

Effectiveness of Melinjo Seed Extract (*Gnetum Gnemon* L.) on Body Weight, Subcutaneous Fat, Visceral Fat, and Cholesterol in Wistar Male White Rats (*Rattus Norvegicus*) With Obesity Given Moderate Intensity Physical Activity

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ABSTRACT

Obesity is a global health issue linked to several metabolic disorders. Natural products, including those containing bioactive compounds, are gaining attention as complementary approaches for weight management. Melinjo seeds (*Gnetum gnemon* L.) are rich in phytochemicals that may support metabolic health. The purpose of this study was to evaluate the impact of melinjo seed extract combined with moderate-intensity physical activity on body weight, abdominal subcutaneous fat, abdominal visceral fat, and cholesterol levels in obese male Wistar rats. A randomized controlled trial was performed with 24 rats, which were assigned to three groups: control (P0), moderate-intensity physical activity (P1), and moderate-intensity physical activity with melinjo extract (P2). Following a 42-day high-fat diet to induce obesity, the rats underwent a 28-day intervention period. Significant improvements were observed in group P2, with reductions in body weight, subcutaneous fat, visceral fat, and cholesterol. Group P1 showed improvements but to a lesser extent, while group P0 showed no significant changes. These results suggest that melinjo seed extract combined with physical activity effectively reduces weight and fat. Future research should investigate the molecular mechanisms and potential human applications.

Keywords: *obesity, melinjo, cholesterol, fat, physical activity*

INTRODUCTION

Obesity has been recognized as a global health problem that continues to increase year after year. The World Health Organization (WHO, 2018) classifies obesity as a global epidemic that requires serious attention due to its association with an increased risk of chronic metabolic diseases. Data from Indonesian Basic Health Research (Riskesdas) in 2018 showed that the prevalence of obesity in the adult population reached 21.8%, a sharp increase compared to 2007 (10.5%) and 2013 (14.8%). This condition illustrates the continuing trend of obesity and has the potential to pose a greater public health burden.

Physiologically, obesity is defined by an abnormal buildup of fat in both subcutaneous and visceral tissues.. While subcutaneous fat, located beneath the skin, is dominant, the

accumulation of visceral fat in the abdominal cavity has been shown to be more dangerous because it can trigger insulin resistance, hyperlipidemia, and hypertriglyceridemia (Masi & Oroh, 2018). The buildup of visceral fat acts as a trigger for several metabolic issues, including type 2 diabetes, coronary heart disease, and stroke.

Furthermore, obesity is closely linked to hypercholesterolemia. Obese individuals generally experience elevated cholesterol levels due to the consumption of high-fat foods, which leads to excess lipids in the blood. This condition contributes to cardiovascular disease, cerebrovascular disease, hypertension, and other metabolic complications (Corine T. Netzer, 2020). Thus, obesity not only results in excess weight but also triggers significant changes in lipid profiles that are detrimental to long-term health.

Obesity management efforts generally involve lifestyle modifications, including diet, physical activity, and behavioral changes, along with pharmacotherapy when necessary. High-intensity physical activity has been shown to effectively reduce body fat reserves by stimulating lipolysis, increasing muscle mass, and improving lipid profiles, including lowering LDL cholesterol (Sarrafzadegan & Mohammadifard, 2017). However, long-term use of pharmacotherapies such as orlistat or statins has side effects ranging from gastrointestinal disturbances, hepatotoxicity, to myopathy (Sa'diyah et al., 2019; Albert et al., 2018). This has prompted the search for safer, natural alternative treatments.

The melinjo plant (*Gnetum gnemon* L.) is a source of natural ingredients with high bioactive compounds, including flavonoids, saponins, tannins, triterpenoids, and resveratrol. These substances are known to have lipid-lowering, anti-inflammatory, and antioxidant qualities (Herlina et al., 2021). Specifically, resveratrol in melinjo seeds can inhibit the HMG-CoA reductase enzyme, which is involved in cholesterol synthesis, thereby lowering cholesterol levels while increasing LDL receptors in the liver membrane (Hafidz et al., 2017; Konno et al., 2013). Previous research also showed that melinjo seed extract is effective in reducing uric acid, inhibiting pancreatic lipase, and increasing HDL levels.

Several experimental studies support the potential of melinjo seeds as an antiobesity agent. Ulfa et al. (2018) reported that melinjo extract had a significant weight-loss effect in animal models of obesity, although human studies are still limited. Conversely, Musthofa (2018) showed that moderate-intensity physical activity in rats can improve body fat levels and increase HDL. However, there is no scientific context regarding the comparison of the effectiveness of administering melinjo extract with moderate-intensity physical activity. Therefore, this study is important to assess the effectiveness of the combination of the melinjo extract with moderate-intensity physical activity on reducing body weight, abdominal fat, visceral fat, and cholesterol levels in obese male Wistar rats (*Rattus norvegicus*).

METHODS

Study Design

A Randomized Post-Test Only with Control Group Design was used in this study. It used an experimental approach, including the collection and processing of samples, preparation of plant material, extraction, phytochemical screening, and measurement of body weight, subcutaneous abdominal fat, visceral abdominal fat, and cholesterol levels. The study

involved three experimental groups: P0 (control group), P1 (moderate-intensity physical activity), and P2 (moderate-intensity physical activity with melinjo seed extract).

Melinjo Seed Extract Preparation

Melinjo seeds were harvested, cleaned, and dried in an oven at temperatures ranging from 50-70°C. Once the seeds had dried, they were pulverized into a fine powder, sieved through a 35-mesh screen, and then sealed in glass containers. To extract the bioactive compounds from the powdered seeds, 70% ethanol was used. The extraction process involved maceration for 72 hours, followed by filtration and concentration using a rotary evaporator to obtain a concentrated extract.

The extract underwent phytochemical analysis to determine whether alkaloids, flavonoids, saponins, tannins, steroids, triterpenoids, and phenols were present, following standard procedures. The rats in Group P2 were then given the melinjo extract orally via a sonde after it had been prepared for oral administration at a dose of 500 mg/kg body weight daily and dissolved in distilled water.

High-Fat Diet Preparation

The high-fat diet was made by blending beef brain and quail eggs, which were steamed, mashed, and mixed with distilled water in a 1:1 ratio. This mixture was administered to the rats daily.

Animal Preparation

A total of 30 male Wistar rats were chosen following Federer's formula: $(n - 1) \times (t - 1) \geq 15$, with an additional 10% reserve to compensate for possible dropouts. The rats underwent a 7-day acclimatization period and were given standard rat food and water ad libitum. During the course of the study, each rat was kept in a cage with regulated lighting and temperature (25°C, 70% humidity).

Experimental Treatment

After 42 days of high-fat diet feeding, rats with obesity (weighing >250 grams, Lee index >300) were randomly divided into three groups: P0: no intervention. P1: Rats performed moderate-intensity swimming for 20 minutes per day. P2: rats performed moderate-intensity swimming and were orally administered melinjo extract at 500 mg/kg body weight per day. The intervention lasted for 28 days. Measurements of body weight, subcutaneous fat, visceral fat, and cholesterol levels were performed on day 28.

Lee Obesity Index = $\sqrt[3]{\text{Body Weight (grams)} \times 1000}$

Naso-anal length (cm)

Rats are categorized as obese if the Lee Obesity Index value exceeds 300 (Mandarim-de Lacerda, et al., 2021).

Body Weight Measurement

After the intervention, body weight was measured in grams using a digital balance.

Cholesterol Measurement

Cholesterol levels were measured by taking blood from the tail of the rats after a 12-18 hour fasting period. The blood was placed on a cholesterol test strip and analyzed using the Easy Touch 3 in 1 device.

Fat Measurement (Subcutaneous and Visceral)

After euthanizing the rats via chloroform inhalation, abdominal fat (subcutaneous and visceral) was collected and weighed using a digital balance and recorded in grams.

Data Analysis

SPSS was used for statistical analyses. The data will be analyzed using descriptive statistics to summarize the characteristics of the variables. The Shapiro-Wilk test and Levene's test will be used to evaluate normality and homogeneity of variance, respectively. Post-hoc LSD will be used in conjunction with One-Way ANOVA for normally distributed data with homogeneous variance; for non-normally distributed or heterogeneous data, the Brown-Forsythe test with post-hoc Games-Howell will be applied. The Kruskal-Wallis test along with the post-hoc Dunn's test will be applied if the data is not regularly distributed. This approach will help identify significant differences in body weight, fat distribution, and cholesterol levels across groups.

RESULTS

Phytochemical Screening

Based on the results of the phytochemical screening test, the extract of melinjo seeds (*Gnetum gnemon* L.) contains saponins, tannins, flavonoids, and terpenoids.

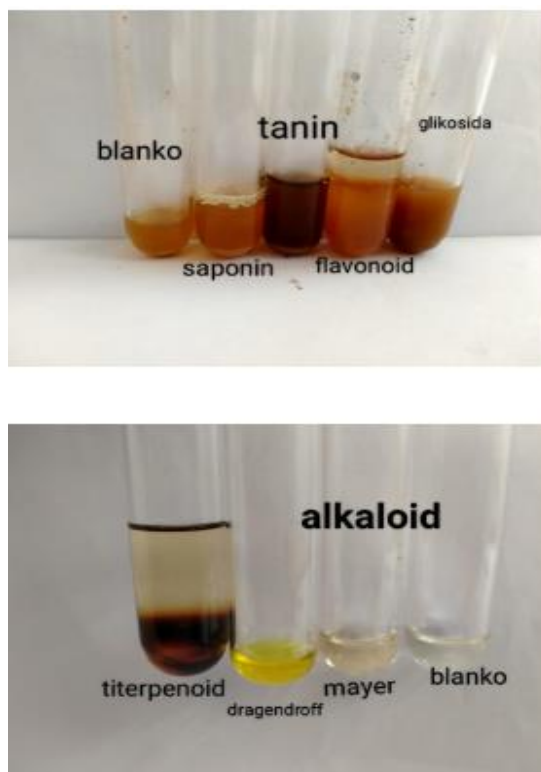


Figure 1. Phytochemical Screening Photo Results

Descriptive Statistics

This study involved 30 male Wistar rats (*Rattus norvegicus*) as subjects. During the study, 6 rats died during the environmental acclimation phase. The remaining subjects were divided into three groups: P0 (control group), P1 (moderate-intensity physical activity), and P2 (moderate-intensity physical activity combined with melinjo seed extract at 500 mg/kg body weight per day, administered via sonde). Each group consisted of 8 rats. The research

was carried out at Universitas Indonesia's Chemistry Laboratory from September to November 2023.

The following table presents the mean values for Lee Index, subcutaneous fat, visceral fat, and cholesterol levels across the treatment groups before and after the intervention:

Table 1. Sample Characteristics

Variable	P0 (Control)	P1 (Physical Activity)	P2 (Physical Activity + Melinjo Extract)
Lee Index after High-Fat Diet	306.63 ± 3.50	306.88 ± 3.80	308.75 ± 4.77
Lee Index Post-Intervention	306.25 ± 3.06	287.88 ± 4.39	279.13 ± 6.49
Visceral Fat (g)	0.98 ± 0.49	0.54 ± 0.27	0.46 ± 0.17
Subcutaneous Fat (g)	0.60 ± 0.13	0.48 ± 0.24	0.34 ± 0.13
Cholesterol (mg/dL)	124.75 ± 6.78	105.88 ± 6.79	101.38 ± 3.11

Before intervention, the Lee Index was similar across all groups, with P0 (306.63 ± 3.50), P1 (306.88 ± 3.80), and P2 (308.75 ± 4.77). After intervention, P0 showed a higher Lee Index (306.25 ± 3.06) compared to P1 (287.88 ± 4.39) and P2 (279.13 ± 6.49). Visceral fat in P2 (0.46 ± 0.17 grams) was significantly lower than P1 (0.54 ± 0.27 grams) and P0 (0.98 ± 0.49 grams). Similarly, subcutaneous fat was lower in P2 (0.34 ± 0.13 grams) compared to P1 (0.48 ± 0.24 grams) and P0 (0.60 ± 0.13 grams). Cholesterol levels in P2 were the lowest (101.38 ± 3.11 mg/dL) after 28 days of moderate-intensity physical activity and melinjo extract supplementation, followed by P1 (105.88 ± 6.79 mg/dL), and P0 (124.75 ± 6.78 mg/dL).

Normality and Homogeneity Tests

Because there were fewer than fifty samples, the Shapiro-Wilk test was used to determine whether the data was normal. Results showed that the Lee Index after the high-fat diet was normal in P0, but not in P1 and P2. However, the Lee Index post-intervention, subcutaneous fat, visceral fat, and cholesterol levels were normally distributed in most groups. Data for cholesterol in P0 and P1 were not normally distributed. Using Levene's test, homogeneity of variance was examined, showing that Lee Index and cholesterol data were homogeneous, while subcutaneous and visceral fat data were not. For non-normal data, Kruskal-Wallis and post-hoc Dunn's test were applied, while One-Way ANOVA and post-hoc LSD were used for normally distributed and homogeneous data, with Brown-Forsythe and Games-Howell used for non-homogeneous fat data.

Comparative Analysis

The following presents a comparative analysis of various variables based on the Lee Index, visceral fat, subcutaneous fat, and cholesterol levels.

Table 2. Comparison of Lee Index between Treatment Groups

Variable	P0 (Control)	P1 (Physical Activity)	P2 (Physical Activity + Melinjo Extract)	p-value
Lee Index after High-Fat Diet	306.63 ± 3.50	306.88 ± 3.80	308.75 ± 4.77	0.375
Lee Index Post-Intervention	306.25 ± 3.06	287.88 ± 4.39	279.13 ± 6.49	<0.001*

*Note: Significant at $p < 0.05$

Before the intervention, the Lee Index values did not differ significantly among the groups, with P0 (306.63 ± 3.50), P1 (306.88 ± 3.80), and P2 (308.75 ± 4.77). However, after the intervention, the P0 group had a higher Lee Index (306.25 ± 3.06) compared to P1 (287.88 ± 4.39) and P2 (279.13 ± 6.49), showing statistically significant differences ($p < 0.001$).

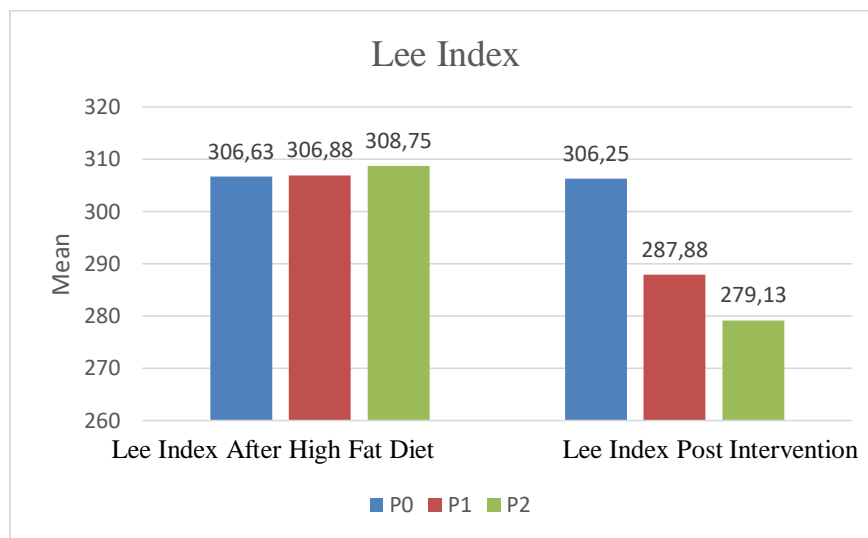


Figure 2. Comparison of Lee Index between treatment groups

Figure 2 illustrates that the Lee Index after the intervention showed significant differences between P0 and both P1 and P2 groups, with P0 showing higher values.

Table 3. Post-Hoc Comparison of Lee Index Post-Intervention

Comparison	p-value
P0 – P1	<0.001*
P0 – P2	<0.001*
P1 – P2	0.002*

Significant differences between P0 and P1 and P2 ($p < 0.001$) and between P1 and P2 ($p = 0.002$) were shown by post-hoc analysis, suggesting that the combination of moderate-intensity physical activity and melinjo extract (P2) was the most effective in lowering the Lee Index.

Table 4. Comparison of Visceral Fat, Subcutaneous Fat, and Cholesterol Levels

Variable	P0 (Control)	P1 (Physical Activity)	P2 (Physical Activity + Melinjo Extract)	p-value
Visceral Fat (g)	0.98 ± 0.49	0.54 ± 0.27	0.46 ± 0.17	0.018*
Subcutaneous Fat (g)	0.60 ± 0.13	0.48 ± 0.24	0.34 ± 0.13	0.028*
Cholesterol (mg/dL)	124.75 ± 6.78	105.88 ± 6.79	101.38 ± 3.11	<0.001*

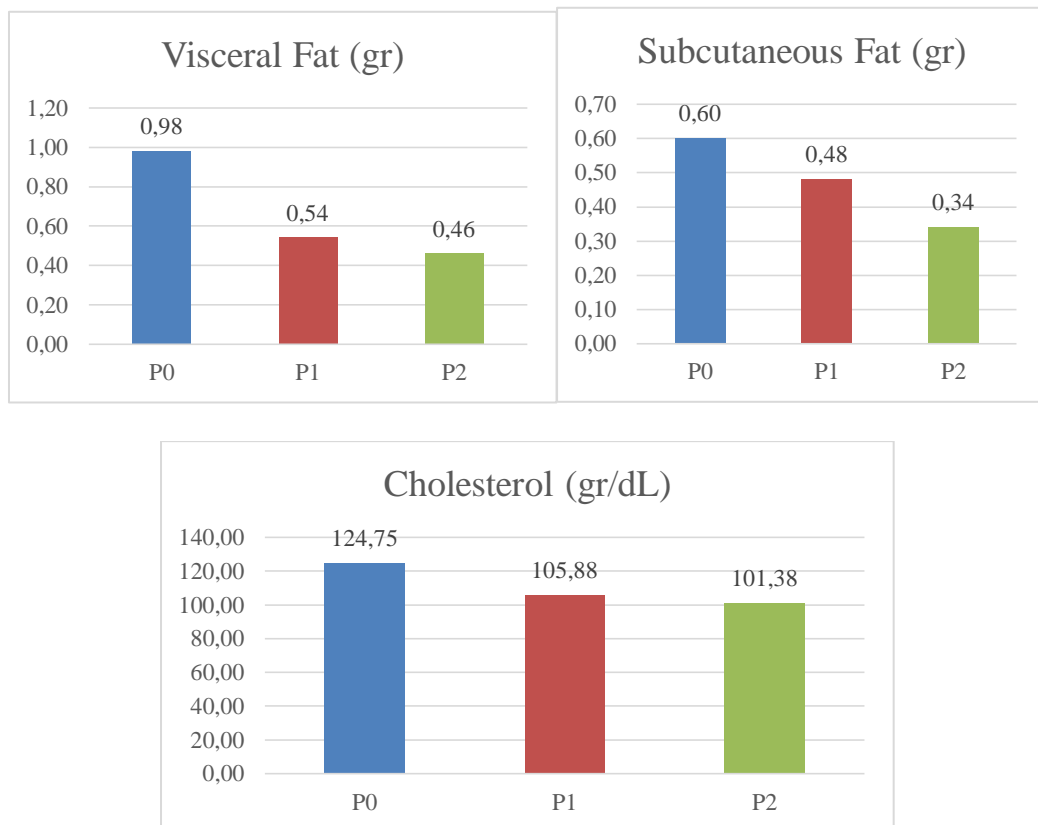


Figure 3. Comparison of treatment groups' levels of visceral fat, subcutaneous fat, and cholesterol

Table 5. Post-Hoc Comparison of treatment groups' levels of visceral fat, subcutaneous fat, and cholesterol

Comparison	p-value
Subcutaneous Fat	
P0 – P1	0.107
P0 – P2	0.048*
P1 – P2	0.773
Visceral Fat	
P0 – P1	0.432
P0 – P2	0.003*

P1 – P2	0.353
Cholesterol	
P0 – P1	0.004*
P0 – P2	<0.001*
P1 – P2	0.330

*Note: Significant at $p < 0.05$

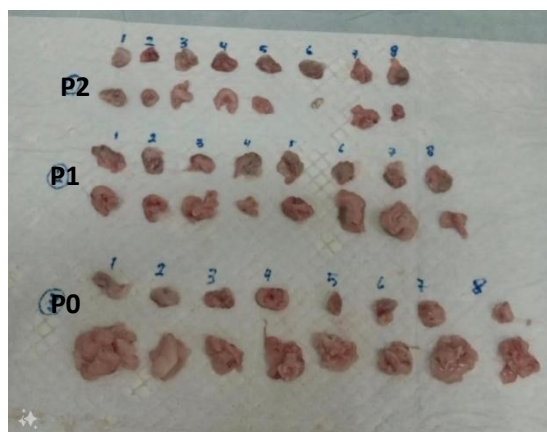


Figure 4. Comparison of visceral fat, subcutaneous fat between treatment groups

Post-Hoc analysis indicated significant differences in visceral fat (P0 vs. P2, $p = 0.003$), subcutaneous fat (P0 vs. P2, $p = 0.048$), and cholesterol levels (P0 vs. P1, $p = 0.004$; P0 vs. P2, $p < 0.001$). The most effective reduction in subcutaneous fat, visceral fat, and cholesterol was observed in the P2 group (moderate-intensity physical activity combined with melinjo seed extract).

DISCUSSION

Effect of Physical Activity and Melinjo Seed Extract on Body Weight

This study's main objective was to evaluate how body weight, visceral fat, subcutaneous fat, and cholesterol levels were affected in Wistar rats by moderate-intensity physical activity and melinjo seed extract. The findings showed that both therapies significantly decreased body weight, with the combination of physical activity and melinjo extract (P2 group) yielding the most significant effect. The Lee Index did not significantly differ across groups prior to the intervention. However, after 28 days of intervention, the P0 (control) group showed no change, while both the P1 (physical activity) and P2 (physical activity plus melinjo extract) groups experienced substantial reductions in body weight and Lee Index ($p < 0.001$), with the P2 group showing the largest decrease.

Phytochemical analysis of the melinjo seed extract identified flavonoids, saponins, tannins, and triterpenoids, all of which are known to influence body weight. Previous studies have shown that flavonoids can promote weight loss by enhancing fat metabolism and reducing lipid absorption (Mahboob et al., 2023). Saponins are also known to modulate appetite-regulating neurons in the hypothalamus, which helps reduce fat absorption and improve lipid metabolism (Cao et al., 2024). Additionally, triterpenoids have been associated with AMPK activation, which increases fat oxidation and stimulates

mitochondrial biogenesis (Chen et al., 2020). These mechanisms likely contributed to the significant weight reduction observed in the P2 group.

Moderate-intensity physical activity plays an important role in weight management by activating AMPK, which regulates cellular metabolism, promoting fat oxidation and inhibiting fat synthesis. The body's capacity to burn fat and create ATP, the energy source, is improved by this activation. The findings from Fang et al. (2022) and Sholikhah and Ridwan (2021) support these results, showing that moderate-intensity physical activity boosts fat metabolism and reduces weight gain, particularly when combined with dietary changes.

Effect of Physical Activity and Melinjo Seed Extract on Visceral and Subcutaneous Fat

Visceral and subcutaneous fat are critical indicators of obesity-related metabolic dysfunctions. The results showed that the combination of moderate-intensity physical activity and melinjo seed extract (P2 group) was more effective in reducing both visceral and subcutaneous fat compared to physical activity alone (P1 group) or the control group (P0). The reduction in visceral fat was statistically significant ($p = 0.018$), with the P2 group showing the lowest levels of visceral fat (0.46 ± 0.17 grams), followed by the P1 group (0.54 ± 0.27 grams) and the P0 group (0.98 ± 0.49 grams). Similarly, subcutaneous fat was also significantly reduced in the P2 group (0.34 ± 0.13 grams) compared to P1 (0.48 ± 0.24 grams) and P0 (0.60 ± 0.13 grams), with a p -value of 0.028.

Flavonoids, saponins, tannins, and triterpenoids in the melinjo seed extract is likely responsible for the reduction in fat accumulation. These compounds are known to regulate fat metabolism by increasing fatty acid breakdown and inhibiting the formation of new fat. Saponins, for instance, can reduce fat absorption and modulate lipid metabolism through gut-liver interactions (Fang et al., 2022). Furthermore, triterpenoids enhance fat breakdown by activating the AMPK pathway, which increases fat oxidation and mitochondrial biogenesis (Huang & Xu, 2025). These findings suggest that the combination of melinjo seed extract and physical activity significantly enhances fat metabolism, particularly in visceral adipose tissue, which is more metabolically active and responsive to interventions.

Effect of Physical Activity and Melinjo Seed Extract on Cholesterol Levels

The P2 group (which combined physical activity with melinjo extract) experienced the greatest reduction in cholesterol levels, averaging 101.38 ± 3.11 mg/dL, compared to the P1 group (physical activity alone, 105.88 ± 6.79 mg/dL) and the P0 group (control, 124.75 ± 6.78 mg/dL). This reduction was statistically significant ($p < 0.001$), suggesting that the combination of physical activity and melinjo seed extract is effective in lowering cholesterol levels.

The bioactive substances in melinjo seed extract, such as flavonoids, saponins, and tannins, are probably what cause its cholesterol-lowering properties. Flavonoids lower total and LDL cholesterol levels by inhibiting HMG-CoA reductase, an enzyme essential to cholesterol production (Herlina et al., 2021). Saponins affect cholesterol in cell membranes, regulating its absorption and excretion (Herlina et al., 2021), while tannins decrease cholesterol absorption in the intestines and promote its excretion (Fang et al., 2022). These compounds likely contributed to the observed cholesterol reduction in the P2 group.

In addition to the effects of melinjo seed extract, moderate-intensity physical activity contributes to lowering cholesterol by increasing lipoprotein lipase activity, enhancing cholesterol esterification, and promoting the transport of cholesterol from peripheral tissues to the liver. Physical activity also inhibits HMG-CoA reductase and boosts LDL receptor activity in the liver, facilitating the removal of LDL cholesterol from the bloodstream (Sholikhah & Ridwan, 2021). The combined impact of physical activity and melinjo seed extract thus has a synergistic effect on reducing cholesterol levels.

This study shows that giving Wistar rats melinjo seed extract along with moderate-intensity physical activity dramatically lowers their body weight, visceral fat, subcutaneous fat, and cholesterol levels. These results demonstrate the potential of melinjo seed extract as a useful adjunct to physical activity in the treatment of obesity and associated metabolic diseases.

The study does have certain drawbacks, though, such as the intervention's brief 28-day length, which might not accurately represent the treatments' long-term benefits. Future studies should look into how physical physical activity and melinjo seed extract affect metabolic health over the long run in both human and animal models. The molecular mechanisms behind the combined effects of physical activity and melinjo seed extract should also be investigated in future research.

CONCLUSION

This study examined the combined effects of moderate-intensity physical activity and melinjo seed extract on body weight, fat distribution, and cholesterol levels in Wistar rats. In comparison to the control and moderate-intensity physical activity-only groups, the results demonstrated that melinjo seed extract and moderate-intensity physical activity significantly decreased body weight, visceral fat, subcutaneous fat, and cholesterol levels. This lends credence to the idea that melinjo seed extract, which is abundant in bioactive substances such as flavonoids, saponins, tannins, and triterpenoids, amplifies the metabolic benefits of physical activity.

The study emphasizes how physical activity and plant-based extracts may be used to treat obesity and associated metabolic diseases, suggesting that melinjo seed extract boosts fat metabolism and improves lipid profiles when combined with moderate-intensity physical activity. However, the study's short duration and reliance on animal models are limitations. Future studies should look into the underlying molecular pathways and examine the long-term impact of physical activity and melinjo seed extract on metabolic health. Additionally, clinical trials involving human participants would be essential to confirm the applicability of these findings in real-world settings. The study lays the groundwork for future research into the combined therapeutic potential of melinjo seed extract and physical physical activity by shedding light on their synergistic benefits in the management of metabolic disorders and obesity.

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