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RESEARCH ARTICLE

Hormonal Regulation in Obesity: The Dose-dependent Impact of *Artocarpus altilis* Extract on Ghrelin, Leptin, and Adiponectin

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Abstract

Background: Obesity is a global health concern linked to metabolic dysregulation, including alterations in key hormones such as ghrelin, leptin, and adiponectin, which regulate appetite, energy metabolism, and adiposity. *Artocarpus altilis* (*Moraceae*) has been explored for its therapeutic potential in obesity management, but its effects on these hormones remain unclear. **Aim:** This study aimed to evaluate the effects of *A. altilis* extract on ghrelin, leptin, and adiponectin levels in obesity-induced rats and compare its efficacy to metformin, a standard anti-obesity agent. **Methods:** Thirty male obesity-induced rats were divided into five groups: Negative Control (NC), positive control treated with metformin 45 mg/kg (PC), and three treatment groups receiving *A. altilis* extract at doses of 200 mg/kg (EA1), 300 mg/kg (EA2), and 400 mg/kg (EA3). Hormone levels were measured, and statistical analysis was performed using ANOVA and post hoc tests. **Results:** ANOVA revealed significant differences ($P < 0.05$) in hormone levels across groups. Ghrelin levels were significantly reduced in all treatment groups, with the most pronounced effect in EA3 (2287 ± 85.84 ng/L, $P < 0.0001$ vs. NC). Leptin levels increased dose-dependently, with EA3 showing the highest levels (16.89 ± 1.129 ng/mL, $P < 0.01$ vs. NC). Adiponectin levels were significantly elevated in EA2 and EA3, with no significant differences between these groups ($P \geq 0.05$). **Conclusion:** *A. altilis* extract demonstrated significant, dose-dependent modulation of ghrelin, leptin, and adiponectin levels, highlighting its potential as a natural therapeutic agent for obesity management.

Major Findings: *A. altilis* extract significantly reduced ghrelin levels, increased leptin in a dose-dependent manner, and elevated adiponectin at higher doses, demonstrating its potential as a natural therapeutic agent for obesity management.

Keywords: Adiponectin, *A. altilis*, Ghrelin, Leptin, Obesity Management

1. Introduction

Obesity represents a significant global health concern, exhibiting a rising prevalence across various countries. Indonesia, in particular, has been identified as one of the nations with a notable incidence of obesity. The prevalence of obesity has reached epidemic proportions, with an annual increase in affected individuals[1]. Projections indicate that by 2030, approximately one in five women and one in seven men will be obese, which would equate to over one billion individuals worldwide[2]. Global obesity rates tend to be higher in women than in men, and the majority of obese individuals are found in developing countries[3]. The data from basic health research indicates a notable increase in the prevalence of obesity in recent years, particularly among the adult population. The prevalence of obesity increased from 28.9 % in 2013 to 35.4 % in 2018. The impact of obesity is disproportionately felt by adult women, with 44.4 % of women being classified as overweight or obese in 2018, compared to 26.6 % of men[4].

The prevalence of obesity is significantly higher in urban areas than in rural areas. In 2018, the basic health research data indicated that the province with the

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highest prevalence of obesity was DKI Jakarta, with an estimated 31.5 % of adult residents classified as obese. In contrast, the prevalence of obesity in rural areas, such as East Nusa Tenggara (NTT), is comparatively lower, at 16.7 %. The high incidence of obesity in urban areas compared to rural areas is thought to be caused by several factors. These include low physical activity due to a practical and modern lifestyle[4]Unbalanced food consumption patterns with excessive portions of saturated fat and synthetic flavourings, but low fibre and vitamins, and higher levels of psychosocial stress related to the demands of living in an urban environment[5]. In contrast, individuals residing in rural areas tend to adhere to more traditional lifestyles, engaging in greater physical activity and consuming diets that are comparatively healthier, with a higher intake of vegetables and fruits. However, there has been an increase in the accessibility of ready-to-eat foods that are high in fat and salt in rural areas over time.

The development of obesity is the result of an imbalance between calorie intake and energy expenditure[6]. This condition is precipitated by a constellation of risk factors, including an unhealthy diet characterised by excessive fat and calorie intake, an increased consumption of processed foods and fast food, and a sedentary lifestyle with low physical activity[5]. A chronic surplus of calories relative to the energy expended by the body will result in an accumulation of excess nutrients, primarily in the form of adipose tissue, leading to progressive weight gain[7]. This alteration in dietary habits and lifestyle is the primary factor contributing to the rising prevalence of obesity in both developed and developing countries, including Indonesia.

From a pathophysiological perspective, obesity is typified by an expansion of adipose tissue, which in turn gives rise to chronic inflammation and a disruption of the intricate hormonal pathways that regulate energy homeostasis and glucose metabolism[8]. Some crucial biomarkers include insulin resistance, dysregulation of appetite hormones (ghrelin, leptin, adiponectin), and elevated levels of inflammatory cytokines (IL-1, IL-6)[9]. Such conditions increase the risk of developing degenerative diseases, including type 2 diabetes and cardiovascular disease.

The treatment and prevention of obesity necessitates a multidisciplinary approach, encompassing lifestyle modification and the utilisation of pharmacological and non-pharmacological therapies. One alternative therapeutic approach is the utilisation of bioactive compounds derived from natural sources, which are generally regarded as safer and may have promising effects. Breadfruit leaves of *A. altilis* (Moraceae) have a long history of use in traditional medicine in several regions. The plant is used for a variety of purposes, including the treatment of hypertension, diabetes mellitus, fever, and other ailments[10].

Additionally, research indicates that compounds derived from the *A. altilis* extract possess antioxidant properties[11]. Extracts of *A. altilis* have been demonstrated to reduce Free Fatty Acid (FFA) levels[12]. Additionally, the ethanol extract of *A. altilis* leaves has been found to possess a high phenolic and flavonoid content[13]. Furthermore, the extract has been demonstrated to exhibit robust free radical capture activity and the capacity to inhibit lipid peroxides[14]. Additionally, *A. altilis* extract has been demonstrated to possess anti-hypertensive effects through its diuretic effect[15]. It can be reasonably assumed that this is related to the diuretic activity of saponin and flavonoid compounds. Furthermore, the extract has been demonstrated to possess antidiabetic properties, which are attributed to its ability to inhibit α-glucosidase and α-amylase enzymes, which are involved in the absorption of carbohydrates. It may therefore be considered a potential antidiabetic agent[16].

Nevertheless, research on the potential of *A. altilis* as an anti-obesity and anti-diabetes agent through the modulation of hormonal and inflammatory factors remains scarce. The research related to the potential of *A. altilis* as an antiobesity and antidiabetic agent through modulation of various hormonal pathways and inflammatory responses is still in its infancy. To date, no studies have examined the effects of *A. altilis* on the regulation of appetite hormones, including leptin, ghrelin, and adiponectin. Indeed, these hormones exert a significant influence on the development of obesity and type 2 diabetes. Furthermore, the impact of *A. altilis* on enhancing insulin sensitivity and glucose tolerance in contexts of insulin resistance or diabetes has yet to be investigated. Similarly, its effect on inflammatory cytokines such as TNF-α, IL-1, and IL-6, as well as anti-inflammatory cytokines such as IL-10, which contribute to both diseases, is worthy of investigation.

It is therefore imperative that further studies be conducted to ascertain the effects of *A. altilis* on the regulation of grelin, leptin, adiponectin, IL-1, IL-6, and insulin resistance in conditions of high-fat feed-induced obesity. The results of this study will provide scientific evidence of the potential of *A. altilis* as an anti-obesity agent through its effects on these key markers.

2. Materials and Methods

2.1 Study Design

This study is a quasi-experimental research with a post-test only control group design. The objective is to evaluate the effects of the ethanol extract of *A. altilis* on various biomarkers related to obesity, including Ghrelin, Leptin, Adiponectin, IL-1, IL-6, and Insulin Resistance. The design allows for comparison between groups treated with different dosages of the extract and a control group.

2.2 Variables

The study examines several key variables. The independent variable is the ethanol extract of *Artocarpus altilis*, while the dependent variables are the levels of Ghrelin, Leptin, Adiponectin, IL-1, IL-6, and Insulin Resistance. In addition, several confounding variables are controlled, including species/strain, sex, age, body weight, diet, fluid intake, and room temperature, all of which could influence the outcomes.

2.3 Subjects

The subjects of this study consisted of 25 male Sprague Dawley rats, aged 2-3 months and weighing between 150-250 grams. These rats were randomly assigned to five treatment groups: (1) obesity-induced rats (NC), (2) rats with metformin (45 mg/kg)-induced obesity (PC), (3) obesity rats treated with *A. altilis* extract at 200 mg/kg (EA1), (4) obesity rats treated with *A. altilis* extract at 300 mg/kg (EA2), and (5) obesity rats treated with *A. altilis* extract at 400 mg/kg (EA3). The concentrations of *A. altilis* extract used in this study (200 mg/kg, 300 mg/kg, and 400 mg/kg) were selected based on preliminary studies and literature that suggest these doses are within the effective range for bioactive compound activity. These concentrations allow for the evaluation of dose-dependent effects, ensuring a comprehensive assessment of the extract's potential therapeutic properties while minimising the risk of toxicity.

2.4 Sample Size Calculation

To determine the appropriate sample size for each group, the Federer formula was applied, resulting in a minimum requirement of five rats per group to ensure sufficient statistical power for the analysis.

2.5 Equipment

The study utilised several pieces of equipment, including a minor set for preparation, an analytical balance for weighing materials, a microscope for any necessary tissue examination, and a perfusion apparatus for euthanising the rats under controlled conditions.

2.6 Materials

The materials used in this research include *A. altilis leaves*, ketamine for anaesthesia, betadine for sterilisation, 0.9 % NaCl, Phosphate Buffered Saline (PBS), 90 % ethanol for maceration, distilled water, and standard rat feed.

2.7 Research Procedure

The research procedure began with obtaining ethical clearance from the Research Ethics Committee of Jenderal Soedirman University (dossier No. 091/KEPK/PE/X/2024). Afterwards, all necessary equipment and materials were prepared for use. The ethanol extract of *A. altili was* prepared by macerating the leaves in 90 % ethanol. The use of 90 % ethanol in the extraction of *A. altilis* leaves was chosen due to its ability to dissolve both polar and nonpolar compounds, enabling a more efficient and comprehensive extraction of bioactive compounds. The process of concentrating the liquid extract was carried out by evaporating the solvent under reduced pressure, followed by the drying process to remove any residual solvent, resulting in a more concentrated and stable extract. Once prepared, the rats were randomly assigned to their respective treatment groups. Obesity was induced in all rats by providing them with a high-fat diet over 10-12 weeks. After the treatment period, the rats were euthanised using gas anaesthesia, such as isoflurane or sevoflurane, to minimise any distress during the termination phase.

2.8 Measurement of Biomarkers

The biomarkers of interest, such as Ghrelin, Leptin, and Adiponectin were measured using the ELISA method, utilizing commercially available kits. Serum samples from the rats were collected to assess the concentration of each of these biomarkers, providing insight into the metabolic changes induced by the different treatments.

2.9 Statistical Analysis

The collected data were analysed for normality using the Shapiro-Wilk test and for homogeneity using Levene's test. For normally distributed and homogeneous data, one-way ANOVA was performed, followed by post hoc LSD tests to identify specific group differences. Non-normally distributed data were analysed using the Kruskal-Wallis test, followed by post hoc Mann-Whitney tests. A significance level of $p<0.05$ was used as the threshold for statistical significance in all analyses.

3. Results

3.1 Effect of *A. altilis* Extract on Ghrelin Levels in Obesity-induced Rats

This study evaluated the effect of *A. altilis* extract on ghrelin levels in obesity-induced rats. The results of ghrelin level measurements are presented in Table 1. Based on the ANOVA analysis, there was a significant difference ($P < 0.05$) in ghrelin levels across the treatment groups. In the Negative Control group (NC), ghrelin levels were the highest, recorded at 6992 ± 299.1 ng/L, indicating that obesity-induced rats without treatment exhibited elevated ghrelin levels. The Positive Control group (PC), which received metformin, showed a reduction in ghrelin levels to 5000 ± 362.4 ng/L, although the levels remained higher than those observed in the treatment groups.

Administration of *A. altilis* extract at various doses demonstrated a dose-dependent reduction in ghrelin levels. At a dose of 200 mg/kg (EA1), ghrelin levels decreased to 3209 ± 265.2 ng/L. A further reduction was observed in the group receiving 300 mg/kg (EA2), with ghrelin levels of 3016 ± 346.1 ng/L. The lowest ghrelin levels were recorded in the group receiving the highest dose, 400 mg/kg (EA3), at 2287 ± 85.84 ng/L. Overall, the analysis indicated that the administration of *A. altilis extract* significantly reduced ghrelin levels compared to the control groups, with the reduction becoming more pronounced at higher doses. This reduction in ghrelin levels highlights the potential of *A. altilis extract* in regulating hormones that play a key role in appetite and energy metabolism, making it a promising candidate for obesity management.

Table 1. Ghrelin level in obesity-induced rats treated with metformin and *A. altilis* extract

Groups	Mean ± SE (ng/L)	P value
NC	6992 ± 299.1	<0.05
PC	5000 ± 362.4	
EA1	3209 ± 265.2	
EA2	3016 ± 346.1	
EA3	2287 ± 85.84	

NC: negative control; PC: positive control (metformin 45 mg/kg); EA1, EA2, EA3: *A. altilis* extract at doses 200 mg/kg, 300 mg/kg, and 400 mg/kg, respectively.

3.2 Effect of *A. altilis Extract* on Leptin Levels in Obesity-induced Rats

The effect of *A. altilis extract* on leptin levels in obesity-induced rats was evaluated, as shown in Table 2. ANOVA analysis revealed a significant difference ($P < 0.05$) in leptin levels among the groups. The Negative Control group (NC) exhibited a mean leptin level of 0.5600 ± 0.02665 ng/mL, while the positive control group (PC) treated with metformin showed a slight increase to 0.7980 ± 0.07351 ng/mL. In contrast, the groups treated with *A. altilis extract* demonstrated a dose-dependent increase in leptin levels. The EA1 group (200 mg/kg) showed a mean leptin level of 1.240 ± 0.1031 ng/mL, which was significantly higher than the NC group ($P < 0.05$, one-way ANOVA). Similarly,

Table 2. Leptin level in obesity-induced rats treated with metformin and *A. altilis extract*

Groups	Mean ± SE (ng/mL)	P value
NC	0.5600 ± 0.02665	<0.05
PC	0.7980 ± 0.07351	
EA1	1.240 ± 0.1031	
EA2	1.352 ± 0.1155	
EA3	1.842 ± 0.03277	

NC: negative control; PC: positive control (metformin 45 mg/kg); EA1, EA2, EA3: A. altilis extract at doses 200 mg/kg, 300 mg/kg, and 400 mg/kg, respectively.

leptin levels continued to increase in the EA2 (300 mg/kg) and EA3 (400 mg/kg) groups, reaching 1.352 ± 0.1155 ng/mL and 1.842 ± 0.03277 ng/mL, respectively.

The results indicate a statistically significant impact of *A. altilis extract* on leptin levels, as revealed by one-way ANOVA. These findings suggest that *A. altilis extract* exerts a potential dose-dependent effect on leptin regulation in obesity-induced rats.

3.3 Effect of *A. altilis* Extract on Adiponectin Levels in Obesity-Induced Rats

The effect of *A. altilis* extract on adiponectin levels in obesity-induced rats was assessed, with results presented in Table 3. ANOVA analysis indicated a significant difference ($P < 0.05$) in leptin levels across the groups. In the Negative Control group (NC), adiponectin levels were recorded at 10.16 ± 1.527 ng/mL. The Positive Control group (PC), which received metformin, showed slightly higher leptin levels at 12.74 ± 0.4311 ng/mL. Interestingly, adiponectin levels in the group treated with *A. altilis* at 200 mg/kg (EA1) were similar to the PC group, at 12.72 ± 0.6435 ng/mL ($P < 0.05$ compared to NC). However, further increases in adiponectin levels were observed in the groups receiving higher doses of the extract.

At a dose of 300 mg/kg (EA2), adiponectin levels increased to 16.31 ± 1.586 ng/mL, and the highest dose of 400 mg/kg (EA3) resulted in adiponectin levels of 16.89 ± 1.129 ng/mL. These results indicate a dose-dependent increase in adiponectin levels following treatment with *A. altilis* extract.

These findings suggest that while low doses of *A. altilis* extract (200 mg/kg) have a comparable effect to metformin on adiponectin levels, higher doses lead to a marked increase in adiponectin concentrations. This dose-dependent elevation in adiponectin could reflect an adaptive metabolic response, suggesting that *A. altilis* may influence adiponectin signaling pathways involved in energy regulation and adiposity.

Table 3. Adiponectin level in obesity-induced rats treated with metformin and *A. altilis* extract

Groups	Mean ± SE (ng/mL)	P value
NC	10.16 ± 1.527	<0.05
PC	12.74 ± 0.4311	
EA1	12.72 ± 0.6435	
EA2	16.31 ± 1.586	
EA3	16.89 ± 1.129	

NC: negative control; PC: positive control (metformin 45 mg/kg); EA1, EA2, EA3: A. altilis extract at doses 200 mg/kg, 300 mg/kg, and 400 mg/kg, respectively.

3.2 Post Hoc Analysis of Biomarker Levels in Treatment Groups

3.2.1 Ghrelin Levels

The post hoc analysis of ghrelin levels, as shown in Figure 1A, revealed significant differences among the treatment groups. The Negative Control group (NC) exhibited the highest ghrelin levels, which were significantly elevated compared to all other groups. The positive control group (PC), treated with metformin, showed significantly lower ghrelin levels than the NC group ($P < 0.0001$) but remained higher than the groups treated with *A. altilis* extract. Among the extract-treated groups, the 200 mg/kg dose (EA1) resulted in a significant reduction in ghrelin levels compared to both NC ($P < 0.0001$) and PC ($P < 0.001$). However, there were no statistically significant differences between the EA1 group and the higher dose groups (300 mg/kg [EA2] and 400 mg/kg [EA3], $P \geq 0.05$). Additionally, no significant difference was observed between the EA2 and EA3 groups ($P \geq 0.05$), suggesting that increasing the dose beyond 200 mg/kg does not lead to further significant reductions in ghrelin levels.

3.2.2 Leptin Levels

The post hoc analysis of leptin levels, as shown in Figure 1B, demonstrated significant differences between the treatment groups. The NC group had the lowest leptin levels, which were significantly lower than those in the positive control group (PC), which was treated with metformin ($P < 0.0001$). However, no significant difference was observed between NC and the group treated with *A. altilis* extract at 200 mg/kg (EA1, $P \geq 0.05$). Treatment with higher doses of *A. altilis* resulted in a marked increase in leptin levels. The 300 mg/kg dose (EA2) significantly increased leptin levels compared to NC ($P < 0.001$), but no significant difference was found compared to the EA1 group ($P \geq 0.05$). The highest leptin levels were observed in the 400 mg/kg dose group (EA3), which exhibited significantly higher levels compared to both EA1 ($P < 0.01$) and EA2 ($P < 0.01$).

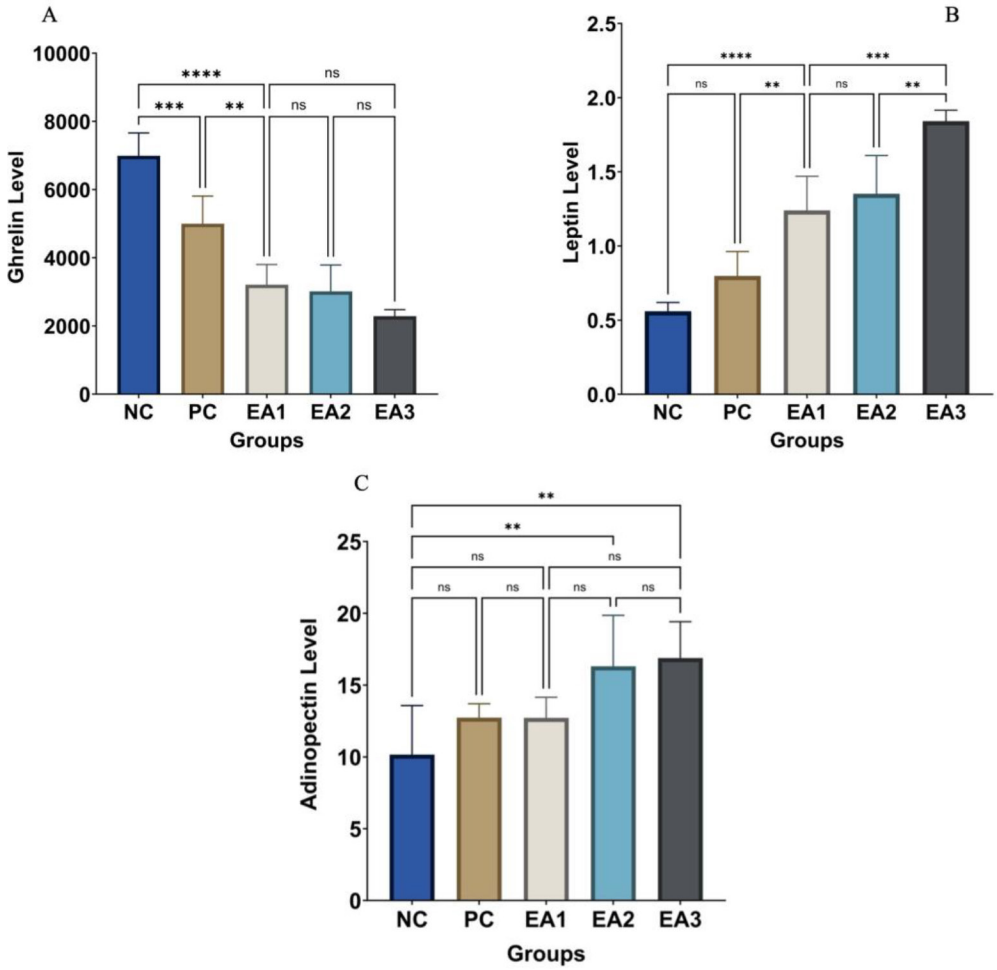


Figure 1. Post hoc analysis among ghrelin, leptin, and adiponectin level in obesity-induced rats (NC), rats with metformin 45 mg/kg-induced obesity (PC), and obbesity rats with extract of *A. altilis* 200 mg/kg (EA1), 300 mg/kg (EA2), 400 mg/kg (EA3). P ≥ 0.05 (ns), P < 0.05 (*), P < 0.01 (**), P < 0.001 (***), P < 0.0001 (****).

3.2.3 Adiponectin Levels

The post hoc analysis of adiponectin levels, as shown in Figure 1C, indicated significant differences between some of the treatment groups. The NC group exhibited the lowest adiponectin levels, which were not significantly different from the PC group (P ≥ 0.05). Treatment with *A. altilis* at 200 mg/kg (EA1) did not significantly alter adiponectin levels compared to the NC or PC groups (P ≥ 0.05). However, higher doses of the extract led to a noticeable increase in adiponectin levels. The 300 mg/kg dose (EA2) significantly elevated adiponectin levels compared to NC (P < 0.01), and the highest levels were recorded in the 400 mg/kg dose group (EA3), which also showed a significant increase compared to NC (P < 0.01). No significant difference was found between the EA2 and EA3 groups (P ≥ 0.05), indicating that both higher doses similarly enhanced adiponectin levels.

4. Discussion

The results of this study indicate that *A. altilis* extract significantly reduces ghrelin levels in obesity-induced rats. This finding aligns with previous research indicating that obesity can increase ghrelin secretion, a hormone that plays a crucial role in appetite regulation and energy metabolism[17,18]. A more pronounced reduction in ghrelin levels was noted in the groups treated with *A. altilis* extract at various doses. These findings demonstrate a clear dose-dependent relationship, where increasing doses of *A. altilis* extract correspond to a greater reduction in ghrelin

levels.. The significant decrease in ghrelin levels may also contribute to reduced food intake and increased energy metabolism, which are critical factors in weight management[19].

The effects of *A. altilis* extract on leptin levels in obesity-induced rats, revealing significant findings that contribute to the understanding of obesity management. Leptin, a hormone primarily produced by adipose tissue, plays a crucial role in regulating energy balance and body weight by signalling satiety to the hypothalamus[20]. Elevated leptin levels indicate a state of leptin resistance commonly associated with obesity[21]. This resistance can lead to disrupted energy homeostasis, perpetuating weight gain and metabolic dysfunction[22]. The leptin levels in the Positive Control group (PC) treated with metformin, a standard anti-hyperglycemic drug, were elevated but not as pronounced as in the *Artocarpus altilis*-treated groups. Metformin is widely recognised for its role in improving insulin sensitivity and reducing body weight in obese individuals[23].

In contrast, the administration of *A. altilis*e extract resulted in a significant, dose-dependent increase in leptin levels. These findings align with previous research indicating that natural extracts, particularly those rich in polyphenols, flavonoids, and alkaloids, can modulate leptin secretion and improve metabolic outcomes in obesity models and improve metabolic profiles in obese models[24].

The mechanism by which *A. altilis* exerts its effects on leptin levels may involve several pathways. Phytochemicals present in the extract, such as flavonoids and polyphenols, have been shown to possess anti-inflammatory and antioxidant properties, which could contribute to improved leptin signalling and reduced adiposity[25]. The present study investigates the effects of *A. altilis* extract on adiponectin levels, a crucial adipokine involved in metabolic regulation and insulin sensitivity. The PC group, treated with metformin, exhibited slightly elevated adiponectin levels. Metformin is well-documented for its role in enhancing insulin sensitivity and increasing adiponectin levels[23].

This dose-dependent increase in adiponectin levels is consistent with the findings of other studies that have demonstrated the potential of natural extracts to modulate adipokine secretion[26]. The observed elevation in adiponectin levels with higher doses of *A. altilis* may indicate an adaptive metabolic response, potentially enhancing the signalling pathways involved in energy regulation and adiposity. The mechanisms underlying the effects of *A. altilis* on adiponectin levels may involve the modulation of inflammatory pathways and the enhancement of insulin sensitivity. Previous research has shown that certain phytochemicals present in *A. altilis* possess anti-inflammatory properties, which could contribute to improved adiponectin signalling[27]. Furthermore, the increase in adiponectin levels may reflect a reduction in visceral fat accumulation, as adiponectin is inversely correlated with body fat percentage[28].

The post hoc analysis of ghrelin, leptin, and adiponectin levels among treatment groups provides valuable insights into the metabolic effects of *A. altilis* extract. Ghrelin, a hormone primarily produced in the stomach, plays a crucial role in appetite regulation and energy homeostasis. Interestingly, the treatment with *A. altilis*a t a EA1 resulted in a significant reduction in ghrelin levels compared to both NC and PC. This suggests a dose-dependent effect of Artocarpus altilis, where 200 mg/kg is optimal for ghrelin suppression. The analysis of leptin levels revealed that higher doses (300 mg/kg and 400 mg/kg) resulted in significant increases in leptin levels, with EA3 exhibiting the highest levels ($P < 0.01$ compared to EA1 and EA2). This elevation in leptin levels with higher doses may indicate a compensatory mechanism in response to increased adiposity or energy storage, as leptin is primarily secreted by adipocytes and is involved in regulating energy balance[22]. The analysis of adiponectin levels further supports the complex interplay between these hormones. Adiponectin is known for its insulin-sensitising effects and anti-inflammatory properties, suggesting that higher doses of *A. altilis* may enhance metabolic health by improving adiponectin secretion[29].

5. Conclusion

Our findings highlight the potential of *A. altilis* as a therapeutic agent for modulating ghrelin, leptin, and adiponectin levels, with implications for appetite regulation and metabolic health. The optimal dose for reducing ghrelin levels appears to be 200 mg/kg, while higher doses may be necessary to enhance leptin and

adiponectin levels. Further studies are warranted to elucidate the underlying mechanisms and long-term effects of *A. altilis* on metabolic parameters.

6. Author Contribution

Wahyudin: Conceptualization, supervision, Writing–original draft, review and editing. Setiawati: Investigation, data curation, writing–original draft, visualization. Viva Ratih Bening: Investigation, writing–review and editing, validation. Rizqi Yanuar Pauzi: Investigation, writing–review and editing, validation. All authors have read and agreed to the published version of the manuscript.

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