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DURIAN SEED EXTRACT AMELIORATES LIPID PROFILES IN METABOLIC SYNDROME MODEL RATS

Ekstrak Biji Durian Memperbaiki Profil Lipid pada Tikus Model Sindrom Metabolik

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ABSTRAK

Sindrom metabolik merupakan sekumpulan kelainan metabolik yang kompleks dan berkaitan dengan terjadinya dislipidemia yang ditandai dengan adanya perubahan profil lipid yang abnormal meliputi peningkatan kadar trigliserida, kadar low-density lipoprotein (LDL) dan rendahnya kadar high-density lipoprotein (HDL). Ekstrak biji durian mengandung senyawa flavonoid, alkaloid, fenolik dan triterpenoid yang berpotensi dalam memperbaiki profil lipid. Penelitian ini bertujuan untuk mengamati ekstrak biji durian dalam perbaikan profil lipid. Penelitian ini merupakan eksperimental laboratorium desain pretest-posttest dengan kelompok kontrol. Sebanyak 30 ekor tikus jantan galur Wistar usia 8 minggu, berat 150-200 g dibagi menjadi 6 kelompok. Kelompok kontrol normal (NG) yaitu tikus yang diberi pakan standar, sedangkan 5 kelompok ainnya dibuat model sindrom metabolik dengan diberi diet High Fat High Fructose (HFHFr) 14 hari dan induksi Streptozotocin (STZ)-Nicotinamide (NA), meliputi kelompok kontrol negatif (NC), yang diberi aquades, dan kelompok kontrol positif (PC), yang diberi simvastatin 0,9 mg/kgBB. Kelompok perlakuan yaitu kelompok perlakuan 1 (TG1), kelompok perlakuan 2 (TG2), dan kelompo perlakuan 3 (TG3), diberikan ekstrak biji durian dosis 100, 200, dan 300 mg/kgBB selama 21 hari. Data dianalisis menggunakan Paired T-test dan One-way ANOVA, dengan signifikansi p<0,05. Hasil menunjukkan setelah 21 hari pemberian ekstrak biji durian terjadi penurunan kadar trigliserida dan LDL serta peningkatan kadar HDL yang signifikan (p<0,05), yang mana perubahan terbesar terjadi pada kelompok dosis 300 mg/kgBB dengan trigliserida sebesar -38,24 ± 6,45 mg/dl, LDL -45,67 ± 2,71 mg/dl dan HDL 54,22 ± 2,72 mg/dl. Pemberian ekstrak biji durian dapat memperbaiki profil lipid pada sindrom metabolik dengan dosis terbaik yaitu 300 mg/kgBB.

Kata kunci: *biji durian, HDL, LDL, sindrom metabolik, trigliserida*

ABSTRACT

Metabolic syndrome is a complex set of metabolic disorders associated with dyslipidemia characterized by abnormal lipid profile changes, including elevated triglyceride levels, low-density lipoprotein (LDL) levels and low high-density lipoprotein (HDL) levels. Durian seed extract contains flavonoids, alkaloids, phenolics and triterpenoids compounds, that can potentially improve lipid profiles. The aim of this study was to investigate durian seed extract in amelioration of lipid profile. This is a laboratory experimental study with a pretest-posttest with control group design. A total of 30 male Wistar rats aged 8 weeks, weighing 150-200 g, were divided into 6 groups. The normal control group (NG) was rats fed with standard food. In contrast, the other 5 groups were modeled metabolic syndrome that given High Fat High Fructose (HFHFr) diet for 14 days and Streptozotocin (STZ)-Nicotinamide (NA) induction, including the negative control group (NC), was given aquadest, the positive control group (PC), was given simvastatin 0.9 mg/kgBB. The

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treatment group 1 (TG1), treatment group 2 (TG2), and treatment group 3 (TG3) were given durian seed extract doses of 100, 200, and 300 mg/kgBB for 21 days. Data were analyzed using Paired T-test and One-way ANOVA. The results showed that after 21 days of durian seed extract administration, there was a significant decrease in triglyceride and LDL and an increase in HDL levels ($p<0.05$), where the biggest change occurred in the 300 mg/kgBB dose group with triglycerides of -38.24 ± 6.45 mg/dl, LDL -45.67 ± 2.71 mg/dl and HDL 54.22 ± 2.72 mg/dl. The administration of durian seed extract can ameliorate lipid profiles in metabolic syndrome with the best dose of 300 mg/kgBB.

Keywords: durian seeds, HDL, LDL, metabolic syndrome, triglycerides

INTRODUCTION

Metabolic syndrome is a group of health problems caused by a complex set of physiological, biochemical, and metabolic factors. These factors include central obesity, insulin resistance, hypertension, and abnormal lipid profile characterized by high levels of triglyceride and low levels of *high-density lipoprotein (*HDL) [1], [2]. Metabolic syndrome is a global health threat because it can increase morbidity and mortality and reduce life expectancy [3]. Globally, the prevalence of metabolic syndrome reaches 25.4%, while the prevalence in Southeast Asia is 25.6% [4]. In Indonesia, the prevalence of metabolic syndrome reached 21.66%, with the highest prevalence of metabolic syndrome components being low HDL levels at 66.41% [5].

The main cause of metabolic syndrome is a complex combination of genetic, environmental and lifestyle factors that affect the body's metabolism. Although there are many contributing factors, one of the most significant causes of metabolic syndrome is the accumulation of adipose tissue, especially in the abdominal area, which is closely associated with insulin resistance and impaired lipid metabolism [6], [7]. Insulin resistance is linked to changes in lipid and lipoprotein metabolism that lead to dyslipidemia [8]. Dyslipidemia represents a primary element of metabolic syndrome. It significantly impacts the progression and consequences that can exacerbate cardiovascular risk and contribute to the progression of metabolic syndrome [9].

Dyslipidemia associated with metabolic syndrome refers to an elevation in triglycerides, reduced levels of HDL, and elevated levels of *low-density lipoprotein* (LDL) in the bloodstream. Central obesity, often defined by excess fat accumulation in the abdominal area, is a characteristic of metabolic syndrome and contributes to the development of dyslipidemia. Visceral adipose tissue, distributed around internal organs, is metabolically active and synthesizes numerous chemicals that influence lipid metabolism [10]. In addition, insulin deficiency or resistance to insulin action is linked to an increase in lipolysis, the metabolically active release of free fatty acids (FFA) into the portal circulation by abdominal fat. The release of FFA will lead to higher quantities of FFA being supplied to the liver via the splanchnic circulation [7], [11]. In the liver, the elevation of FFA results in an augmentation of triglyceride synthesis and the generation of triglycerides that include apolipoprotein B. These triglycerides are particularly abundant in small LDL. The liver synthesizes triglycerides which are then discharged into the bloodstream as *very low-density lipoprotein* (VLDL) [7]. VLDL is a lipoprotein that contains triglycerides and cholesterol where the increase in VLDL concentration goes hand in hand with the increase in triglyceride and cholesterol concentrations in the bloodstream. Subsequently, these molecules activate cholesteryl ester transfer protein (CETP), which assists in transferring triglycerides from VLDL to HDL, which will increase HDL clearance and reduce its concentration [12], [13].

Lipid profile is an integral part of metabolic syndrome and is the main cause of cardiovascular disease and type 2 diabetes mellitus in metabolic syndrome patients if it is abnormal [14]. So, there is a need for treatment in improving lipid profiles to control

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metabolic syndrome. One way to overcome this is with pharmacological therapy. Pharmacological therapy is a therapy using drugs, one of which is simvastatin, which aims to overcome dyslipidemia and the risk of cardiovascular disease in metabolic syndrome [15]. However, the use of this drug can cause nausea, constipation, dehydration, urinary tract infection and ketoacidosis as side effects that may occur if consumed in the long term [16].

Although recently, the treatment of metabolic syndrome continues to be innovated, these drugs cannot suppress the development of metabolic syndrome. Therefore, alternatives are needed to help overcome metabolic syndrome, namely with more effective natural ingredients that have minimal side effects, minimal toxicity and are relatively cheaper. One of the plants that can be utilized in overcoming metabolic syndrome isdurian seeds. Durian seed extract contains bioactive compounds, namely alkaloids, triterpenoids, phenolics and flavonoids [17]. Some of these compounds are reported to function as antihyperlipidemic agents [18].

Durian seeds contain rutin, which is a group of flavonoids that can inhibit pancreatic lipase enzymes and function as antihyperlipidemic agents by preventing LDL oxidation, thereby reducing LDL levels in the blood. This enzyme is responsible for the process of lipid emulsification in the intestine. If pancreatic lipase is inhibited, fat absorption in the intestine will be inhibited, which can reduce cholesterol and triglyceride levels in the blood [18]. On the other hand, lupeol a kind of triterpenoid compounds also have benefits in treating hyperlipidemia by inhibiting endogenous cholesterol formation by blocking the activity of the enzyme 3- hydroxy-methyl-glutarylcoenzyme A (HMG-CoA) reductase in the liver. HMG-CoA reductase serves as the controlling enzyme in the production of cholesterol in the liver. Exogenous cholesterol and LDL degradation decrease the enzyme level through increased LDL receptor expression. Inhibition of the enzyme activity will increase the density of LDL receptors on hepatocytes and decrease LDL concentrations [19], [20]. Previous research examining durian seeds in fermented form was reported to have an effect on lowering cholesterol with the best dose at 0.15 g [21]. However, there have been no studies that have documented the adverse effects of durian seeds. Charoenphund & Klangbud [22] reported that the flour extract of chanee durian seeds exhibited lower cytotoxicity compared to other parts, including the peel and pulp.

Research on durian seed extract is currently limited, and no studies report its effects on lipid profiles in metabolic syndrome. Therefore, researchers are interested in studying how durian seed extract improves lipid profiles using animal models of metabolic syndrome. This study aims to determine the effect of durian seed extract in improving lipid profiles, including triglyceride, LDL, and HDL levels in metabolic syndrome model rats.

METHODS

Type, Place and Time of Research

This laboratory experimental study uses a pretest and posttest with control group design. Preparation of extracts, maintenance, and treatment of experimental animals were conducted at the Laboratory of the Center for Food and Nutrition Studies, Universitas Gadjah Mada, Yogyakarta, during the period of March-April 2024. This research obtained approval from the Research Ethics Committee of the Faculty of Medicine, Universitas Muhammadiyah Surakarta, under the reference number 5195/A.1/KEPK-FKUMS/III/2024.

Population and Sample

The study population consisted of male white rats of the Wistar strain (*Rattus norvegicus*) aged 8 weeks, weighing approximately 150-200 g. These rats were obtained from the laboratory of the Center for Food and Nutrition Studies, Pre-clinical Services

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and Animal Development of Universitas Gadjah Mada, Yogyakarta. The study consisted of 30 rats divided into 6 groups, with each group containning 5 rats. The group include the normal control group (NG), a group of healthy rats given standard feed, the negative control group (NC) is a group of metabolic syndrome rats that are not given treatment, the positive control group (PC) is a group of metabolic syndrome rats that were given standard drugs, spesifically simvastatin at a dose of 0.9 mg/kgBW, treatment group 1 (TG1) is a group of metabolic syndrome rats treated with durian seed extract at a dose of 100 mg/kgBW, treatment group 2 (TG2) is a group of metabolic syndrome rats treated with durian seed extract at a dose of 200 mg/kgBW and treatment group 3 (TG3) is a group of metabolic syndrome rats treated with durian seed extract at a dose of 300 mg/kgBW. Sample selection using consecutive sampling techniques based on inclusion, exclusion and dropout criteria. Inclusion criteria include Wistar rats, male, 8 weeks old, weighing 150-200 g and healthy condition during observation. Exclusion criteria are rats experiencing diarrhea, characterized by a change in the shape of the stool to liquid. Dropout criteria are rats that die during treatment.

Preparation of Durian Seed Extract

Durian seeds were obtained from Simalungun Regency, North Sumatra, which had been cleaned, thinly sliced, and dried with a cabinet dryer at 40°C. The dried durian seeds were then pulverized and sieved using a 60-mesh sifter and then macerated using 70% ethanol with 2 macerations. The macerate was filtered and evaporated at 50°C until it became a thick extract. The dose of durian seed extract given in the study refers to previous studies on rats modeling type 2 diabetes mellitus [23]. The doses were 100, 200, and 300 mg/kgBW for 21 days.

Development of Metabolic Syndrome Animal Model

Mice that were acclimatized for 7 days and then modeled metabolic syndrome by giving *High Fat High Fructose* (HFHFr) feed for 14 days with a feed composition consisting of a mixture of standard Comfeed feed 23 g, duck egg yolk 28 g, beef fat 40 g, chicken liver 12 g and butter4 g and 10% fructose [24], [25]. After 14 days of HFHFr feed, followed by STZ-NA induction by inducing a nicotinamide (NA) dose of 110 mg/kgBW, 15 minutes later, streptozotocin (STZ) was induced intraperitoneally. Rats are considered to have metabolic syndrome if their blood glucose levels exceed 200 mg/dl, they experience a weight change is 8% of their initial body weight, their systolic blood pressure is at or above 130 mmHg, their HDL levels are less than 35 mg/dl, their triglycerides levels exceed 150 mg/dl, and their total cholesterol levels are above 110 mg/dl [26].

Animal Care and Treatment

30 rats were subjected to a 7-day acclimatization period. The acclimatization process to control the condition of the rats was carried out during the study by keeping them in a stainless steel cage measuring 20x30x17 cm. The rats were kept in a room with temperature control of 25-28°C with light settings of 12 hours of darkness and 12 hours of light and humidity of 70-75%. After acclimatization, 25 rats were then subjected to metabolic syndrome modeling. After the modeling of metabolic syndrome was achieved, then proceed with the intervention in all groups, namely the NG (normal rats given standard food and distilled water), NC (metabolic syndrome rats given standard food and distilled water), PC (metabolic syndrome rats given standard food, distilled water, and simvastatin at a dose of 0.9 mg/kgBW), TG1 (metabolic syndrome rats given standard food, distilled water, and durian seed extract 100 mg/kgBW), TG2 (metabolic syndrome rats given standard food, distilled water, and durian seed extract 200 mg/kgBW) and TG3 (metabolic syndrome rats given standard food, distilled water, and durian seed extract 300 mg/kgBW), the intervention was carried out for 21 days.

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Blood Sampling

Blood sampling was done twice, before and after 21 days of treatment. Blood samples were taken with the retro orbital plexus technique. Blood sampling of rats is done utilizing rats conditioned in a comfortable state and then held and clampedat the nape of the neck with a finger. Microhematocrit was scraped on the medial canthus, which is under the eyeball to towards the foramen and rotated until it injures the plexus then the the blood was collected in Eppendorf [27].

Lipid Profile Examination

A lipid profile examination was conducted twice, before and after 21 days of treatment. Triglyceride levels were measured by enzymatic calorimetry using *Glyceryl Phospo Para Amino Phenazone* (GPO-PAP), and LDL and HDL levels were measured by enzymatic calorimetry using *Cholesterol Oxidase-Peroxidase Aminoantypirin* (CHOD-PAP) [28].

Statistical Analysis

The statistical analysis was conducted using the Statistical Program for Social Science (SPSS) 26 software. The data were presented as mean ± standard deviation (SD). The Shapiro-Wilk test was utilized to assess the normality of the data, while the Lavene test was implementes to evaluate the homogenity of the data. The Paired T-test was employed to assess the differences between the before treatment and after treatment conditions. The one-way Analysis of Variance (ANOVA) test, followed by the Tukey HSD test, was employed to compare data between groups with a normal distribution. The Kruskal-Wallis test, followed by the Dunn test, was employed to compare non normally distributed data between groups. Statistical tests were performed at a confidence level of 95%, and the difference was considered significant if $p<0.05$.

RESULTS

Lipid profile measurements were performed after metabolic syndrome induction or before intervention and after 21 days of durian seed extract administration to evaluate the treatment's effect on the lipid profile of metabolic syndrome model rats. Before each treatment, rats must be confirmed to have metabolic syndrome by measuring the parameters of metabolic syndrome, which can be seen in Table 1.

Table 1. Parameters of Metabolic Syndrome on Rats

Groups	Mean ± SD BW changes (%)	Mean ± SD laboratory examination			
		Blood Glucose (mg/dl)	Total Cholesterol (mg/dl)	Triglyceride (mg/dl)	HDL (mg/dl)
NG	7.56 ± 0.77	67.34 ± 0.69	86.46 ± 2.16	73.78 ± 1.91	89.25 ± 1.89
NC	25.09 ± 0.73	266.41 ± 1.60	200.94 ± 3.86	129.19 ± 2.97	26.39 ± 1.62
PC	25.43 ± 0.49	272.52 ± 5.29	201.21 ± 1.68	127.92 ± 1.80	25.17 ± 1.07
TG1	26.07 ± 0.48	268.06 ± 1.43	200.54 ± 4.69	127.21 ± 2.06	25.57 ± 1.03
TG2	25.69 ± 0.59	270.58 ± 5.79	201.62 ± 4.22	126.64 ± 2.47	23.95 ± 1.94
TG3	26.71 ± 0.63	272.16 ± 5.46	187.07 ± 3.79	127.21 ± 3.04	24.89 ± 1.41

Description:
NG) Group of healthy rats
NC-TG3) Groups of rats given HFHFr diet and STZ-NA

After the HFHFr diet and STZ-NA induction, metabolic syndrome parameters were measured to determine the success of the experimental animals' modeling. Table 1 shows that the NG group showed lower percentage changes in BW, GDP, total cholesterol, and triglyceride levels and higher values in HDL levels compared to the groups fed the HFHFr diet and STZ-NA induction, namely in the NC, PC, TG1, TG2, and TG3 groups. Based on the Table 1, it is found that rats in the NC, PC, TG1, TG2 and

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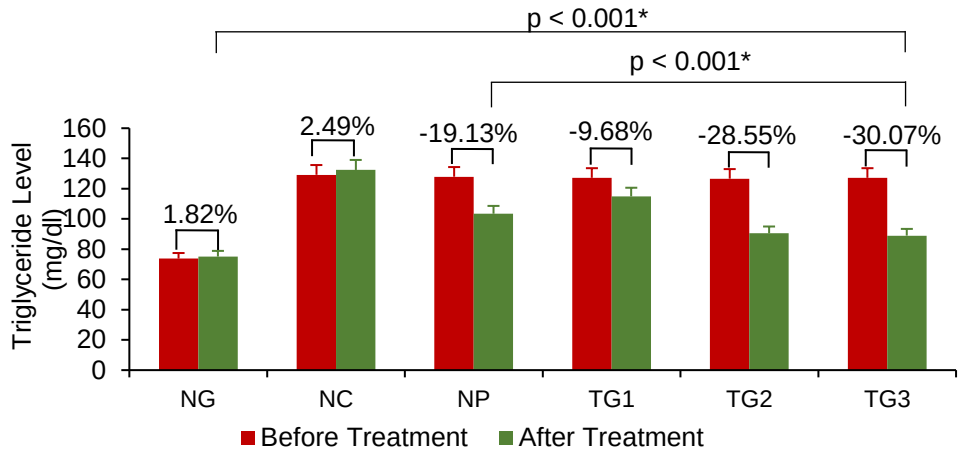
TG3 groups experienced metabolic syndrome characterized by an increase in body weight (>8%), increased blood glucose levels (>250 mg/dL), increased total cholesterol levels (>110 mg/dL), and decreased HDL levels (<45 mg/dL).

Table 2. Mean Triglyceride Levels in Metabolic Syndrome Model Rats

Groups	Triglyceride Level (mg/dl)			p^A
	Before Treatment	After Treatment	Δ	
NG	73.78 ± 1.91[a]	75.12 ± 2.18[a]	1.39 ± 0.34	0.001*
NC	129.19 ± 2.97[b]	132.41 ± 2.80[b]	3.23 ± 1.16	0.003*
PC	127.92 ± 1.80[b]	103.45 ± 2.44[c]	-24.47 ± 3.69	<0.001*
TG1	127.21 ± 2.06[b]	114.89 ± 2.95[d]	-12.31 ± 3.80	0.001*
TG2	126.64 ± 2.47[b]	90.48 ± 2.30[e]	-36.16 ± 1.11	<0.001*
TG3	127.21 ± 3.04[b]	88.96 ± 4.44[e]	-38.24 ± 6.45	<0.001*
p^B	0.000*	0.000*		

Description:
*) there is a significant difference ($p<0.05$)
p^A) Paired T-test results
p^B) One-way ANOVA test results
[a,b,c,d,e]) post-hoc test results, the same notation indicates no significant difference

Table 2 showed the durian seed extract administration results on triglyceride levels in metabolic syndrome rats. According to the Paired T-test, there was a statistically significant difference between before treatment and after treatment in all groups ($p<0.05$). These results indicate an effect of durian seed extract on triglyceride levels in metabolic syndrome rats. The findings of the one-way ANOVA test indicated a statistically significant difference between the groups after 21 days of treatment ($p<0.001$). Based on the post-hoc test revealed significant differences between groups except in groups TG2 and TG3 ($p>0.05$). To make it easier to see changes in triglyceride levels can be seen in Figure 1.



Picture caption: NG (normal control), NC (negative control), PC (positive control), TG1 (treatment 1), TG2 (treatment 2), TG3 (treatment 3), a negative sign in percent change indicates a decrease.

Figure 1. Changes in Triglyceride Levels Before and After Treatment

Figure 1 demonstrates that triglyceride levels in all groups before treatment (NC, PC, TG1, TG2, and TG3) have higher results than the NG group. These results indicate that HFHFr feeding and STZ-NA induction can increase triglyceride levels in metabolic syndrome rats. After 21 days of treatment there was an increase in triglyceride levels in the NG group by 1.82%(1.39 ± 0.34 mg/dl) and the NC group by 2.49% (3.23 ± 1.16 mg/dl), while in other groups decreased with the largest decrease in order, namely in the

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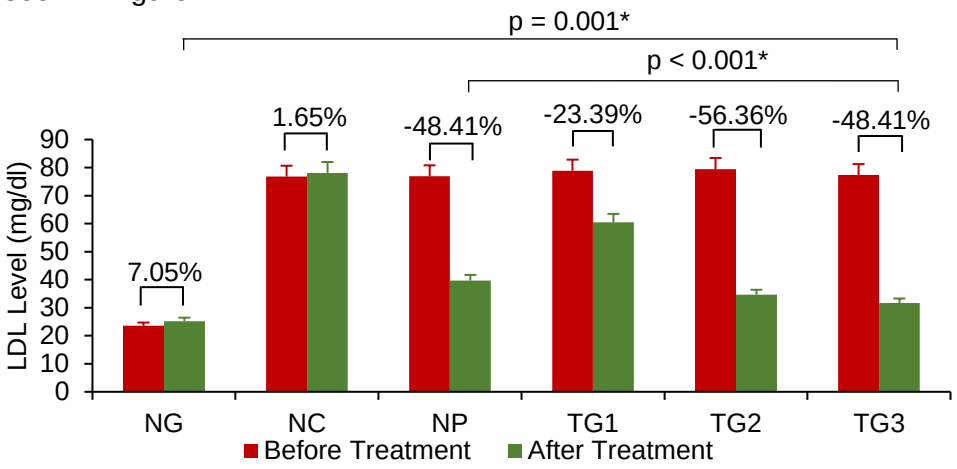
TG3 group by 30.07% (-38.24 ± 6.45 mg/dl), TG2 28.55% (-36.16 ±1.11 mg/dl), PC 19.13% (-24.47 ± 3.69 mg/dl), and TG1 by 9.68% (-12.31± 3.80 mg/dl).

Table 3. Mean LDL Levels in Metabolic Syndrome Model Rats

Groups	Mean ± SD LDL Level (mg/dL)			p^A
	Before Treatment	After Treatment	Δ	
NG	23.53 ± 1.09[a]	25.19 ± 1.17[a]	1.66 ± 0.07	<0.001*
NC	76.81 ± 1.62[b]	78.08 ± 1.70[b]	1.26 ± 0.39	0.002*
PC	76.95 ± 1.42[b]	39.70 ± 2.26[c]	-37.25 ± 3.29	<0.001*
TG1	78.89 ± 2.68[b]	60.44 ± 1.53[d]	-18.45 ± 3.00	<0.001*
TG2	79.45 ± 1.65[b]	34.67 ± 3.03[e]	-44.78 ± 2.18	<0.001*
TG3	77.37 ± 2.16[b]	31.70 ± 2.74[e]	-45.67 ± 2.71	<0.001*
p^B	<0.001*	<0.001*		

Description:
*) there is a significant difference (p<0.05)
p^A) Paired T-test results
p^B) One-way ANOVA test results
[a,b,c,d,e]) post-hoc test results, the same notation indicates no significant difference

Table 3 showed the durian seed extract administration results on LDL levels inmetabolic syndrome rats. According to the Paired T-test, there was a statistically significant difference between before treatment and after treatment in all groups (p<0.05). These results indicate an effect of durian seed extract on LDL levels in metabolic syndrome rats. The findings of the one-way ANOVA test indicated a statistically significant difference between the groups after 21 days of treatment (p<0.001). Based on the post-hoc test revealed significant differences between groups except in groups TG2 and TG3 (p>0.05). To make it easier to see changes in LDL levels can be seen in Figure 2.



Picture caption: NG (normal control), NC (negative control), PC (positive control), TG1 (treatment 1), TG2 (treatment 2), TG3 (treatment 3), a negative sign in percent change indicates a decrease.

Figure 2. Changes in LDL Levels Before and After Treatment

Figure 2 shows that LDL levels in all groups before treatment (NC, PC, TG1, TG2, and TG3) have higher results than the NG group. These results show that HFHFr feeding and STZ-NA induction can increase LDL levels in rats with metabolic syndrome. After 21 days of treatment there was an increase in LDL levels in the NG group by 7.05% (1.66 ± 0.07 mg/dl) and the NC group by 1.65% (1.26 ± 0.39 mg/dl), while in other groups decreased with the largest decrease in order, namely in the TG3 group by 59.03% (-45.67 ± 2.71 mg/dl), TG2 56.36% (-44.78 ± 2.18 mg/dl), PC 48.41% (-37.25 ± 3.29 mg/dl), and TG1 by 23.39% (-18.45 ± 3.00 mg/dl).

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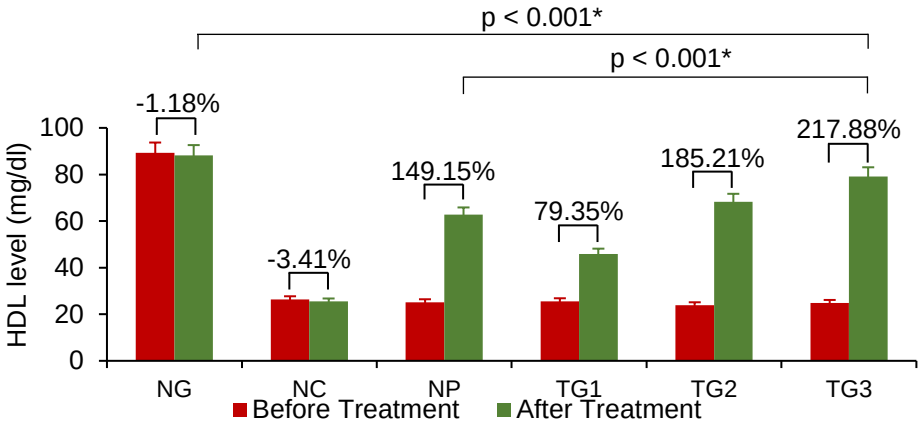
Table 4. Mean HDL Levels in Metabolic Syndrome Model Rats

Groups	Mean ± SD HDL Level (mg/dl)			p^A
	Before Treatment	After Treatment	Δ	
NG	89.25 ± 1.89[a]	88.20 ± 1.98[a]	-1.05 ± 0.32	0.002*
NC	26.39 ± 1.62[b]	25.49 ± 1.41[b]	-0.90 ± 0.44	0.010*
PC	25.17 ± 1.08[b]	62.71 ± 2.46[c]	37.54 ± 3.23	<0.001*
TG1	25.57 ± 1.03[b]	45.86 ± 1.69[d]	20.28 ± 1.06	<0.001*
TG2	23.94 ± 1.95[b]	68.28 ± 1.41[e]	44.33 ± 2.31	<0.001*
TG3	24.89 ± 1.41[b]	79.12 ± 1.64[f]	54.22 ± 2.72	<0.001*
P^B	<0.001*	<0.001*		

Description:
*) there is a significant difference (p<0.05)
p^A) Paired T-test results
p^B) One-way ANOVA test results
[a,b,c,d,e,f]) post-hoc test results, the same notation indicates no significant difference

Table 4 showed the durian seed extract administration results on HDL levels in metabolic syndrome model rats. According to the Paired T-test, there was a statistically significant difference between before treatment and after treatment in all groups (p<0.05). These results indicate an effect of durian seed extract on HDL levels in metabolic syndrome rats. The findings of the one-way ANOVA test indicated a statistically significant difference between the groups after 21 days of treatment (p<0.001). Based on the post-hoc test revealed significant difference between each group (p>0.05). To make it easier to see changes in HDL levels can be seen in Figure 3.



Picture caption: NG (normal control), NC (negative control), PC (positive control), TG1 (treatment 1), TG2 (treatment 2), TG3 (treatment 3), a negative sign in percent change indicates a decrease.

Figure 3. Changes in HDL Levels Before and After Treatment

Figure 3 shows that HDL levels in all groups before treatment (NC, PC, TG1, TG2, and TG3) have lower results than in the NG group. These results show that HFHFr feeding and STZ-NA induction can reduce HDL levels in rats with metabolic syndrome. After 21 days of treatment, there was a decrease in HDL levels in the NG group by 1.18% (-1.05 ± 0.32 mg/dl) and the NC group by 3.41% (-0.90 ± 0.44 mg/dl). Meanwhile, the other groups experienced an increase with the largest increase in order, namely in the TG3 group by 217.88% (54.22 ± 2.72 mg/dl), TG2 185.21% (44.33 ± 2.31 mg/dl), PC 149.15%(37.25 ± 3.29 mg/dl), and TG1 by 79.35%(20.28 ± 1.06 mg/dl).

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DISCUSSION

This study examined the administration of durian seed extract on lipid profile including triglyceride, LDL, and HDL levels of rats with metabolic syndrom. The rats were generated with metabolic syndrome by being fed by HFHFr diet for 14 days, followed by a low dose injection of STZ-NA. Metabolic syndrome parameters observed in this study include increased BW, blood glucose levels, total cholesterol levels, triglyceride levels and decreased HDL levels. After the induction of metabolic syndrome, the NC, PC, TG1, TG2, and TG3 groups had increased of BW change, triglyceride and LDL and decreased HDL levels compared to the NG group. In this study, triglyceride levels in the group of rats fed the HFHFr diet and STZ-NA induction had not reached the cut-off parameter of metabolic syndrome, which is above 150 mg/dl. This could be due to the 2-week HFHFr diet, where a significant increase in triglyceride levels generally occurs after 4 weeks of the HFHFr diet [26]. However, in this study, the development of metabolic syndrome model rats has been successful. This result refers to the criteria of the National Cholesterol Education Program-Adult Treatment Panel III (NCEP-ATP III), which stated that metabolic syndrome is considered to have at least 3 health problems from the parameters of metabolic syndrome that have been previously mentioned [13].

The findings of this study correlates with previous research indicating that the administration of HFHFr to weight gain and aberrant lipid profiles, including elevated triglyceride levels and LDL, as well as reduced levels of higher HDL, as compared to rats given merely a high-fat diet [29]. The administration of STZ-NA in this study serves as a diabetogenic agent to make animals experience increased blood glucose levels. STZ is considered a better diabetogenic agent than alloxan because it is stable in solution before and after injection into test animals and has higher effectiveness and lower side effects [26]. However, STZ administration can cause organ and tissue damage. To minimize its toxic effects, NA is needed. NA administration aims to protect pancreatic β-cells from experiencing massive damage [30].

Administration of durian seed extract at doses of 100, 200, and 300 mg/kgBW has shown improvements in lipid profiles in rats with metabolic syndrome as indicated by decreased levels of triglyceride and LDL, as well as increase levels of HDL, in the group receiving durian seed extract doses of 100, 200, and 300 mg/kgBW for a duration of 21 days, compared to the NC group. This study also shows the effectiveness of durian seed extract on each parameter, including triglyceride and LDL levels, namely in the TG3 group (dose of 300 mg/kgBW), showing the largest decrease of 30.07% and 59.03%, respectively, and the largest increase in HDL levels also occurred in the TG3 group with an increase of 217.88%. Furthermore, the TG3 group exhibited the most substantial enhancement in triglyceride, LDL, and HDL levels and had a more notable improvement impact compared to the group treated with the usual medication. Furthermore, the findings of the TG3 group exhibited the highest degree of similarity to the NG group, which served as the standard control in this investigation. The proximity observed suggests that the intervention in the TG3 group successfully restored the lipid profile that closely approximated the normal level observed in the NG group. Thus, this effect has contributed to the improvement of metabolic syndrome symptoms due to dyslipidemia. The results of this study support previous clinical studies that the administration of water-soluble polysaccharide crude extract from durian seeds for 4 weeks in hyperlipidemic rats can decrease triglyceride levels by 38.48%, decrease LDL levels by 72.23% and increase HDL levels by 182.16% [31]. Other studies reported that fermented durian seeds, which showed improvements in lipid profiles, namely levels of triglycerides, LDL and HDL with the best dose of 0.15 g [21].

Durian seed extract contains bioactive compounds, namely flavonoids, phenolics, alkaloids, and triterpenoids [17]. Previous research reported that durian seed extract has a total flavonoid content of 23.24 mg QE/g and a total phenolic content of 0.33 mg GAE/g

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[32], [33]. These bioactive compounds have different mechanisms for improving lipid profiles [34].

The mechanism of flavonoids in ameliorating lipid profiles is by reducing cholesterol biosynthesis, particularly in supressing the activity of HMG-CoA reductase, an important enzyme involved in cholesterol biosynthesis [35]. Another target of flavonoid action is reducing the requirement for NADPH in the production of fatty acids and cholesterol [36]. Flavonoids can contribute to the amelioration of hypercholesterolemia by altering lipoprotein metabolism. This can be achieved by increasing the absorption of LDL trough the upregulation of LDL receptors or by raising the activity of lecithin cholesterol acyl transferase (LCAT) [37]. LCAT is an enzyme that transforms free cholesterol into hydrophobic cholesterol esters, allowing them to attach to lipoprotein core particles to produce new HDL [38]. In addition, flavonoids can inhibit pancreatic lipase enzymes and function as antihyperlipidemic agents by preventing LDL oxidation, thereby reducing LDL levels in the blood. This enzyme is responsible for the process of lipid emulsification in the intestine. If pancreatic lipase is inhibited, fat absorption in the intestine will be inhibited, which can reduce cholesterol and triglyceride levels in the blood [18].

Improvement of lipid profiles in rats is also based on the role of alkaloid and triterpenoid content in durian seeds. Alkaloids play a role in inhibiting the activation of lipase enzymes so that lipase enzyme activity decreases. This decrease in enzyme activity can reduce triglycerides entering the small intestine [39]. Triterpenoids have the same mechanism as simvastatin: inhibiting endogenous cholesterol formation by blocking HMG-CoA reductase activity in the liver. HMG-CoA reductase is an enzyme that regulates liver cholesterol biosynthesis. Exogenous cholesterol and LDL degradation decrease the enzyme level through increased LDL receptor expression. Inhibition of the enzyme activity will increase the density of LDL receptors on hepatocytes and decrease LDL concentration [40]. Based on these results and discussions, this study offers innovation by exploring durian seed extract as a natural ingredient that has the potential to improve lipid profiles. This provides new insights into the development of nature-based therapies for metabolic syndrome. However, this study still has limitations. The metabolic syndrome parameters studied are still limited to lipid profiles, so a complete understanding of the effect of durian seed extract on metabolic syndrome as a whole is limited.

CONCLUSION

Durian seed extract can potentially ameliorate lipid profiles (triglycerides, LDL, and HDL) in rats with metabolic syndrome. Administration of durian seed extract at 100, 200, and 300 mg/kgBW doses can significantly reduce triglyceride and LDL levels and increase HDL levels. Among the three doses, 300 mg/kgBW is the most effective dose in improving lipid profiles (reducing triglyceride and LDL levels while increasing HDL levels) in rats with metabolic syndrome. Additional research is required to examine the effects of administering durian seed extract on metabolic syndrome parameters such as body weight, blood glucose, insulin resistance, blood pressure and inflammatory status that may occur in metabolic syndrome.

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