing blood glucose levels (Gropper & Smith, 2012). Insoluble dietary fiber will go to the large intestine and be converted into a substrate that bacteria can ferment in the large intestine. The fermentation results (short-chain fatty acids acetate, propionate, and butyrate) will be reabsorbed into the bloodstream. Acetate will inhibit the process of glucose utilization in tissues and increase insulin sensitivity by reducing free fatty acids in the bloodstream. Propionate will inhibit the work of HMG CoA reductase so that fat mobilization is inhibited and gluconeogenesis does not occur in the liver (Gropper & Smith, 2012; Velázquez-

López et al., 2016). This mechanism caused a decrease in TG levels and an increase in HDL levels in the blood, so the IAP value of rats in a group (P) decreased by 0.45 after the intervention of sorghum flour (Table 4).

These results are in line with research on the effect of sorghum on lipid profiles and antioxidant activity in hyperlipidemic rats (in vitro and in vivo studies), which showed that sorghum could reduce triglyceride levels and increase HDL cholesterol levels to reduce the risk of cardiovascular disease (Ortíz Cruz et al., 2015). These results align with research on sorghum's effect on lipid profiles and antioxidant activity in hyperlipidemic rats (in vitro and in vivo studies), which showed that sorghum could reduce triglyceride levels and increase HDL cholesterol levels to reduce the risk of cardiovascular disease.

Conclusion

The administration of sorghum flour affected the lipid profile and atherogenic plasma index (IAP) in DM rats. Administration of sorghum flour at a five g/rat/day dose reduced LDL, triglycerides, total cholesterol, and IAP and increased HDL in DM rats.

Suggestions, a good diet, such as increasing the consumption of local foods high in fiber and antioxidants and low glycemic index, and a healthy lifestyle are essential components in preventing non-communicable diseases. Therefore, educating the public about food diversification from sorghum flour is necessary. It has expected to be another alternative food for DM sufferers with high fiber, antioxidant content, and low glycemic index by involving universities, government, food industry players, and community groups.

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References

Abd El-Twab, S. M., Mohamed, H. M., & Mahmoud, A. M. (2016). Taurine and pioglitazone attenuate diabetes-induced testicular damage by abrogation of oxidative stress and up-regulation of the pituitary–gonadal axis. *Canadian Journal of Physiology and Pharmacology*, *94*(6), 651–661. https://doi.org/10.1139/cjpp-2015-0503

Amanda, E., Juniarto, A. Z., Afifah, D. N., Muniroh, M., Al-Baarri, A. N., & Fitranti, D. Y. (2021). Perbaikan kadar trigliserida dan Hs-CRP pada tikus Wistar Diabetes Mellitus tipe 2 dengan biskuit biji bunga matahari. *AcTion: Aceh Nutrition Journal*, *6*(2), 189–198. https://doi.org/10.30867/action.v6i2.560

Ananda, K., Kumarappan, C. T., Christudas, S., & Kalaichelvan, V. K. (2012). Effect of Biophytum sensitivum on streptozotocin and nicotinamide-induced diabetic rats. *Asian Pacific Journal of Tropical Biomedicine*, *2*(1), 31–35. https://doi.org/10.1016/S2221-1691(11)60185-8

Balikai, F., Deshpande, N., Javali, S., Shetty, D., Benni, J., Shindhe, V., Jaalam, K., & Kapoor, N. (2020). The relationship between serum triglyceride level and heart rate variability in type 2 diabetes mellitus patients of North Karnataka. *Journal of Diabetology*, *11*(3), 191. https://doi.org/10.4103/jod.jod_7_20

Basiak-Rasała, A., Różańska, D., & Zatońska, K. (2019). Food groups in dietary prevention of type 2 diabetes. *Roczniki Panstwowego Zakladu Higieny*, *70*(4), 347–357. https://doi.org/10.32394/rpzh.2019.0086

E.Jyothsna, Hymavathi, D. T. V., & Kumar, D. G. K. (2015). Effect of sorghum based resistant starch rich product supplementation on lipid profile of healthy individuals. *IOSR Journal of Nursing and Health Science (IOSR-JNHS)*, *4*(3), 50–54. https://doi.org/10.9790/1959-04335054

Firdaus, F., Rimbawan, R., Marliyati, S. A., & Roosita, K. (2016). Model Tikus Diabetes Yang Diinduksi Streptozotocin-Sukrosa Untuk Pendekatan Penelitian Diabetes Melitus Gestasional. *JURNAL MKMI*, *12*(1), 29–34. https://doi.org/https://doi.org/10.30597/mkmi.v12i1.550

Fukaya, M., Tamura, Y., Chiba, Y., Tanioka, T., Mao, J., Inoue, Y., Yamada, M., Waeber, C., Ido-Kitamura, Y., Kitamura, T., & Kaneki, M.

(2014). Protective effects of a nicotinamide derivate, isonicotinamide, against streptozotocin-induced β-cell and diabetes in mice. *Biochemical and Biophysical Research Communications*, *442*(0), 92–98. https://doi.org/10.1016/j.bbrc.2013.11.024.Protective

Ghasemi, A., Khalifi, S., & Jedi, S. (2014). Streptozotocin-nicotinamide-induced rat model of type 2 diabetes (review). *Acta Physiologica Hungarica*, *101*(4), 408–420. https://doi.org/10.1556/APhysiol.101.2014.4.2

Gropper, S. S., & Smith, J. L. (2012). *Advanced nutrition and human metabolism*. Cengage Learning.

Hamid, A., Ilyas, M., & Kalsoom, S. (2017). Effect of Wheat and Corn Bran and Barley and Sorghum β-Glucan Extracts on the Plasma Cholesterol Level of Dietary-Induced Hypercholesterolemic Rats. *Pakistan Journal of Zoology*, *49*(5). https://doi.org/10.17582/journal.pjz/2017.49.5.1631.1637

International Diabetes Federation. (2021). IDF Diabetes Atlas. In *www.diabetesatlas.org* (10th Editi). https://doi.org/10.1242/jeb.64.3.665

Iqbal, J., Al Qarni, A., Hawwari, A., Alghanem, A. F., & Ahmed, G. (2017). Metabolic Syndrome, Dyslipidemia and Regulation of Lipoprotein Metabolism. *Current Diabetes Reviews*, *14*(5), 427–433. https://doi.org/10.2174/1573399813666170705161039

Isdamayani, L., & Panunggal, B. (2015). Kandungan Flavonoid, Total Fenol, Dan Antioksidan Snack Barsorgum Sebagai Alternatif Makanan Selingan Penderita Diabetes Mellitus Tipe 2. *Journal of Nutrition College*, *4*(2), 342–349. https://doi.org/https://doi.org/10.14710/jnc.v4i4.10108

Karunia, S., Wati, S., Putra, I. B., & Jusuf, N. K. (2021). Relationship between plasma atherogenic index and xanthelasma palpebrarum. *Bali Medical Jurnal*, *10*(3), 1010–1014. https://doi.org/10.15562/bmj.v10i3.2813

Kementerian Kesehatan Republik Indonesia. (2020). INFODATIN : Diabetes Melitus. In *Pusat Data dan Informasi Kementrian Kesehatan RI*.

Kim, J., & Park, Y. (2012). Anti-diabetic effect of sorghum extract on hepatic gluconeogenesis of streptozotocin-induced diabetic rats. *Nutrition and Metabolism*, *9*(106), 1–7. https://doi.org/10.1186/1743-7075-9-106

Lee, R. D. (2010). Energy Balance and Body Weight. In S. L. R. Marcia Nelms, Kathryn P. Sucher, Karen Lacey (Ed.), *Nutrition Therapy and Pathophysiology.* (2nd editio, pp. 245–248). Cengage Learning.

Mahdi, C., Citrawati, P., & Hendrawan, V. F. (2020). The Effect of Rice Bran on Triglyceride Levels and Histopatologic Aorta in Rat (Rattus norvegicus) of High Cholesterol Dietary Model. *IOP Conference Series: Materials Science and Engineering*, *833*(012022), 1–9. https://doi.org/10.1088/1757-899X/833/1/012022

Monikasari, M., Widyastiti, N. S., Mahati, E., Syauqy, A., & Al-Baarri, A. N. (2023). Pengaruh pemberian ekstrak bekatul beras hitam (Oryza sativa L. indica) terhadap kadar MDA, SOD dan trigliserida pada tikus diabetes mellitus tipe 2. *AcTion: Aceh Nutrition Journal*, *8*(1), 129–138. https://doi.org/10.30867/action.v8i1.731

Nuraini, I., Sulchan, M., & Dieny, F. (2017). Resitensi Insulin pada Remaja Stunted Obesity Usia 15-18 Tahun di Kota Semarang. *Journal of Nutrition College*, *6*(2), 164–171. https://doi.org/10.14710/jnc.v6i2.16906

Ortíz Cruz, R. A., Cárdenas López, J. L., González Aguilar, G. A., Astiazarán García, H., Gorinstein, S., Canett Romero, R., & Robles Sánchez, M. (2015). Influence of Sorghum Kafirin on Serum Lipid Profile and Antioxidant Activity in Hyperlipidemic Rats (In Vitro and In Vivo Studies). *BioMed Research International*, *2015*, 1–8. https://doi.org/10.1155/2015/164725

Park, J. H., Lee, S. H., Chung, I.-M., & Park, Y. (2012). Sorghum extract exerts an anti-diabetic effect by improving insulin sensitivity via PPAR-γ in mice fed a high-fat diet. *Nutrition Research and Practice*, *6*(4), 322. https://doi.org/10.4162/nrp.2012.6.4.322

Pinakesty, A., & Azizah, R. N. (2020). Hubungan

Profil Lipid dengan Progresivitas Diabetes Melitus Tipe 2. *JIMKI: Jurnal Ilmiah Mahasiswa Kedokteran Indonesia*, *8*(2), 66–72. https://doi.org/10.53366/jimki.v8i2.131

Punthakee, Z., Goldenberg, R., & Katz, P. (2018). Definition, Classification and Diagnosis of Diabetes, Prediabetes and Metabolic Syndrome. *Canadian Journal of Diabetes*, *42*, S10–S15. https://doi.org/10.1016/j.jcjd.2017.10.003

Sa'adah, N. N., Purwani, K. I., Nurhayati, A. P. D., & Ashuri, N. M. (2017). Analysis of lipid profile and atherogenic index in hyperlipidemic rat (Rattus norvegicus Berkenhout, 1769) that given the methanolic extract of Parijoto (Medinilla speciosa). *AIP Conference Proceedings*, *1854*(020031), 1–8. https://doi.org/10.1063/1.4985422

Salimi, Y. K. (2012). *Peranan Ekstrak dan Tepung Sorgum (Sorghum bicolor L.) dalam Penghambatan Kanker secara in vitro dan in vivo pada Mencit BALB/c*. Institut Pertanian Bogor.

Savych, A., & Marchyshyn., S. (2017). Investigation of pharmacological activity the new antidiabetic plant gathering in streptozotocin-nicotinamide-induced diabetes in the rats. *The Pharma Innovation Journal*, *6*(3), 175–177.

Setyawati, T. (2014). Peroxisome Proliferator Activated Receptor- γ (Ppar- γ) coactivator 1- α (PGC-1 α) Pada Diabetes Melitus Tipe 2 (DMT2) dan perannya dalam fungsi mitokondria. *Jurnal Ilmiah Kedokteran Medika Tadulako*, *1*(1), 54–62.

Shen, R.-L., Zhang, W.-L., Dong, J.-L., Ren, G.-X., & Chen, M. (2015). Sorghum resistant starch reduces adiposity in high-fat diet-induced overweight and obese rats via mechanisms involving adipokines and intestinal flora. *Food and Agricultural Immunology*, *26*(1), 120–130. https://doi.org/10.1080/09540105.2013.876976

Velázquez-López, L., Muñoz-Torres, A. V., García-Peña, C., López-Alarcón, M., Islas-Andrade, S., & Escobedo-de la Peña, J. (2016). Fiber in Diet Is Associated with Improvement of Glycated Hemoglobin and Lipid Profile in Mexican Patients with Type 2 Diabetes. *Journal of Diabetes Research*, *2016*, 1–9. https://doi.org/10.1155/2016/2980406

Wresdiyati, T., Hartanta, A. B., & Astawan, M. (2012). Tepung Rumput Laut (Eucheuma Cottonii) Menaikkan Level Superoksida Dismutase (Sod) Ginjal Tikus Hiperkolesterolemia. *Jurnal Veteriner*, *12*(2), 125–135.

Yustina, I., Nurhasanah, A., & Antarlina, S. S. (2021). Karakteristik muffin sorghum (Sorghum bicolor) varietas KD 4 dengan perlakuan perendaman biji dan konsentrasi tepung sorgum. *Jurnal Penelitian Pascapanen Pertanian*, *18*(6), 37–44. https://doi.org/10.21082/jpasca.v18n1.2021.37-44