



## Effects of Ambon Banana Juice on Glucose Levels and Lipid Profile in Diabetic Rats

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### ABSTRACT

Consumption of fruit juice is an alternative for diabetic patients who cannot consume fresh. Banana is one of the recommended fruits for diabetic patients because it has flavonoid content. This study aims to evaluate the effect of Ambon banana juice on fasting blood glucose (FBG), triglycerides, and total cholesterol levels in diabetic Wistar rats. The type of research is an experimental laboratory study with a pre-posttest design. The research sample was 21 male Wistar rats divided into 3 groups, T1 (control), T2 (10% fructose), and T3 (4 ml of Ambon banana juice) which were administered for 21 days. The FBG, triglycerides, and total cholesterol levels were examined using the colourimetric enzymatic method. The data were analyzed using one-way ANOVA, and post hoc tests. Ambon banana juice can improve FBG levels compared to control ( $p < 0.01$ ). Ambon banana juice can increase triglyceride levels but is significantly different from T2 ( $p < 0.01$ ). Ambon banana juice did not significantly increase total cholesterol levels compared to T2 ( $p < 0.01$ ). In conclusion, Ambon banana juice was demonstrated to decrease FBG and did not increase triglyceride and total cholesterol levels.

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#### Kata kunci:

Jus Pisang Ambon  
Glukosa Darah Puasa  
Trigliserida  
Kolesterol Total

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### ABSTRAK

Konsumsi jus buah merupakan alternatif bagi penderita diabetes yang tidak dapat mengonsumsi buah segar. Pisang termasuk jenis buah yang direkomendasikan penderita diabetes, karena memiliki senyawa flavonoid. Tujuan penelitian ini untuk mengevaluasi efek jus pisang Ambon terhadap glukosa darah puasa (GDP), kadar trigliserida dan kolesterol total pada tikus diabetes. Jenis penelitian yaitu eksperimental laboratorium dengan desain pre-post test. Sampel penelitian berjumlah 21 ekor wistar jantan yang dibagi dalam 3 kelompok, T1 (kontrol), T2 (10% fruktosa), dan T3 (4ml jus pisang Ambon) yang diberikan selama 21 hari. Kadar GDP, trigliserida dan kolesterol total diukur menggunakan metode kolorimetri enzimatis. Data dianalisis menggunakan one-way ANOVA dan tes post hoc. Jus pisang ambon dapat membantu menurunkan kadar GDP dibanding kontrol ( $p < 0,01$ ). Jus pisang Ambon dapat meningkatkan kadar trigliserida tetapi signifikan berbeda dibanding T2 ( $p < 0,01$ ). Jus pisang ambon tidak signifikan meningkatkan kadar kolesterol total dibanding T2 ( $p < 0,01$ ). Oleh karena itu, jus pisang ambon dapat membantu menurunkan kadar GDP dan tidak meningkatkan kadar trigliserida dan kolesterol total.

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## INTRODUCTION

Diabetes Mellitus (DM) is a metabolic disease which its prevalence has risen in the last decades. Based on the International Diabetes Federation (IDF) report in 2021, prevalence of global diabetes is 537 million people while the prevalence diabetes in Indonesia is 10.6% (IDF, 2021). The DM disease is characterized by hyperglycemia due to impaired insulin function and/or impaired insulin production (Chatterjee et al., 2017). IDF reports that the highest risk of DM development is obesity and the global prevalence of obesity and overweight are 49.5% and 35.5%, respectively (IDF, 2021; Bawady et al., 2020). Based on the survey conducted in the United States, high intake of carbohydrates and fats in the US adults results in the accumulation of fats in the human body and the increase of body weight (BW) (Lee et al., 2018).

Many factors such as hereditary, environment, and metabolism, contribute to the development of type 2 DM (Nasution et al., 2021). For example, an individual with a family history of type 2 DM has higher risk of getting type 2 DM than an individual without a family history of type 2 DM (Hariawan et al., 2019). Other studies have also revealed that obesity and unhealthy diet play an important role in type 2 DM development in urban areas (Dafriani, 2017; Aravinda, 2019). Therefore, the higher increase of BW is more likely to increase insulin resistance in the muscle and white fat cells (Kim et al., 2018). A meta-analysis study showed that obese men and women in the United States and Europe have seven times and 12 times more risk to develop type-2 DM than normal men and women (Guh et al., 2012).

A bad eating pattern is another modifiable factor that improves glucose metabolism in patients with type-2 DM (Hisni et al., 2014). They are recommended to consume a balanced nutrition, which consists of 45–65% carbohydrates of total energy intake, especially highly complex carbohydrates, 20–25% fats, and 10–15% protein. According to the Indonesian Society of Endocrinology, the principle of DM diet management is regular eating time, food choice, and calorie content (Perkeni, 2019). Patients with type 2 DM have to eat 3 main meals, 2–3 interlude meals at more frequent intervals and moderate portions. In addition, they should pay attention to consume foods with low to moderate glycemic indexes. The number of daily calories should be balanced between energy intake and energy expenditure, based on gender, age, physical activity and BW (Suryani dan Septiana, 2016; Perkeni, 2019). From the PERKENI recommendations, patients with type 2 DM are recommended to consume 150g/day fruits to fulfill their daily intake of fibre and to help reduce their blood glucose levels (Nour et al., 2017). Besides high fiber levels, fruits also contain many phytochemicals such as flavonoid, which help lower blood glucose, triglyceride and total cholesterol levels, inhibit absorption of cholesterol in the small intestine and increase of bile acid formation (Faadlilah and Ardaria, 2016; Sun et al., 2021; Mahmoud et al., 2019).

Fructose is the other nutrient that is mainly found in some fruits and gives sweet taste. For example, banana juice contains 14% sugar (glucose, sucrose and fructose), and which consists of 15.63g/L fructose (Tan et al., 2019). However, patients with type 2 DM are not allowed to consume pure fructose because it is a simple carbohydrate and can increase LDL levels (Perkeni, 2019) and triglyceride synthesis in the liver levels (Stanhope et al., 2011). A recent study reported that the administration of 10, 30, and 60% of oral pure fructose in Wistar rats for 8 weeks could significantly increase cholesterol, Low-Density Lipoprotein

(LDL), and triglycerides levels, compared to the control group (Susanti et al., 2019).

Banana (*Musa acuminata*) is one of the recommended fruits for patients with type 2 DM and Ambon or Cavendish banana is one of the most popular bananas in the world (Adedayo et al., 2016; Falcomer et al., 2019; Wulandari et al., 2018). 100g Ambon banana contains 108 kcal, 24.3g carbohydrate, 1.9g fibre and 1g protein (Kemenkes, 2018). Furthermore, the dry Ambon banana contain 851µg QE flavonoids (Al Amri and Hossain, 2018) are bioactive compounds to reduce the risk of cardiovascular diseases and type 2 DM (Visvanathan & Williamson, 2021; Manavi et al. 2021). A recent study reported that patients with type-2 DM who consumed 250 g of bananas per day for 4 weeks could improve blood glucose and increases serum adiponectin levels (Cressey et al., 2014). Another action of banana's flavonoids may increase insulin sensitivity due to potentiation of the insulin signaling pathway (Vicente & Boscaiu, 2018).

A meta-analysis study has proven that the consumption of whole fresh fruits in some Western countries can be substituted by drinking a half or 1 glass of unsweetened 100% fruit juice, especially people who cannot consume fresh fruits (Scheffers *et al.*, 2020; Benton & Young, 2019; Murphy et al., 2017). Tijjani et al (2020) reported that banana juice has flavonoids, saponins and other phytochemicals which have a hypolipidemic effect on blood cholesterol level of experimental rats (Tijjani et al., 2020). However, no studies investigate the effect of Ambon banana juice on blood glucose, triglycerides, and total cholesterol levels. Therefore, this study aimed to evaluate the effects of Ambon banana juice on fasting blood glucose, triglyceride and total cholesterol levels in diabetic Wistar rats.

## METHODS

Streptozotocin (STZ) was purchased from Bio World, USA and Nicotinamide (NA) was provided by sigma Aldrich, USA. Fresh Ambon bananas were purchased from a local market in Jebres, Surakarta City and pure fructose was purchased from Lansida Herbal Technology, Yogyakarta. The rat standard food (594 diets) was obtained from the Charoen Pokphand Indonesia, Surabaya. Male Wistar rats and drinking water were provided by the Laboratory of Pharmacology – Toxicology, Universitas Setia Budi, Surakarta.

### Research Design

This was an experimental study with the pre-posttest group design and it was calculated using a resource equation (Arifin & Zahiruddin, 2017). This study was carried out in the Laboratory of Pharmacology – Toxicology, Universitas Setia Budi, Surakarta from June to July 2021. The selected rats were randomly divided into three groups. T1 (control) group only received the standard food 594 diets and tap water while treatment (T2 and T3) groups were given standard food and 10% fructose solution or 4ml/day Ambon banana juice at 9 am every day for 21 days.

### Making Ambon banana juice

Ambon banana juice was prepared in this study, based on a previous study performed by Shetgar et al (2017). In brief, 75 mg peeled Ambon banana was mixed with 25 ml pure water and then were blended for 3 minutes. The Ambon

banana juice was freshly prepared every day before the feeding time in the morning.

### Animal model

Twenty-one male Wistar rats aged 8 weeks with around 200 g bodyweight were acclimatized in 3 standard cages (7 rats/cage) with 12-hour light/dark cycles at 25–27 °C. The total amount of standard food, which was daily given to all rats, was 10% body weight. Before induction with STZ-NA reagents, the rats were fasted for 12 hours. The following day, they were injected intraperitoneally with 230 mg/kg BW NA and were followed by an intraperitoneal injection of 65 mg/kg BW STZ. FBG levels were measured before and after 7 days injection, using Accu-Check glucometer. The diabetic rat model was confirmed by hyperglycemia with increased FBG levels  $\geq 126$  mg/dl (Rouhi et al., 2017). However, body weight was measured by digital scale in 3 times (initial weight, after induction and intervention).

### Measurement of fasting blood glucose, triglyceride, and total cholesterol levels

To measure FBG, triglyceride and cholesterol levels, the whole blood from the orbital vein of each rat was taken before, during and after interventions (day 0, 14 and 21). Collected whole blood was separated by centrifugation at 3.000 rpm for 20 minutes to obtain blood serum. FBG levels were determined using the Glucose Oxidase-Peroxidase Aminoantipyrin (GOD-PAP) method. The triglyceride and total cholesterol levels were determined using the Glycerol-3-Phosphate Oxidase Phenol Aminophenazone (GPO-PAP) and Cholesterol Oxidase-Peroxidase Aminoantipyrin (CHOD-PAP) methods respectively.

### Data analysis

All data were analyzed using the SPSS program version 18.0 and presented as mean  $\pm$  Standard Deviation. The normality data were tested using the Shapiro Wilk test. Mean differences of FBG and cholesterol levels were statistically analyzed using the One Way-ANOVA, with the Least Significant Difference (LSD) while triglyceride levels among groups were analyzed using the Games Howell test. The p-value  $< 0.05$  was considered statistically significant.

## RESULTS AND DISCUSSION

Table 1. Sample Characteristics

Body Weight (g)	T1 (mean $\pm$ SD)	T2 (mean $\pm$ SD)	T3 (mean $\pm$ SD)	p
Before Induction	192.42 $\pm$ 14.04	199.71 $\pm$ 15.01	196.85 $\pm$ 13.89	0.078
After Induction	195.71 $\pm$ 15.39	191.85 $\pm$ 18.41	187.14 $\pm$ 17.91	0.039
After Intervention	206.57 $\pm$ 12.86	214.42 $\pm$ 11.54	218.57 $\pm$ 22.50	0.013*
p	0.065	0.043*	0.032*	

Data were presented as mean $\pm$ SD (n=7). \*) showed significant differences between different groups using ANOVA,  $p < 0.05$

Table 1 shows the difference in mean body weight before induction, after induction, and after treatment. Body weight before and after induction in the three groups showed no difference in mean weight between groups ( $p > 0.05$ ). This indicates that group randomization has been successful. The average body weight after induction at T2 and T3 showed a decrease in body weight, in contrast to T1 which experienced a continuous increase in body weight.

Figure 1 shows the mean difference for fasting blood glucose, tested with One Way-ANOVA. Before the treatment,

the FBG levels in T2 and T3 were similar ( $173.85 \pm 16.54$  vs  $178.71 \pm 8.61$ ) and did not show a statistically significant difference, indicating that randomization had been achieved for the objective. The average FBG levels in T2 at 14 and 21 days of treatment increased more significantly than that in T3 ( $p = 0.001$ ). Interestingly, the fasting blood glucose levels in T2 and T3 at day 21 reduced significantly compared to those at 14 days of treatment ( $p < 0.05$ ). In addition, the reduction of fasting blood glucose levels in T3 almost reached the fasting blood glucose levels at 0 days of treatment.

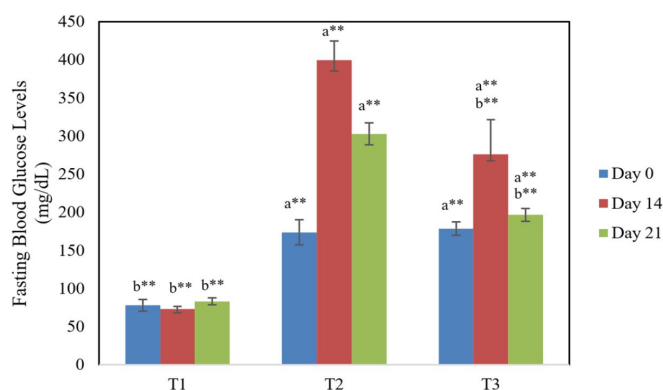


Figure 1. Effect of Ambon banana juice on fasting blood glucose levels

Data were presented as mean $\pm$ SD (n=7). Different superscripts (\*,\*\*) showed significant differences between different groups using ANOVA and post hoc statistical analysis tests. a=compared to T1 group, b=compared to T2 group, \*( $p < 0.05$ ), \*\*( $p < 0.01$ ).

From the perspective of lipid metabolism, fructose in blood circulation will be converted into triglyceride in the liver. Table 2 indicated that the administration of Ambon banana juice was able to significantly increase serum triglyceride levels. The average triglyceride levels in T2 were

significantly higher than that in T3 and significantly different on day 14 and day 21. In contrast to FBG levels at 21 days of treatment, the average triglyceride levels increased in both groups ( $199.42 \pm 1.08$  vs  $179.57 \pm 6.83$ ) at day 21.

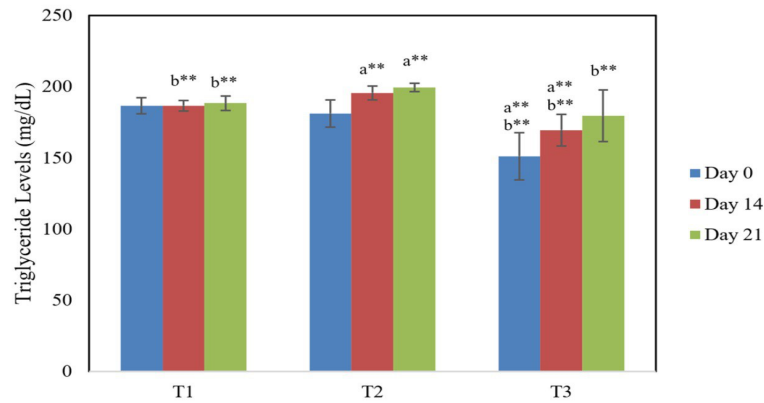


Figure 2. Effect of Ambon banana juice on triglyceride levels.

Data were presented as mean±SD (n=7). Different superscripts (\*,\*\*) showed significant differences between different groups using ANOVA and post hoc statistical analysis tests. a=compared to T1 group, b=compared to T2 group, \*( $p < 0.05$ ), \*\*( $p < 0.01$ ).

Figure 3 shows the mean difference for total cholesterol levels after being tested with One Way-ANOVA and Repeated Measure ANOVA. Among groups before treatment, there were not any significant differences but T1 and T3 shows the significant difference compared to T2 tested with post hoc

LSD test. On day 21, T1 compared to T3 did not show a statistically significant difference. In contrast to T2, total cholesterol levels were increased significantly while in the T3 group was not seen.

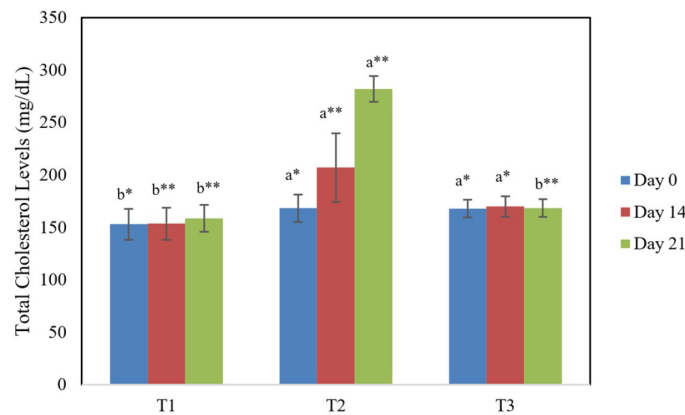


Figure 3. Effects of Ambon banana juice on total cholesterol levels.

Data were presented as mean±SD (n=7). Different superscripts (\*,\*\*) showed significant differences between different groups using ANOVA and post hoc statistical analysis tests. a=compared to T1 group, b=compared to T2 group, \*( $p < 0.05$ ), \*\*( $p < 0.01$ ).

In the present study, we have evaluated the administration of Ambon banana juice in terms of fasting blood glucose, triglycerides, and total cholesterol levels, compared to the administration of pure fructose. The administration of 4 ml of Ambon banana juice could increase triglyceride and decrease total cholesterol levels, lower than the administration of 10% fructose. However, the administration of Ambon banana juice and fructose can increase triglyceride levels almost at the same amount.

Fructose metabolism in the liver causes de novo hepatic lipogenesis and lipotoxicity mechanisms (Todoric et al.,

2020). Fructose pure over-consumption increases body weight and changes food consumption patterns and lipid profile. It could be partly responsible for the epidemic increase in obesity and metabolic syndrome (Sandeva et al., 2015). A recent study reported that the consumption of more than 100 g/day of fructose can increase blood glucose levels (Macdonald, 2016). Figure 1 shows that administration of Ambon banana juice can reduction almost reached fasting blood glucose levels at 0 days of treatment. However, the decreased fasting blood glucose level still had a high level when compared to day 0. Furthermore, the T3 group given

Ambon banana juice for 21 days can reduce fasting blood glucose levels but still not reach normal blood glucose levels. This is presumably because Ambon bananas are included in the fruit group with a high glycemic index compared to other fruits so that the effect of lowering blood glucose levels caused has not yet reached normal blood glucose levels (Falcomer et al., 2019). However, the administration of T3 still had an effect in lowering fasting blood glucose levels in diabetic rats which were probably due to the presence of phytochemicals in the fruit, such as flavonoids, saponins, tannins, and alkaloids (Tijjani et al., 2020). In addition, the possible decreasing effect given to Ambon banana juice is also influenced by the fibre and vitamin C content. Currently, the consumption of important fruit is recommended for people with diabetes because it is useful in controlling blood glucose (Beidokhti & Jäger, 2017).

Figure 2 showed that the administration of Ambon banana juice for 21 days in diabetic Wistar rats could increase triglyceride levels, but it was not as high as in T2. This occurred due to the metabolism of fructose converted into fat in the liver through the process of lipogenesis (Edebor & Fasanmade, 2019; Softic et al., 2017). Theoretically, fructose can synthesize triglycerides in the liver (Ayoub-Charette et al., 2019; Guimarães et al., 2019). Triglyceride levels in T3 showed no difference between giving Ambon banana juice compared to control. In addition, it might be caused by the presence of phytochemicals such as flavonoid antioxidants in bananas that can prevent an increase in triglycerides (P, Venkateswara Rao et al., 2017; Sun et al., 2021). Fruit juices can have an impact on increasing triglycerides due to the presence of fructose which induces lipogenesis so that lipid accumulation occurs (Ruxton and Myers, 2021; Inada et al., 2020). The content in fruit that allows it to have an effect in inhibiting the increase in triglycerides is dietary fibre and vitamin C. Research by Munasika et al (2018) reported that the water-soluble fibre in banana juice is absorbing water as it passes through the digestive tract and is fermented by bifidobacteria to produce short-chain fatty acids. An increase in short-chain fatty acids is known to reduce fat synthesis in the body (Zakaria et al., 2020).

Furthermore, the effect of Ambon banana juice on reducing fasting blood glucose levels from flavonoid compounds is through the inhibitory pathway of digestive enzyme activity,  $\alpha$ -glucosidase,  $\alpha$ -maltase and  $\alpha$ -amylase (Anggraini, 2020; Barber et al., 2021). These three enzymes are enzymes that function in the process of absorption and breakdown of carbohydrates (polysaccharides) that are consumed into simpler ones (monosaccharides) in the digestive system. So that if these three enzymes are inhibited, it will have an impact on decreasing the breakdown of polysaccharides into glucose and making fasting blood glucose levels controlled (Al-Ishaq et al., 2019; Sarian et al., 2017). In line with the research of Hebi et al (2018) and Sasmita et al (2017) proved that the flavonoids of some plants have an anti-diabetic effect through the inhibitory pathway of the  $\alpha$ -glucosidase enzyme in the digestive system in rat models of diabetes mellitus. The antidiabetic effect of flavonoids apart from being an inhibitor of glucose absorption, flavonoids can control blood glucose levels through the gluconeogenesis pathway. Gluconeogenesis is the process of forming glucose which does not come from carbohydrates but amino acids, lactate, and glycerol (Tornhiem, 2018).

Theoretically, diabetes mellitus has increased gluconeogenesis in the liver due to impaired insulin function so that it contributes to hyperglycemia (Zhang et al., 2019).

Patients with diabetes mellitus experience a decrease in glucose transporter type 4 (GLUT 4) translocation which results in lower glucose uptake, increased insulin resistance, reduced insulin signalling, and decreased glycogen in the liver (Saligram et al., 2012; Al-Ishaq et al., 2019). Flavonoids can exert antidiabetic effects in several pathways, namely the glucose transporter pathway by activating the synthesis of GLUT 4 translocations, the hepatic enzyme pathway by increasing hexokinase activity in the liver, the beta-cell apoptosis pathway by reducing pancreatic beta apoptosis, the Peroxisome Proliferator-Activated Receptors (PPARs) pathway by activating Peroxisome Proliferator-Activated Receptor Gamma (PPAR- $\gamma$ ) expression to enhance glucose uptake, AMP-Activated protein kinase (AMPK) and Nuclear factor-kappa B (NF- $\kappa$ B) activation pathway (Al-Ishaq et al., 2019). In line with Shodehinde's study (2015) reported that administration of plantain fruit for 14 days has an antihyperglycemic effect in rat models of diabetes mellitus, possibly influenced by phytochemical content such as quercetin, kaempferol, apigenin, myricetin and rutin in bananas because they provide protective properties against diabetes mellitus. In addition, Ariani & Yunita's study (2016) reported administered Ambon banana (*Musa paradisiaca var. sapientum (L.) Kunt*) in male Wistar rats model diabetes mellitus can reduce blood glucose levels possibly influenced by tannin compounds by stimulating glucose metabolism so that glucose accumulation can be reduced, through the pathway of increasing glycogenesis and inhibiting glucose absorption in the small intestine. Several studies have also reported that flavonoid compounds can help to control fasting blood glucose levels in diabetes mellitus by increasing glycogen synthesis by modulating Phosphoinositide 3-kinase (PI3K/AKT) signalling in liver, muscle, and adipose tissue as well as by decreasing gluconeogenesis activity in the hepar (Sarian et al., 2017; Al-Ishaq et al., 2019; Chen et al., 2020; Dwi tiyanti et al., 2020).

In addition to the flavonoid content, it turns out that Ambon banana juice can control blood glucose levels, possibly due to the fibre content. According to Kemenkes (2018), it is reported that Ambon banana has a fibre content of 1.9 g/100 g. Foods that contain dietary fibre and resistant starch are known to lower blood glucose through various mechanisms (Marsono et al., 2020). Physiologically oligosaccharides and resistant starch are dietary fibres that cannot be digested in the small intestine but are fermented by microflora in the colon (Marsono et al., 2020). Banana is a type of food rich in resistant starch and has the potential to control blood glucose levels. The effect of decreasing fasting blood glucose levels after being given Ambon banana juice for 21 days may be due to the fibre and resistant starch content. Research on the emergence of antihyperglycemic effects from the effect of consumption of fibre and resistant starch in diabetic rats was also conducted by Zhou et al (2014) which demonstrated that resistant starch can regulate blood sugar metabolism by lowering blood glucose levels in rat models of diabetes mellitus. Resistant starch when digested very slowly so it can help to control the increase in blood sugar in diabetes mellitus. In addition, the benefits of fibre and resistant starch have the ability to release glucose slowly and the body will follow to secrete low insulin (Lockyer & Nugent 2017).

Fibre is part of the plant that is composed of carbohydrates and is resistant to the digestive process. In theory, fibre has the function to absorb water and bind glucose so that it can reduce the availability of carbohydrates in diabetes mellitus (Santoso, 2011). The application of a diet with enough fibre will cause the digestibility of

carbohydrates to decrease. This situation is able to inhibit the increase in blood glucose and keep it under control (Gipyapuri et al., 2019). Therefore, it is possible that the effect of reducing blood glucose levels caused is influenced by the fibre nutrients in Ambon banana juice. Several studies have also proven that the fibre content in food has an influence in controlling and reducing blood glucose levels for diabetes mellitus (Kurniasari, 2014; Immawati & Wirawanni, 2014; Soviana & Maenasari, 2019; Gipyapuri et al., 2019). Research by Pratiwi et al (2020) also revealed that the antioxidant properties of phenolic compounds and anthocyanins can reduce free radical activity and oxidative damage to pancreatic beta cells in rat models of diabetes mellitus. In addition, the antioxidant effect can also reduce pancreatic cell apoptosis, repair mitochondria in pancreatic cells, increase insulin secretion so that it affects blood glucose levels.

Based on Figure 2 it can be seen that Ambon banana juice can increase serum triglyceride levels for 21 days. However, T3 triglyceride levels at day 21 were still lower than T2 and significantly different. An increase in triglyceride levels can occur presumably due to the presence of fructose in Ambon bananas but it is not dangerous compared to pure fructose. This is in line with the research of Cressey et al (2014) which revealed that daily consumption of 1-2 bananas (@250g/day) was not harmful to diabetics and marginally beneficial to non-diabetic hypercholesterolemic patients. The mechanism of fructose in increasing lipid accumulation is through an increase in de-novo hepatic lipogenesis (DNL) which results in increased production and secretion of VLDL so that serum triglyceride and cholesterol levels will increase (Wang et al., 2015). Consumption of fructose can increase lipogenesis in the liver because the liver is the main site in fructose metabolism. In addition, the presence of fructose in the glycolytic pathway via fructose-1-phosphate bypasses the main controller of glycolysis catalyzed by phosphofructokinase, thereby providing the lipogenic substrates of acetyl CoA and glycerol-3-phosphate in excessive amounts. (Hernandez-Diazcouder., 2019) Based on its metabolic pathway, fructose consumed after entering the duodenum will enter the liver via Glucose Transporter-2 (GLUT-2) and Glucose Transporter-8 (GLUT-8) (Hannou et al., 2018; Jegatheesan & De Bandt, 2017). Fructose that enters the liver will pass through the fructolysis pathway to produce glycerol 3-phosphate and triacylglycerol or triglycerides (Liu et al., 2016; Tappy & Rosset, 2019). Furthermore, fructose can also activate sterol receptor element-binding protein-1c (SREBP-1c) independently so that genes involved in the DNL process will be active (Stanhope & Havel, 2008; DiNicolantonio et al., 2018; Hernandez-Diazcouder., 2019)

Research by Faeh et al (2015) reported that a high-fructose diet can increase fasting DNL by 2-9% with the amount of fructose 75g/day served in the diet menu a day for 12 weeks in abdominal obesity men. This is evidenced by a significant increase in fasting DNL of 12.3 – 16.5% within 4 to 8 hours after eating. Meanwhile, Ramos et al (2017) reported that Wistar rats given a 20% fructose solution for 60 days would increase triglyceride levels 31.27 mg/dL higher than the control group. Several studies have determined the effect of fructose intake on total cholesterol levels. A significant increase in total cholesterol levels occurred in individuals with very high fructose intake (>100g/day). Consumption of fructose can directly alter the expression of genes involved in lipid metabolism by increasing liver fat accumulation or reducing liver fat secretion body (DiStefano, 2020). However, based on the results of a meta-analysis of Zhang et al (2013)

reported the effect of increasing total cholesterol depending on the dose of fructose consumed. The results of the study reported that 10% fructose in the diet for 10 weeks was able to increase total cholesterol levels but did not increase triglyceride levels. The increase in total cholesterol tends to be faster than triglyceride levels in experimental animals induced using 10% fructose (Indriyani, 2019).

In addition, the effect of lowering serum lipids such as triglyceride and total cholesterol levels is thought to be due to the content of soluble fibre, phytochemicals and vitamin C in the fruit. Soluble fibre has a total cholesterol-lowering effect by increasing the excretion of bile acids and cholesterol in the faeces. Soluble fibre is also able to bind bile acids and increase the viscosity of the small intestine so that it can inhibit the absorption of lipids and reduce the absorption of bile acids from the intestine (Yuliatmoko et al., 2021; Njapdounke et al., 2021). According to Indriawati and Khalifah (2018) flavonoids act as free radical scavengers that have a hydroxyl group (OH-) on the aromatic ring and stop the lipid peroxidation chain reaction by protecting cells and chemicals in the body. The mechanism of action of antioxidants such as flavonoids lowers plasma cholesterol levels by inhibiting cholesterol in the intestine and increasing the reaction for the formation of bile acids from cholesterol to be excreted through faeces.

Vitamin C is the most important radical-scavenging antioxidant in the extracellular fluid. Vitamin C or ascorbic acid is a six-carbon lactone called an antioxidant because, by donating its electrons, it prevents other compounds from being oxidized (Bashandy et al., 2018; Popovic et al., 2015). The role of antioxidant vitamin C in reducing cholesterol is by increasing the conversion of cholesterol into bile salts and bile acids in the liver and excreting it into the intestines to be subsequently excreted with feces (Rompies et al., 2021). In addition, vitamin C also plays a role in maintaining arterial walls which can alter cholesterol metabolism by modulating the conversion of cholesterol into bile acids, meanwhile affecting plasma triglyceride levels through modulation by lipoprotein lipase activity (Hilstrom et al., 2003). Based on the results of research Munasika et al (2018) reported giving banana juice with different variants such as plantain, kepok banana, and Cavendish banana amount 0.7mL/day for 7 days with a frequency of 8 times can reduce total cholesterol levels of each group by 16.5%, 9.3%, and 6.8% in mice induced by a high cholesterol diet. In contrast, T3 given Ambon banana juice did not show a decrease in cholesterol levels but increased from day 0 to day 21 as much as 0.86mg/dl but this increase had not yet reached hypercholesterolemia. This could be due to the duration of the intervention and the number of doses of fructose used so that it shows the highest triglyceride levels compared to T3.

## LIMITATION OF THE STUDY

The limitation in this study was that it did not use a negative control so it could not compare the group that was administration Ambon banana juice with that which was not administration on fasting blood glucose, triglyceride, and total cholesterol levels. This study did not measure the phytochemical content of Ambon banana juice to determine its effect on reducing fasting blood glucose, triglycerides, and total cholesterol in diabetes mellitus.

## CONCLUSIONS AND SUGGESTIONS

Our findings revealed that the administration of Ambon banana juice did not increase triglyceride and total cholesterol levels compared to pure fructose and could help reduce fasting blood glucose levels in diabetic wistar rats. Further research is needed to use a negative control group and measure the content of other phytochemical compounds in Ambon banana juice to determine the mechanism of the relevant antidiabetic effect before recommending Ambon banana juice for diabetes mellitus.

## ETHICAL CONSIDERATIONS

The experimental protocol was approved by the Health Research Ethics Commission of Universitas Sebelas Maret number 25/UN27.06.6.1/KEP/EC/2021.

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No funding was received for conducting this study

## Conflict of Interest Statement

None declared

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