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The effects of raja banana (*Musa acuminata*) peel extract on body weight, body mass index, body fat percentage, and visceral fat mass in male rats with obesity

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ABSTRAK

Latar Belakang: *Obesitas menjadi faktor risiko penyakit sindrom metabolik yang dapat meningkatkan angka kematian. Penderita obesitas seringkali mengalami kegagalan dalam menurunkan berat badan (BB) melalui terapi non farmakologi. Obat sintetik obesitas dapat menimbulkan efek samping maka diperlukan bahan alami sebagai terapi alternatif.*
Tujuan: *Penelitian ini bertujuan untuk mengetahui pengaruh pemberian ekstrak kulit pisang raja (RBPE) terhadap BB, Indeks Massa Tubuh (IMT), body fat percentage (BFP), dan massa lemak viseral pada tikus jantan obesitas.*
Metode: *Subjek penelitian adalah 30 ekor tikus wistar jantan berumur delapan minggu dengan BB 125-200 g. Induksi obesitas dengan diberikan pakan tinggi lemak tinggi fruktosa atau High Fat High Fructose (HFHFr) selama 28 hari. Tikus dirandomisasi dan dibagi menjadi lima kelompok yaitu kelompok kontrol negatif (KN) diberi pakan standar dan aquades, kontrol positif (KP) diberi pakan standar dan obat orlistat, perlakuan 1 (P1), perlakuan 2 (P2), dan perlakuan 3 (P3) yang diberi pakan standar dan RBPE dosis 200 mg/kgBB/hari, 400 mg/kgBB/hari, dan 800 mg/kgBB/hari. Data sebelum dan sesudah induksi obesitas dianalisis menggunakan uji paired t-test. BB, IMT, dan massa lemak viseral dianalisis menggunakan uji One-Way Analysis of Variance (ANOVA) dan Repeated Measure ANOVA. BFP dianalisis menggunakan uji Kruskal Wallis dan uji Friedman.*
Hasil: *: RBPE secara signifikan dapat menurunkan BB (p=0,026), IMT (p<0,001), dan BFP (p<0,001). Namun, tidak ada perbedaan yang signifikan pada massa lemak viseral antar semua kelompok (p=0,187). P3 merupakan kelompok dengan rata-rata BB, IMT, BFP, dan massa lemak viseral yang paling rendah meskipun penurunan BB tertinggi selama masa intervensi terjadi pada K+.*
Kesimpulan: *RBPE berpotensi sebagai terapi alternatif untuk obesitas karena dapat menurunkan BB, IMT, dan BFP. Penelitian selanjutnya dapat meneliti pengaruh RBPE pada parameter obesitas lainnya seperti profil lipid.*

KATA KUNCI*: obesitas; pisang; ekstrak kulit pisang; musa acuminata; pisang raj*

ABSTRACT

Background: *Obesity is a risk factor for metabolic syndrome which can increase mortality. Obese sufferers often fail to lose body weight (BW) through non-pharmacological therapy. Obesity synthetic drugs can cause side effects, so natural ingredients are needed as alternative therapies.*

Objectives: *This study aims to determine the effect of raja banana peel extract (RBPE) on BW, body mass index (BMI), body fat percentage (BFP), and visceral fat mass in obese male rats.*

Methods: *The research subjects were 30 male Wistar rats weighing 125-200 g, aged eight weeks. Obesity was induced by being given high-fat high fructose (HFHFr) feed for 28 days. Rats were randomized and divided into five groups: the negative control group (C-) was given standard feed and distilled water, the positive control (C+) was given standard feed and orlistat, treatment 1 (T1), treatment 2 (T2), and treatment 3 (T3). Which were given standard feed and RBPE doses of 200 mg/kgBW/day, 400 mg/kgBW/day, and 800 mg/kgBW/day. Data before and after the induction of obesity were analyzed using paired t-tests. BW, BMI, and visceral fat mass were analyzed using the One-Way Analysis of Variance (ANOVA) and Repeated Measure ANOVA tests. BFP was analyzed using the Kruskal-Wallis test and the Friedman test.*

Results: *RBPE can significantly reduce BW (p=0.026), BMI (p<0.001), and BFP (p<0.001). However, all groups had no significant difference in visceral fat mass (p=0.187). T3 was the group with the lowest average BW, BMI, BFP, and visceral fat mass although the highest weight loss during the intervention period occurred in C+.*

Conclusions: *RBPE has the potential as an alternative therapy for obesity because it can reduce BW, BMI, and BFP. Future studies can investigate the effect of RBPE on other obesity parameters such as lipid profiles.*

KEYWORD*:* *obesity; banana; banana peel extract; musa acuminata; raja banana*

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INTRODUCTION

Currently, obesity has become a common health problem in the global community. Obesity can be a risk factor for metabolic syndrome diseases such as DM type 2 and cardiovascular diseases which can increase mortality (1). The prevalence of obesity continues to increase in both developed and developing countries (2). According to Lobstein et al. (2023), as many as 2.6 billion (38%) of the world's population were overweight and obese in 2020 and this prevalence is expected to continue to increase to 42% in 2025 whereas the prevalence of obesity in Indonesian children is estimated to increase by 7.9% and 5.8% in adults in 2035 (3). Indonesian basic health research Riskesdas also shows that the prevalence of obesity in residents aged > 18 years has increased by 50% in five years, from 14.8% in 2013 to 21.8% in 2018 (4).

Dietary habits that often consume foods high in energy and fat, snacking at night, and lack of physical activity can cause excess energy (5). Excess energy leads to fat accumulation in adipose tissue. Fat accumulation in subcutaneous adipose tissue, skeletal muscle, and metabolic organs can cause an increase in body weight (BW), while fat accumulation in visceral adipose tissue causes a decrease in adiponectin levels and oxidation of triglycerides. This causes adipose tissue dysfunction, increasing BW above the standard limit, and obesity will occur (6,7). Obesity is also influenced by genetic, stress, hormonal, and environmental factors such as gut microbiota dysbiosis (8–10). Obesity I is characterized by a Body Mass Index (BMI) of 25-29.9 kg/m2, and obesity II with BMI ≥30 kg/m2 (11). In addition, obesity can also be diagnosed by measuring the body fat percentage (BFP). Obesity in men is

characterized by a BFP >25% and in women >35% (12). For children, there are no accepted international standard cut-offs for BFP. However, several studies have reported that 30% for girls and 25% for boys are associated with obesity (13).

Non-pharmacological therapies such as dietary adjustments and physical activity often fail to be carried out by obese people, while pharmacological therapy using synthetic drugs such as orlistat can cause side effects if consumed for a long time (14,15). Common side effects include nausea, vomiting, diarrhea, constipation, and gastrointestinal disturbances (16). Therefore, natural ingredients are needed that contain certain active compounds that can be used as an alternative in pharmacological therapy for obesity.

Banana is one of the tropical fruits that contribute to 16.8% of the world's fruit supply (17). Banana is the most common fruit produced in Indonesia, a total of 9.6 million tons of banana was produced in 2022 (18). The high production and consumption of bananas cause an increase in banana peel waste because each banana consists of 40% peel. Banana peel waste is usually used as animal feed and organic waste, but many benefits are produced by banana peel waste (19). Banana peel contains nutrients and several active compounds such as flavonoids, phenols, tannins, alkaloids, and saponins which have the potential for pharmacological therapy of obesity (20). A previous research conducted showed that giving banana peel extract added to phosphatidylcholine (PC) can reduce BW, blood glucose levels, and insulin in rats that are given a high-fat diet (21). However, until now, no research has been conducted to determine the effect of raja banana peel extract (RBPE) on obesity. This study aimed to determine the effect of RBPE administration on BW, BMI, BFP, and visceral fat mass in obese male rats.

MATERIALS AND METHODS

Extraction of RBPE

The skin of ripe, yellow banana was obtained from a fruit seller in Klaten City, Central Java, Indonesia. Extraction was carried out at the Phytochemical Laboratory of Setia Budi University, Surakarta. The extraction process began with manufacturing of banana peel flour using the method developed by Maulana (2018), using a cabinet dryer temperature of 80oC for 8 hours (22). Banana peel flour was extracted using the maceration method and was carried out by modifying the method developed by Aboul-Enein et al. (2016) (23). As much as 1 kg of banana peel flour was soaked in 80% methanol solvent (Shisam Mas Chemical Pharmacy) with a ratio of 1:10 (v/v) for 72 hours. The solution was filtered using whatman filter paper to produce filtrate, then redissolved twice. The filtrate obtained from the three screenings was then concentrated with a rotary evaporator at a temperature of 80oC at 80 rpm. Next, the concentrated results were dried using an oven blower (Binder FD 56) with a temperature of 45-50oC for 12 hours until a thick extract was obtained and stored at 4oC before use.

Research Design

This type of research was a laboratory experimental research design pre-posttests with control group for the measurement of BW, BMI, and BFP as well posttest only for visceral fat mass. The inclusion criteria in this study were white Wistar male rats, 8 weeks old, weighing 125-200 g, and in good health. The number of research samples was calculated using the degree of freedom (E) formula. Each group consisted of five rats with the addition of 10% of the minimum number of samples to overcome drop-out so that each group consisted of six rats (24).

Generating a Rat Model with Obesity

The maintenance of rats was carried out at the Integrated Laboratory Technical Implementation Unit of Universitas Sebelas Maret using cage polypropylene; each cage contained three rats. The cage was placed in a room with a temperature of 22-27oC, 37-56% humidity, and a light-dark cycle for 12 hours (25). Rats were adapted for seven days, given standard Comfeed Broiler-2 (BR-2) (PT. Japfa Comfeed Indonesia Tbk.), and drank regularly. Obesity induction was carried out by providing high-fat or high-fructose feed High Fat High Fructose (HFHFr) for 28 days. Based on research conducted by Sundari (2022), the composition of HFHFr consisted of 54.64% fat and 10% fructose (26). Feed was given every morning and evening. After the rats became obese, the rats were randomized into five groups, namely the negative control (C-), positive control (C+), treatment 1 (T1), treatment 2 (T2), and

treatment 3 (T3). C- was a group that was only given standard feed and aquadest. C+ was given standard feed and orlistat (Novell Pharmaceutical Laboratories) at 12.3 mg/kg BW (27). Groups T1-T3 were given standard feed and RBPE doses of 200 mg/kgBW/day, 400 mg/kgBW/day, and 800 mg/kgBW/day for 28 days. The Research Ethics Committee of Faculty of Medicine, Universitas Sebelas Maret approved the research protocol (No. 50/UN27.06.11/KEP/EC/2023).

Measurement of BW, BMI, BFP, and Visceral Fat Mass

The naso-anal length was obtained by measuring the rat's body length (BL) from the tip of the nose to the anus of the rat. Anthropometric data (BW and BL) were measured using digital scales (Joil) and Metlin (OneMed), which were measured before, during, and after the intervention. BMI was calculated using the Rohrer index formula: [body weight (g)/naso-anal length (cm)3] × 103. Rats were declared obese with a Rohrer index > 30 (28). BFP was calculated by the formula body fat percentage by calculating the TM index (28,29).

TM Index = [body weight (g)/naso-anal length (cm)2,823] × 103

BFP = 0.581 × [TM index] – 22.03

At the end of the intervention, the rats were sacrificed to gain fat mass using the following method: the rats were dissected, and the fat attached to the epididymal and retroperitoneal areas located in the kidneys were taken, then weighed to determine the mass of visceral fat in the rats (12).

Statistical Analysis

Numerical data were presented in terms of mean and standard deviation using SPSS version 26. The Shapiro-Wilk test and the Levene test were used to test the data normality and the homogeneity of variants, respectively. Paired t-tests were used to determine the difference before and after obesity induction. BW, BMI, and visceral fat mass were analyzed using the One-Way ANOVA and continued with the post hoc test Least Significance Different (LSD) to determine the average difference between groups at one measurement time. Repeated Measure ANOVA followed with Bonferroni test were used to determine the mean differences between groups of rats at the time before, during, and after the intervention. BFP was analyzed using Kruskal Wallis and Friedman's test. Significant data continued with the test post hoc Mann-Whitney and Wilcoxon. The p-value <0.05 was considered as statistically significant.

RESULTS AND DISCUSSIONS

Table 1 shows that all groups of rats induced by obesity experienced a significant increase in BW, BMI, and BFP (p<0.001). The highest increase in BW occurred in G2 with an increase of 65.50±25.85, while the lowest increase in BW occurred in G1 with an increase of 46.67±12.97. There was no significant difference in the mean BW between groups either before induction (p=0.153) or after induction (p=0.548). The highest increase in BMI and BFP occurred in G2, with an increase of 6.18±1.49 and 6.22±1.39, respectively. The lowest increase in BMI and BFP occurred in G1, with an increase of 6.22±1.39 and 5.24±1.58, respectively. The mean BMI between groups did not differ significantly either before induction (p=0.076) or after induction (p=0.888). The same thing happened to the average BFP before induction (p=0.089) and after induction (p=0.952).

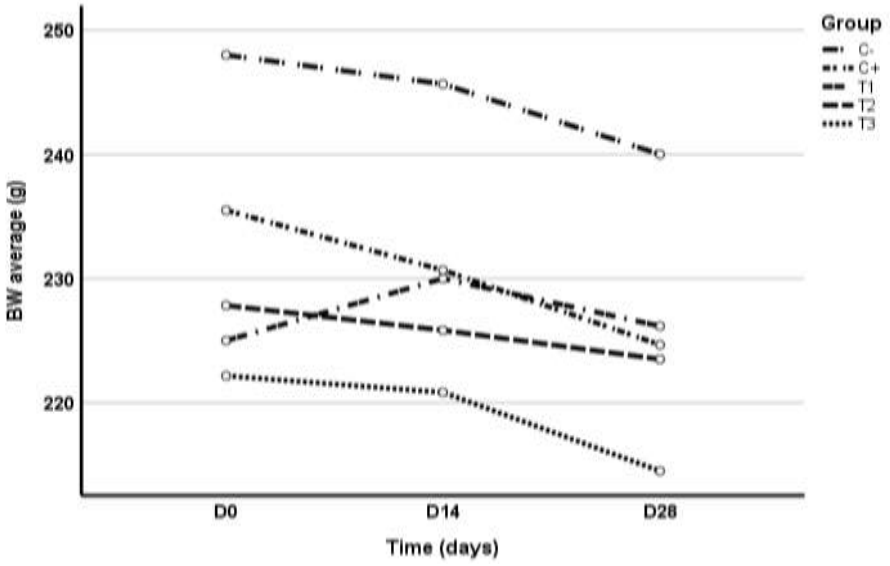
Table 1. Average BW, BMI, and BFP of Rats Before and After Obesity Induction

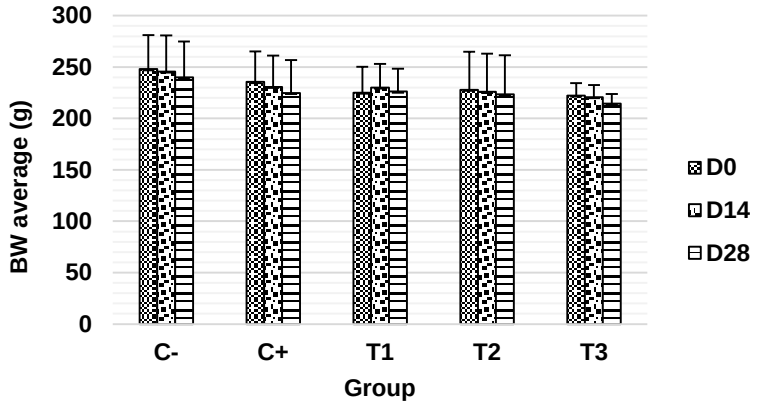
Obesity Parameters	Group	Before Induction	After Induction	Δ	p^a
BW (g)	G1	175.50±9.73	222.17±12.35	46.67±12.97	<0.001*
	G2	170.00±17.29	235.50±29.63	65.50±25.85	<0.001*
	G3	174.83±21.15	225.00±25.23	50.17±14.92	<0.001*
	G4	192.83±16.40	248.00±33.11	55.17±17.78	<0.001*
	G5	168.67±20.37	227.83±37.05	59.17±24.94	<0.001*
	p^b	0.153	0.548		
BMI (g/cm^3)	G1	26.29±1.37	31.55±1.28	5.27±1.71	<0.001*
	G2	24.72±0.30	30.90±1.58	6.18±1.49	<0.001*

Obesity Parameters	Group	Before Induction	After Induction	Δ	p^a
	G3	25.38±1.21	31.04±1.54	5.65±1.19	<0.001*
	G4	25.30±0.42	30.87±1.34	5.57±1.30	<0.001*
	G5	25.16±0.70	31.30±0.90	6.15±1.23	<0.001*
	p^b	0.076	0.888		
BFP (%)	G1	3.65±1.28	8.89±1.20	5.24±1.58	<0.001*
	G2	2.15±0.32	8.37±1.36	6.22±1.39	<0.001*
	G3	2.81±1.24	8.43±1.57	5.62±1.14	<0.001*
	G4	2.87±0.47	8.44±1.32	5.57±1.21	<0.001*
	G5	2.54±0.69	8.69±0.95	6.15±1.27	<0.001*
	p^b	0.089	0.952		

*p^a) simple paired t test; p^b) One-Way ANOVA; *) p<0.05*
Group 1 (G1), Group 2 (G2), Group 3 (G3), Group 4 (G4), Group 5 (G5)

The average BMI in all groups after induction is >30 indicating successful induction of obesity (28). Rats treated with HFHFr tended to experience increased food intake and decreased energy expenditure (30). High-fat consumption and lack of energy expenditure cause Free Fatty Acid (FFA) in the form of triglycerides will be distributed and stored in adipose tissue resulting in hyperplasia and hypertrophy of adipose tissue and can increase BW (7,31). Fructose can enter liver cells without requiring insulin signaling due to the presence of the GLUT5 transporter. High fructose consumption can cause greater absorption of fructose and triglyceride levels in the blood and liver will increase. In addition, fructose is mediated by GLUT2 in the liver causing fructose that enters the hepatocyte cytoplasm to be phosphorylated into Fructose 1-phosphate, which can increase fatty acid synthesis, inhibit fat distribution to mitochondria, and cause hypertrophy increasing BW (32,33). After the induction period, the groups underwent a randomization process and were divided into 2 control groups and 3 treatment groups. The control groups consisted of a negative control group (C-), originally G4, and a positive control group (C+), originally G2. The treatment group consisted of treatment group 1 (T1), which was originally G3, treatment group 2 (T2), which was originally G5, and treatment group 3 (T3), which was originally G1. All groups experienced a significant reduction in BW after being given the intervention for 28 days (p=0.026). Figure 1. (a) shows a significant difference between D14 and D28 (p<0.001). In C+, there was the highest decrease in BW, with a decrease of 10.83±23.69. In T1, it experienced an increase in BW of 1.17±9.48. In T2 and T3, there was a decrease in BW but not as much as the decrease in BW in the C+ group, namely 4.33±12.57 and 7.67±10.27, respectively. Figure 1. (b) shows that there was no difference between groups before the intervention (p=0.548), during the intervention (p=0.656), and after the intervention (p=0.672).



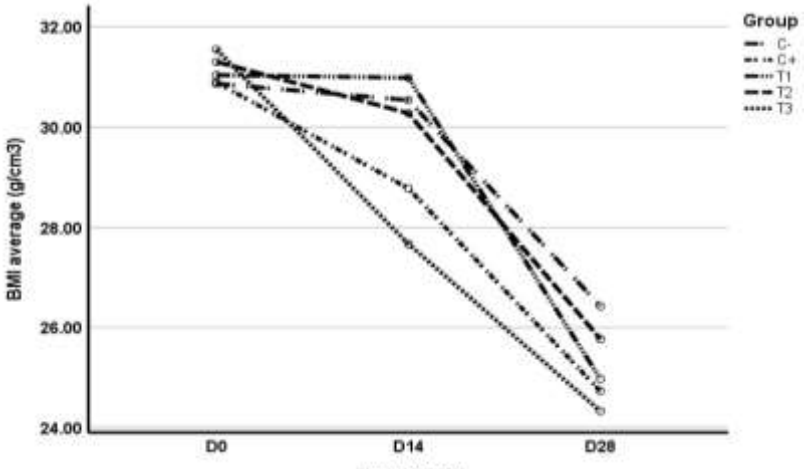


(b)

Figure 1. The RBPE administration reduce rats' BW in the dose-dependent manner. Figure1.(a) indicates significant BW reduction among groups after 14 days and 28 days of RBPE treatment (p<0.05) and Figure 1.(b) indicates slight reduction of rats' BW within groups (p>0.05).

All groups experienced a significant reduction in BMI after 28 days of intervention (p<0.001). **Figure 2**. (a) shows significant differences of BMI between D0 and D14, D0 and D28, and D14 and D28 (p<0.001). The group that experienced the highest decrease occurred in T3 with a decrease of 7.23±1.83, while the group with the lowest decrease occurred in C- with a decrease of 4.44±0.79. Figure 2. (b) shows that on day 0, there was no significant difference between groups (p=0.888), but on days 14 and 28, there was a significant difference between groups with p=0.010 and 0.011, respectively. After 14 days of intervention, there was a significant difference between C- and T3 (p=0.006) and C+ and T1 (p=0.029). After 28 days of intervention, there was a significant difference between C- and C+, T1, and T3 (p≤0.021).

(a)



(b)

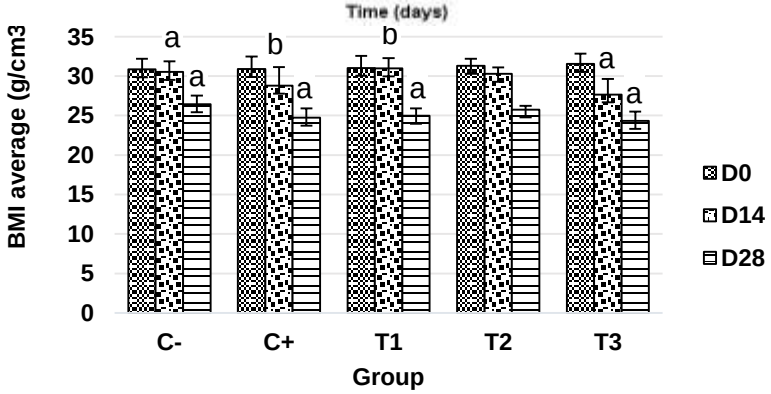


Figure 2. The RBPE administration reduce rats' BMI in the dose-dependent manner. Figure 2.(a) indicates significant BMI reduction among groups on day 0 and after 14 days and 28 days of RBPE treatment (*p*<0.05) and Figure 2.(b) indicates significant mean differences of rats BMI within groups (*p*<0.05).

All groups experienced a significant reduction in BFP after 28 days of intervention ($p<0.001$). **Figure 3**. (a) shows that there are significant differences between D0 and D14, D0 and D28, and D14 and D28 ($p\leq0.001$). The group that experienced the highest decrease occurred in T3 with a decrease of 6.77±1.70, while the group with the lowest decrease occurred in C- with a decrease of 4.20±0.74. **Figure 3**. (b) shows that on day 0, there was no significant difference between groups ($p=0.863$), but on days 14 and 28, there was a significant difference between groups with $p=0.042$ and 0.006, respectively. After 14 days of intervention, there was a significant difference between C- and T3 ($p=0.037$). After 28 days of intervention, there was a significant difference between C- and C+, T1, and T3 ($p\leq0.025$).

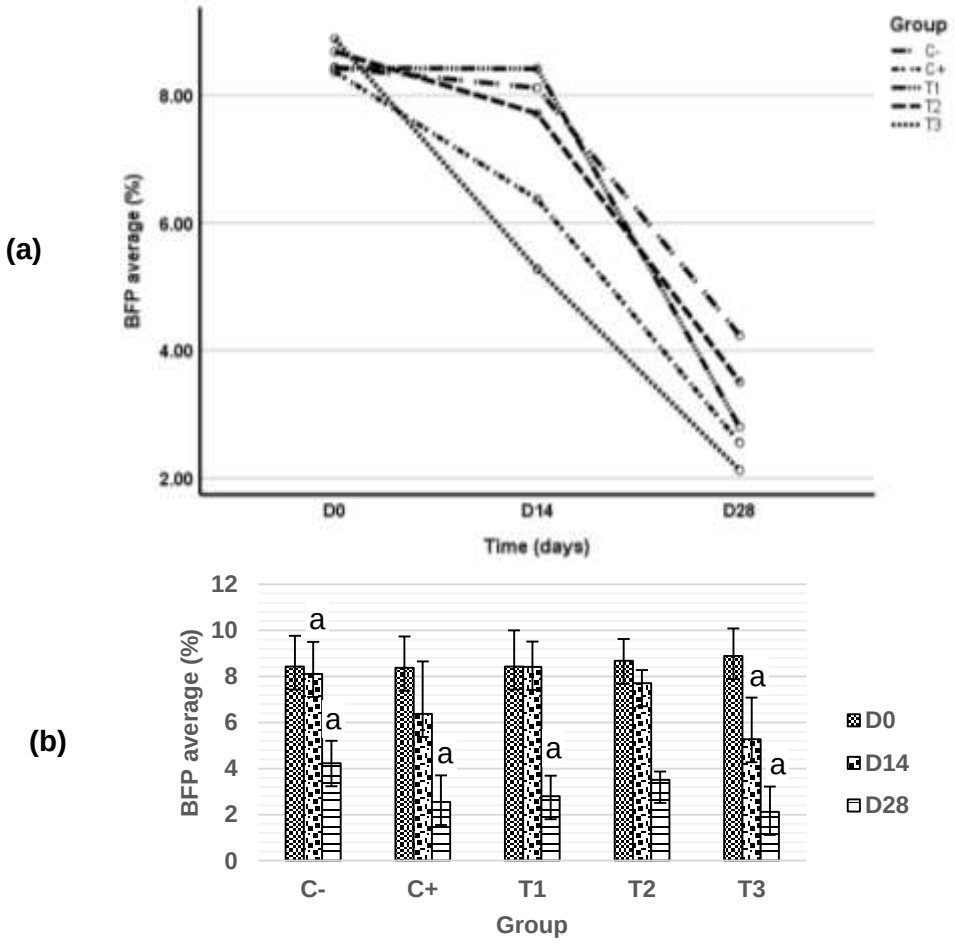


Figure 3. The RBPE administration reduce rats' BFP in the-dose dependent manner. Figure 3.(a) indicates significant BFP reduction among groups on day 0 and after 14 days and 28 days of RBPE treatment (*p*<0.05) and Figure 3.(b) indicates significant mean differences of rats BFP within groups (*p*<0.05).

The highest BW loss occurred in C+, but the lowest average BW was in the group given RBPE at 800 mg/kgBW/day (T3). Meanwhile, the highest decrease in BMI and BFP and the lowest average BMI and BFP were owned by T3. This research is in line with Jomard's study (2021), which stated that the group of obese rats given banana peel extract added to phosphatidylcholine (PC) had the lowest average BW when compared to the other groups (21). In addition, research conducted by Bagabaldo et al. (2022) stated that '*saba*' banana skin extract (*Musa acuminata x balbisiana BBB* Group), which grows a lot in the Philippines, can reduce fat accumulation in the body so that it can reduce BW, BMI, and BFP (34).

Visceral fat mass in each group did not experience a significant difference in either the control or treatment groups, which was indicated by the value of *p*=0.187. T3 was the group with the lowest visceral fat mass while C- was the group with the highest visceral fat mass (1.02±0.49 vs 1.58±0.37).

Table 2. Mean differences in visceral fat mass of rats with obesity with or without RBPE administration

Group	Mean ± SD (g)	*p*
	After 28 days of intervention	
C-	1,58±0.37	
C+	1,52±0.39	
T1	1,25±0.50	0.187
T2	1,23±0.42	
T3	1,02±0.49	

p) One-Way ANOVA

There was no significant difference in visceral fat mass in all groups (p=0.187). However, when compared to all groups, T3 had lower visceral fat mass when compared to other groups, including C+. This may have happened because, in this study, no physical activity was carried out on experimental animals, while the decrease in visceral fat mass did not only occur due to dietary interventions but also required physical activity (35). Research conducted by Wijaya and Surdijati (2020) stated that obese male Wistar rats supplemented with virgin coconut oil had a visceral fat mass of 2.40 g, and rats given coconut oil supplementation had a visceral fat mass of 2.77 g (36). In this study, the visceral fat mass was lower. The difference in visceral fat mass may be due to differences in BW in the experimental animals after the intervention and the type of intervention given. The average BW of rats in the study by Wijaya and Surdijati (2020) was 258.25 g, while in this study, it was 225.77 g. BW has a positive correlation with visceral fat mass, so the greater the BW, the greater the visceral fat mass (37).

The results of this study indicate that RBPE produces a positive effect in obesity therapy. This may be caused by compounds in RBPE, such as quercetin, a flavonoid derivative compound. Previous research that has examined the quercetin compound in green tea and grape seeds states that the mechanism of quercetin, which acts as an anti-obesity agent, is carried out by inhibiting pancreatic lipase activity. Quercetin can reduce the body's absorption of fatty acids by as much as 50% (38). In addition, research on rat models of metabolic syndrome states that quercetin can reduce abdominal circumference by reducing visceral fat mass (39).

Lipogenesis is a fat deposition process that begins with the conversion of glyceraldehyde-3-phosphate (GDP) to lysophosphatidic acid (LPA) by Glycerol-3-phosphate acyltransferase (GPAT). Furthermore, LPA changes to phosphatidic acid (PA), a biosynthetic acylglycerol precursor. These changes are assisted by Lysophosphatidic acid acyltransferase theta (LPAATθ). PA will be converted into

diacylglycerol (DAG) by Lipin1, and then DAG will be synthesized into triglycerides by Diacylglycerol O-Acyltransferase 1 (DGAT1). The quercetin compound can inhibit the action of LPAATθ, Lipin1, and DGAT1, causing a decrease in fat accumulation and triglycerides (40,41).

This study shows a difference in the decrease between the average BW, BMI, and BFP. Fat mass did not significantly differ, but T3 had a lower fat mass than C+. T3 also had a lower average BW than the control group, but during the intervention period, the highest average decrease occurred in C+. In addition, T3 was the group with the lowest average BMI and BFP and experienced the highest average decline during the intervention period. Therefore, further research is needed to evaluate the effect of higher dose of RBPE on obesity. Whilst our study shows a significant reduction of obesity, the mechanism is still unclear, whether it is caused by the quercetin compound contained in RBPE or other compounds, so further study is needed to examine the effect of pure quercetin compound from RBPE on obesity.

CONCLUSIONS AND RECOMMENDATIONS

RBPE can reduce BW, BMI, and BFP in obese model rats although there is no difference in visceral fat mass between groups. Therefore, RBPE has the potential as an alternative pharmacological therapy for the treatment of obesity. Further research is needed to isolate the quercetin compound in RBPE so that a pure quercetin compound is obtained and RBPE testing can be carried out on other obesity parameters such as lipid profiles.

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