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THE EFFECT OF *DURIO ZIBETHINUS* L. SEED EXTRACT ON FASTING BLOOD GLUCOSE AND INSULIN RESISTANCE IN METABOLIC SYNDROME MODEL RATS

Siti Aisyah[1]✉, Dhani Redhono Harioputro[2], Ida Nurwati[3,4]

[1]Master Program of Nutritional Sciences, Graduate School, Universitas Sebelas Maret, Surakarta, Indonesia
[2]Internal Medicine Department, Faculty of Medicine, Universitas Sebelas Maret, Surakarta, Indonesia
[3]Doctoral Program of Medical Sciences, Faculty of Medicine, Universitas Sebelas Maret Surakarta, Indonesia
[4]Department of Biochemistry, Faculty of Medicine, Universitas Sebelas Maret, Surakarta, Indonesia

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ABSTRACT

Metabolic syndrome is known as insulin resistance syndrome, characterized by chronic hyperglycemia. Management of metabolic syndrome involves several combinations, including lifestyle modifications and pharmacological interventions. Durian seeds are one source of antioxidants that have the potential to improve blood glucose homeostasis and insulin sensitivity. The objective is to analyze the effect of durian seed extract on changes in fasting blood glucose and insulin resistance. This was an experiment laboratory with a randomized pre-posttest control group design. The sample amounted to 30 rats, divided into six treatment groups: KN (normal group), K- (metabolic syndrome rats), K+ (metabolic syndrome rats + metformin 9 mg/kgBB), P1, P2, and P3 metabolic syndrome rats were given durian seed extract doses of 100, 200 and 300 mg/kgBB, respectively. The metabolic syndrome rats were fed a diet high in fat and fructose for 14 days before receiving nicotinamide and streptozocin. Data results were analyzed by ANCOVA and *one-way* ANOVA or *Kruskall-Wallis* test with a significant value of <0.05. The results indicate that following 21 days of intervention, there is a significant difference in the HOMA-IR and fasting blood glucose ($p<0.05$). The highest decrease is found in the P3 group at a dose of 300 mg/kgBB with blood glucose levels and HOMA-IR values of 90.00 ± 2.70 mg/dl and 3.55 ± 0.11. The findings of this study indicate that intervention of durian seed extract for 21 days can effectively improve the condition of rats with metabolic syndrome.

Kata Kunci:

Ekstrak biji durian;
Kadar glukosa; darah puasa;
Resistensi insulin;
Sindrom metabolik

ABSTRAK

Sindrom metabolik dikenal sebagai sindrom resistensi insulin yang ditandai dengan hiperglikemia kronis. Penatalaksanaan sindrom metabolik melibatkan beberapa kombinasi termasuk modifikasi gaya hidup dan intervensi farmakologis. Biji durian sebagai salah satu sumber antioksidan yang berpotensi memperbaiki homeostatis glukosa darah dan sensitivitas insulin. Tujuan penelitian ini adalah untuk menganalisis pengaruh ekstrak biji durian terhadap perubahan glukosa darah puasa dan resistensi insulin. Penelitian ini bersifat eksperimental laboratoris dengan rancangan acak kelompok kontrol pretest-posttest. Sampel berjumlah 30 ekor tikus, dibagi menjadi enam kelompok perlakuan: KN (kelompok normal), K- (tikus sindrom metabolik), K+ (tikus sindrom metabolik + metformin 9 mg/kgBB), P1, P2, dan P3 tikus sindrom metabolik yang masing-masing diberi ekstrak biji durian dosis 100, 200 dan 300 mg/kgBB. Tikus sindrom metabolik diberi diet tinggi lemak dan fruktosa selama 14 hari, sebelum diinduksi *streptozocin* dan *nicotinamide*. Hasil data dianalisis menggunakan uji ANCOVA dan *one-way* ANOVA atau *Kruskall-Wallis*, signifikan jika $p<0,05$. Hasil penelitian menunjukkan bahwa setelah 21 hari intervensi, terdapat perbedaan yang signifikan pada HOMA-IR dan glukosa darah puasa ($p<0,05$). Penurunan tertinggi terdapat pada kelompok P3 dosis 300 mg/kgBB dengan kadar glukosa darah dan nilai HOMA-IR sebesar 90,00 ± 2,70 mg/dl dan 3,55 ± 0,11. Temuan penelitian ini menunjukkan bahwa konsumsi ekstrak biji durian selama 21 hari secara efektif dapat memperbaiki kondisi tikus dengan sindrom metabolik.

✉ ***Corresponding Author:***
Siti Aisyah
Telp. 082273157153
Email: staisyah0502@gmail.com

INTRODUCTION

Metabolic syndrome is a group of metabolic disorders that affect the human metabolic system, including central adiposity, hyperglycemia, dyslipidemia, and hypertension (Huang *et al*., 2022). It is estimated that metabolic syndrome affects over one billion individuals worldwide and is increasing yearly (Rodríguez-Correa *et al*., 2020). Currently, 20–25% of adults globally have metabolic syndrome, and by 2035, that number is predicted to rise to 53% (Alkhulaifi & Darkoh, 2022; Mujayanah *et al*., 2023a). Metabolic syndrome affects 12–37% of people in the Asian region. In Indonesia, 23.3% of the population suffers from metabolic syndrome (Gartika *et al*., 2023; Sigit *et al*., 2020).

The pathophysiology of metabolic syndrome is a variety of complex pathways and has yet to be completely understood. Metabolic syndrome is mainly caused by insulin resistance, which is caused by, neurohormonal activity, an increase of free fatty acids (FFA) from adipose tissue, and chronic inflammation (Marušić *et al*., 2021; Neri-Numa *et al*., 2020). Insulin resistance occurs due to a metabolic disorder characterized by a decreased sensitivity of organs such as muscle, liver, and adipose tissue to insulin secretion (Neri-Numa *et al*., 2020). Insulin resistance produces inadequate glucose metabolism and enhanced hepatic gluconeogenesis uptake and utilization, resulting in increased blood glucose or hyperglycemia, leading to type 2 diabetes mellitus (T2DM) (Fahed *et al*., 2022). Insulin resistance is measured using the HOMA-IR index. HOMA-IR involves assessing fasting plasma glucose and insulin levels using mathematical modeling to determine insulin sensitivity (Rahman *et al*., 2019).

Individuals with the condition of metabolic disorder have a five-fold higher risk of T2DM and 2-3-fold higher risk of morbidity and mortality because they are more likely to develop cardiovascular disease. Therefore, appropriate treatment is needed to reduce these risks (Alkhulaifi & Darkoh, 2022; Sigit *et al*., 2020). Management of metabolic syndrome involves several combinations, including lifestyle modifications and pharmacological interventions. However, drug therapy tends to have side effects, such as nausea, vomiting, dizziness, tremors, constipation, and hypoglycemia (Rahman *et al*., 2019). Utilization of nutraceuticals and functional foods will reduce drug use and thus minimize medication side effects (Carresi *et al*., 2020; Rahman *et al*., 2019). The utilization of natural ingredients as an alternative therapy in addition to drug therapy has begun to be widely developed (Lasker *et al*., 2019).

Durian *(Durio zibethinus* L.) is an abundant Bombaceae in the Southeast Asian region, including Indonesia. It is widely recognized that all components of the durian plant, including the fruit pulp, leaves, outer skin, inner skin, and seeds, have potential health benefits (Sani *et al*., 2022). Durian seeds contain good nutrients and minerals and are high in antioxidants and anti-inflammatory, among other qualities. Durian seeds contain various phytochemical compounds, including flavonoids, phenolics, phenolic glycosides, flavonoids, coumarins, triterpenoids, alkaloids, and simple sugars (Charoenphun & Klangbud, 2022; Nayik & Gull, 2020). The flavonoid groups found in durian seeds are rutin, isoquercitrin and quercitrin (Aziz & Jalil, 2019). The flavonoid group improves the body to absorb glucose properly by lowering the absorption of carbohydrates from the small intestine, preventing tissue gluconeogenesis, and lowering insulin resistance by encouraging beta cells to produce higher levels of insulin (Han *et al*., 2022; Martín & Ramos, 2021).

In Addition, flavonoids are a class of phenol compounds known as antioxidant agents that have beneficial effects on obesity, insulin resistance, T2DM, and cardiovascular disease (Neri-Numa *et al*., 2020). Flavonoids modulate the expression of different genes and gut microbiota, pro-inflammatory cytokines, enzymes, and metabolites by preventing and inhibiting free radicals, thereby suppressing oxidative stress and inflammation as well as metabolic inhibition, which in turn reduce body weight, blood pressure, and blood glucose, and insulin resistance (Neri-Numa *et al*., 2020; Pertiwi, 2023). Therefore, the flavonoid content in durian seeds is expected to contribute to improving human health by decreasing oxidative stress, which triggers degenerative diseases (Kumoro *et al*., 2020).

The objective of this study is to know the effectiveness of durian seed extract on reducing fasting blood glucose (FBG) and insulin resistance, as determined by the HOMA-IR index in rats with metabolic syndrome. Developing durian seeds, which could potentially re-used as food ingredients with valuable bioactive compounds, is the objective of this study. It is also beneficial for humans and has the potential to be used as a reference for future studies.

MATERIALS AND METHODS

Type of Research

This research employed an experimental laboratory with a randomized pretest and posttest control group design.

Place and Time of Research

The durian seed extract was manufactured, and the experimental animals were maintained and treated in the Food and Nutrition Study Center laboratory at Gadjah Mada University in Yogyakarta. The study occurred from March to April 2024 and was approved by the Universitas Muhammadiyah Surakarta Faculty of Medicine's Health Research Ethics Committee (No. 5196/A.1/KEPK-FKUMS/III/2024).

Population and Sample

Male white rats (Rattus novergicus) of the Wistar strain were the subject of the study. The inclusion criteria were that the rodents be eight weeks old, weigh 150-200 g, and be in a healthy and normal state during the observation period. Inactive movements, diarrhea with liquid stool consistency, and mortality during treatment are all exclusionary criteria for sick rats. The sample size for this research was calculated using the Federer formula, which consisted of a total of 30 rats distributed into six treatment groups. Each group was randomly assigned five rats. A total of six treatment groups: the normal group (KN), the negative control group was metabolic syndrome rats (K-), the positive control group given metformin 9 mg/kgBW (K+), the durian seed extract 100 mg/kgBW (P1), the durian seed extract 200 mg/kgBW (P2), and the durian seed extract 300 mg/kgBW (P3).

Procedure

Preparation of Durian Seed Extract

Durian seeds were obtained from the Simpang Raya area, Simalungan Regency, North Sumatra. Durian seeds *(Durio zibethinus* L.*)* that had been collected were then cleaned, drained of water, thinly sliced, and dried without direct sunlight after the sample was dried ground with a flour grinding machine at speed 2 for 2 minutes until smooth and then dried Weighed. The maceration method, which entailed soaking the sample in an ethanol solvent, was used to carry out the extraction process. Samples were weighed as much as 500 g and then soaked in 70% ethanol solution in a closed container for 48 hours. The extraction was repeated and filtered using *Whatman* paper to separate the pulp and filtrate. Additionally, a rotary evaporator was used to concentrate the filtrate at 500C until the solvent evaporated, producing a thick extract. The thick extract is stored in a bottle at refrigerator temperature (± 4^0C) and protected from sunlight to avoid damage to nutrients (Aisyah *et al*., 2024). Previous studies report that 70% ethanol has a different effect on yield, total phenols, total flavonoids, and DPPH radical inhibitory activity of extracts (Suhendra *et al*., 2019).

Animal Treatment

A total sample of 30 rats was acclimatized for 7 days, Next, the rats were randomized at random to 6 groups, each containing 5 rats. The rats were kept in a dedicated chamber within a sanitary cage constructed from polypropylene with adequate lighting and ventilation, room temperature of 27-29^0 C, a 12-hour dark-light cycle, and 70-90% humidity. Rats were grouped and then given an HFHFr diet for 14 days. After that, rats were induced NA 110 mg/KgBW in 2 ml/200 gr saline, and after 15 minutes, *streptozocin* (STZ) 45 mg/KgBW that had been dissolved in cold citrate buffer intraperitoneally. Rats were then adapted for 72 hours, then FBG and HOMA-IR index were measured. Rats are hyperglycemic with FBG levels >135 mg/dl (Husna *et al*., 2019). The intervention of ethanol durian seed extract was given by sonde 1x/day at 9.00-10.00 WIB for 21 days at a dose of 100, 200, and 300 mg/kgBB.

Energy intake from HFHFr feeding was hoped to cause hyperglycemia due to failure of insulin signaling, leading to decreased glycogen and increased gluconeogenesis. HFHFr is converted into FFA, leading to insulin resistance (Khoirunnisa *et al*., 2023; Mujayanah *et al*., 2023b). Meanwhile, STZ is a chemical substance that is toxic to pancreatic β-cells and inhibits insulin production, STZ may affect DNA strands and degrade β-cell membranes, which can result in cell death. Nicotinamide (NA) administration before induction with STZ can protect β-cells from the toxic effects of STZ and inhibit

DNA methylation (Gunawan *et al*., 2021; Husna *et al*., 2019). HFHFr feeding for 14 days and low-dose STZ-NA injection showed metabolic syndrome components that met the minimum requirements based on NCEP-ATP III standards.

Data Collection

Blood Sampling

Rat blood samples were obtained twice by the retro-orbital plexus procedure through the sinus orbitalis, namely before (0 days) and after (21 days) intervention of durian seed extract. After that, the blood was centrifuged at 4000 rpm for 15 minutes at 4000 C to collect the blood serum. After measuring FBG levels and HOMA-IR values before treatment (pretest), EBD intervention was given according to the treatment group for 21 days.

Measurement of blood glucose levels

The levels of FBG were determined using the GOD-PAP method, an enzymatic calorimetric test utilizing glucose oxidase and phenol four amino phenazone. This test was carried out twice, namely before and after giving durian seed extract for 21 days (Putri *et al*., 2022).

Measurement of HOMA-IR index

The HOMA-IR (Homeostatic Model Assessment Insulin Resistance) index determined by analyzing FGB and insulin levels to evaluate insulin resistance, is generated by multiplying FGB levels by insulin and then dividing by 405 as a constant value (Ekafentie *et al*., 2023; Tian *et al*., 2021).

Data Analysis and Processing

The means and standard deviations of the data were presented. The data were analyzed using ANCOVA and one-way ANOVA with a post-hoc test to determine the differences between the groups. Lauvene's test of variance was employed to analyze homogeneity ($p>0.05$) and the Shapiro-Wilk test for normality. The data was significant because the p-value was less than 0.05.

RESULT

After 21 days of intervention with durian seed extract, this study concludes that it significantly improved the condition of rats with metabolic syndrome through decreased FBG and insulin resistance, as measured by the HOMA-IR index.

Measurement of Fasting Blood Glucose Levels

The Glucose Oxidase-Peroxidase-Antipyrine (GOD-PAP) method was used to determine blood glucose levels twice before and after treatment. Data on FBG levels from all test animals were statistically analyzed with an ANCOVA test employed to evaluate FBG levels before and after treatment, and the one-way ANOVA test was utilized to examine treatment group differences. Changes in FBG levels during treatment are presented in Table 1.

Table 1. Mean Difference of FBG Before and After Treatment

Group	Mean ± SD FBG Level (mg/dl)		Δ	p^a
	Pretest	Posttest		
KN	67.34 ± 0.69	68.54 ± 1.35	1.20 ± 0.72	
K-	266.40 ± 1.60	268.10 ± 1.87	1.70 ± 0.52	
K+	273.16 ± 2.81	111.09 ± 1.64	-162.07 ± 4.36	<0.001*
P1	268.05 ± 12.43	162.77 ± 2.28	-105.28 ± 11.11	
P2	270.58 ± 5.80	106.86 ± 1.19	-163.72 ± 5.01	
P3	272.16 ± 5.46	90.00 ± 2.70	-182.16 ± 6.19	
p^b	<0.001*	<0.001*	<0.001*	

Note: p^a: ANCOVA test; p^b: one-way ANOVA; *: There is a significant difference ($p<0.05$).

Table 1 shows a significant difference in FBG before and after treatment for 21 days ($p<0.05$). The highest dosage of durian seed extract that improves in lowering FBG levels is found in the P3 group,

with a value of -182.16 ± 6.19 mg/dl, followed by the P2 group (-163.72 ± 5.01 mg/dl), K+ (-162.07 ± 4.36 mg/dl), and P1 (-105.28 ± 11.11 mg/dl).

Based on the result, there are significant variations in all the groups, both in the treatment group and the control group ($p<0.001$). Figure 1 shows that there are differences between treatment groups except in the K+ group with P2 ($p>0.05$). This means that the intervention of a metformin dose of 9 mg/kgBW has the same effect as a durian seed extract dose of 200 mg/kgBW in reducing FBG in metabolic syndrome model rats.

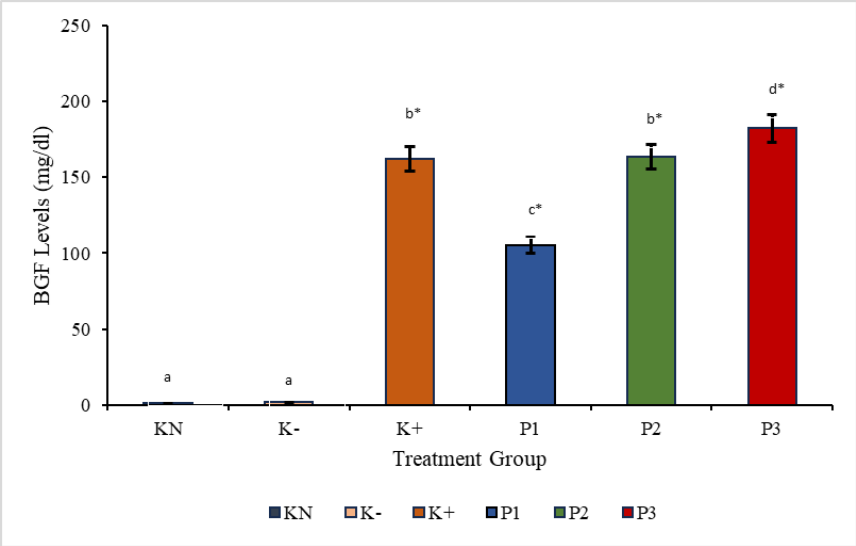

Figure 1: Post-Hoc Tukey LSD Analysis of

*Mean ± SD shown as data

Note: a,b,c,d: The similar letter shows there is not a significance based on the post hoc test

Measurement of HOMA-IR index

The intervention of durian seed extract for 21 days positively affects the reduction of insulin resistance in metabolic syndrome model rats, as indicated by the results of statistical tests. Differences in the HOMA-IR index as a marker of insulin resistance are shown in Table 2.

Table 2. Mean Difference of HOMA-IR Index Before and After Treatment

Group	Mean ± SD HOMA-IR index		Δ	p^a
	Pretest	Posttest		
KN	2.78 ± 0.70	2.77 ± 0.10	-0.01 ± 0.03	
K-	9.39 ± 0.16	9.28 ± 0.20	-0.11 ± 0.05	
K+	9.66 ± 0.13	4.14 ± 0.06	-5.52 ± 0.13	<0.001*
P1	9.38 ± 0.52	5.92 ± 0.11	-3.46 ± 0.48	
P2	9.42 ± 0.29	4.17 ± 0.08	-5.25 ± 0.23	
P3	9.45 ± 0.16	3.55 ± 0.11	-5.90 ± 0.16	
p^b	<0.001*	<0.001*	<0.001*	

Note: p^a: ANCOVA test; p^b: one-way ANOVA; *: There is a significant difference ($p<0.05$).

Table 2 shows that following a 21-day intervention with durian seed extract, the HOMA-IR index significantly decreases for all treatment groups at dosages of 100, 200, and 300 mg/kgBW ($p<0.05$), but the normal control group does not experience a decrease in HOMA- IR values because they were only given distilled water. In this study, the most significant decrease in HOMA-IR index is the P3 treatment dose of 300 mg/kgBW, followed by the positive control group given 9 mg/kgBW metformin, P2 (200 mg/kgBW) and P1 (100 mg/kgBW) with a sequential percentage decrease of 62.43% (-5.90 ± 0.16), 57.14% (-5.52 ± 0.13), 55.73% (-5.25 ± 0.23) and 36.89% (3.46 ± 0.48).

The one-way ANOVA statistical analysis shows significant variations in the changes in the HOMA-IR index among the treatment groups ($p<0.05$). All treatment groups are identical ($p>0.05$) except the KN group, which comprises P2 and P3; the post hoc test reveals a significant difference between the treatment groups (Figure 2). Therefore, in rats with metabolic syndrome, the HOMA-IR index is decreased similarly by the administration of durian seed extract at doses of 200 and 300 mg/kgBW in addition to the metformin at a dose of 9 mg/kgBW. The administration of durian seed extract for 21 days has a positive effect on the reduction of insulin resistance in metabolic syndrome model rats.

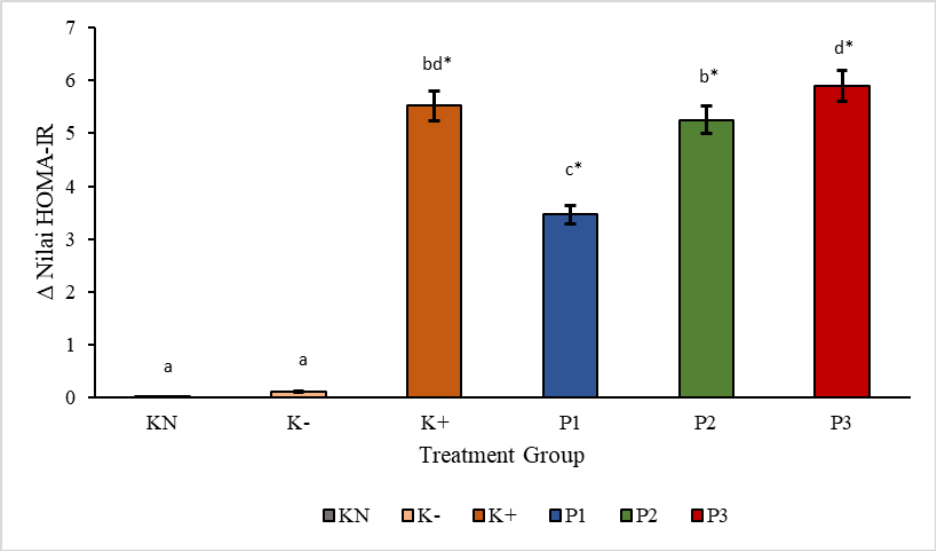

Figure 2. Post-Hoc Tukey LSD Analysis of HOMA-IR Indeks

*Mean ± SD shown as data

Note: a,b,c,d: The similar letter shows there is not a significance based on the post hoc test

DISCUSSION

Effect of Durian Seed Extract to Reduce Fasting Blood Glucose Levels

Sugar produced from carbohydrates in meals and stored as glycogen in the liver and skeletal muscles is known as blood glucose. Insulin is a hormone derived from the pancreas that converts carbohydrates into glucose as a source of energy for the body (Soelistijo *et al*., 2021). BGF levels in all groups after giving an HFHFr diet for 14 days and STZ-NA induction have experienced hyperglycemia conditions with BGF levels >200 mg/dL, and blood glucose levels of metabolic syndrome rats tend to be higher than those of normal rats. The rats experienced hyperglycemia after 14 days of HFHFr induction and low-dose STZ-NA. STZ-NA induction can cause impaired insulin secretion, increasing BGF levels because insulin does not function properly (Gunawan *et al*., 2021). High BGF levels over a long period, called chronic hyperglycemia, occur due to insulin resistance, where the body becomes less responsive to the insulin produced (Freeman *et al*., 2024). T2DM can develop in individuals with metabolic syndrome due to impaired insulin responsiveness, which can make it difficult to regulate blood glucose levels (Marušić *et al*., 2021).

The findings show that rats with metabolic syndrome have lower BGF levels following a 21-day intervention with ethanol extract from durian seeds. The decrease in BGF levels in the durian seed intervention group is due to the antioxidant content in durian seeds, including flavonoids of the rutin compound group, isoquercitrin, quercitrin, and phenolic compounds that provide antihyperglycemic effects because they can reduce blood glucose levels (Charoenphun & Klangbud, 2022; Mungmai *et al*., 2023). The results of this study are based on previous research showing that giving durian seeds fermented with red yeast for 28 days can reduce BGF levels by 12.89% in rats with DM (Gamay *et al*., 2024).

The mechanism of flavonoids in reducing BGF levels during 21 days of durian seed intervention in rats with metabolic syndrome is by inhibiting α-amylase and α-glucosidase enzymes that can delay

the process of carbohydrate digestion so that glucose absorption in the gluconeogenesis process decreases and improves blood glucose levels in metabolic syndrome (Melinda *et al*., 2023). Flavonoids are bioactive compounds that can degrade free radicals and regulate signals to various cells in the body (Putri *et al*., 2022). Through the activation of GLUT4 translocation in muscle, hexokinase activity in the liver, a decrease in pancreatic β-cell apoptosis, PPARϒ expression to enhance glucose uptake, activation of the AMPK pathway for energy homeostasis, inhibition of tyrosine kinase activity, and activation of NF-Kb is a flavonoid function (Al-Ishaq *et al*., 2019).

This study also shows a difference in the percentage reduction in BGF levels in each treatment group. The findings show that the most effective dose of durian seed extract in reducing BGF levels after the intervention of durian seed extract for 21 days is a dose of 300 mg/kgBW or group P3, with the average BGF levels in group P3 being 90.00 ± 2.70 mg/dl. This intervention group is the closest group to normal blood glucose levels. This means that in this study, the higher the extract dose given, the decrease in BGF levels in metabolic syndrome model rats will increasingly lead to normal groups.

Based on the results of this study, durian seed extract has the same effect as metformin at a dose of 9 mg/kgBB in reducing blood glucose levels, which means that durian seed extract can be an alternative therapy for metabolic syndrome. Metformin is an anti-hyperglycemia drug that helps reduce liver gluconeogenesis and increase insulin sensitivity in peripheral tissues to help maintain the balance of FBG levels in plasma (Behrouzi *et al*., 2021). Having a mechanism similar to metformin, the flavonoid content in durian seeds can reduce FGB because it is reported to have antioxidant and antidiabetic effects (Charoenphun & Klangbud, 2022; Juarah *et al*., 2021).

Effect of Durian Seed Extract to Reduce Insulin Resistance

The HOMA-IR index is an established and commonly utilized method of evaluating insulin sensitivity. It is a simple and efficient method validated and used in numerous previous investigations (Afandi & Marpaung, 2019; Dioni *et al*., 2020; Putri *et al*., 2022). The use of HOMA-IR in measuring insulin resistance is believed to represent the state and function of insulin during the process of regulating blood glucose in the body (Afandi & Marpaung, 2019).

The intervention of durian seed extract for 21 days has a positive effect on the reduction of insulin resistance in metabolic syndrome model rats, as indicated by the results of statistical tests. Doses with the highest decrease are 300 mg/kgBW or group P3, with an average blood glucose level and HOMA-IR index of 3.55 ± 0.11. The limit of the HOMA-IR index differs depending on the population size and the average BMI of the sample (Diniz *et al*., 2020). However, in general, insulin resistance occurs when the HOMA-IR index is >4.0 (Pasaribu *et al*., 2021; Putri *et al*., 2022). The increased HOMA-IR index suggests that the body's cells are experiencing disruptions in the assimilation and utilization of glucose, which leads to an increase in the blood glucose level and higher insulin resistance that occurs (Diniz *et al*., 2020; Lewandowski *et al*., 2019).

Based on the result of this study, consumption of durian seed extract at a dose of 200 and 300 mg/kgBW has a similar effect to metformin at a dose of 9 mg/kgBW in reducing insulin resistance in metabolic syndrome rats. The mechanism of action of metformin in reducing insulin resistance is the same as the mechanism of flavonoids because metformin plays a role in increasing insulin sensitivity in body tissues so that the body is more responsive to insulin. Metformin is a common therapy for individuals with T2DM because it can improve muscular absorption of glucose while inhibiting the liver's synthesis of glucose (Herman *et al*., 2022; Xiao *et al*., 2020).

In this study, flavonoids, which are popular compounds, can regulate insulin signaling pathways in body cells, including regulation of enzyme activity involved in glucose and lipid metabolism, as well as regulation of gene expression associated with insulin sensitivity (Neri-Numa *et al*., 2020; Zhou *et al*., 2023). Flavonoids will increase the IRS-1, GLUT-2, GLUT-4, and α-glucosidase pathways, thus improving insulin sensitivity (Martín & Ramos, 2021). Increased insulin sensitivity will stimulate insulin secretion from pancreatic beta cells, which are responsible for regulating blood glucose levels, thereby reducing the HOMA-IR index in diabetic rats after 21 days of combined administration of sappanwood and gotu kola extracts, which are known to contain flavonoid compounds (Putri *et al*., 2022).

CONCLUSION AND SUGGESTION

Durian seed extract can be provided in 100, 200, and 300 mg/kgBW for 21 days to rats with metabolic syndrome. Insulin resistance and FBG levels decrease due to the treatment, as indicated by a

lower HOMA-IR index. The optimal dose of P3 treatment to improve the condition of rats with metabolic syndrome is 300 mg/kgBW. Further research is needed so that durian seeds can be considered a therapy to decrease the HOMA-IR index and FGB in Individuals suffering from metabolic syndrome. Durian seeds can also be developed as supplements or processed products with high economic value.

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