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Modulatory Effects of *Artocarpus altilis* Leaf Extract on Metabolic and Inflammatory Markers in Obesity

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ABSTRACT

Obesity is a pathological condition characterized by excessive fat accumulation, which significantly increases the risk of developing metabolic disorders like insulin resistance and chronic inflammation. This study aimed to investigate the effects of *Arthocarpus altilis* leaf extract on insulin, DPP4, GLP-1, IL-1*β*, and CRP levels in obese rats. We employed a quasi-experimental design using 25 male Sprague Dawley rats, all induced with obesity via a high-fat diet for 10-12 weeks. The rats were divided into five groups: a negative control (NC) receiving a high-fat diet and vehicle only, a positive control treated with metformin (PC) at doses 45 mg/kg, and three groups treated with *A. altilis* extract at doses of 200 mg/kg (EA1), 300 mg/kg (EA2), and 400 mg/kg (EA3). Biomarker levels were measured using the ELISA method. The results showed there were significant differences among groups for all biomarkers ($p < 0.001$). The extract had a dose-dependent effect, progressively increasing insulin and GLP-1 levels while reducing DPP4, IL-1*β*, and CRP levels. The highest dose (EA3) produced effects on insulin, GLP-1, and CRP that were comparable to metformin. Notably, the EA3 group demonstrated a stronger DPP4-inhibitory effect than metformin. The anti-inflammatory effect on IL-1*β* and CRP was most pronounced at the highest dose, suggesting a therapeutic threshold. *A. altilis* extract effectively modulates key biomarkers of obesity and metabolic dysfunction, with the highest dose showing efficacy comparable to or exceeding the standard drug, metformin. These findings position *A. altilis* extract as a promising natural therapeutic agent for managing obesity-related metabolic complications.

Keywords: Obesity, *Artocarpus altilis*, *Insulin*, *Dipeptidyl peptidase*-4, *Glucagon-like peptide-1*, *Interleukin*-1*β*, C - reactive protein

Introduction

Obesity is a medical condition defined by excessive fat accumulation, which markedly elevates the risk of several metabolic disorders, including type 2 diabetes, cardiovascular diseases, and systemic inflammation.[1] A key pathophysiological mechanism underlying obesity is the disruption of glucose metabolism, closely linked to insulin resistance.[2] Insulin resistance is a condition wherein the body's become less sensitive to insulin, necessitating more insulin production to sustain normal blood glucose levels.[3] Moreover, obesity is linked to persistent low-grade inflammation, which intensifies insulin resistance and heightens the likelihood of metabolic problems.[4] In this context, the gastrointestinal hormone *glucagon-like peptide*-1 (GLP-1) and the enzyme *dipeptidyl peptidase*-4 (DPP4) play central roles in glucose metabolism and inflammation regulation.[5]

GLP-1 is a hormone secreted by intestinal cells that stimulates insulin secretion in response to food intake. Optimal GLP-1 activity is crucial for maintaining glucose homeostasis, as it enhances glucose-dependent insulin secretion, slows gastric emptying, and increases satiety.[6]

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However, in obesity, GLP-1 activity is often insufficient to effectively regulate glucose, and its action is terminated by DPP4.[7] DPP4, which degrades GLP-1, is commonly elevated in obesity, further hindering GLP-1's ability to regulate insulin secretion and reducing its anti-inflammatory effects.[8] Thus, DPP4 inhibition could offer therapeutic potential by enhancing GLP-1 activity and improving glucose metabolism in individuals with obesity.[5]

Furthermore, obesity is associated with increased levels of CRP (C-reactive protein) and IL-1*β* (*interleukin*-1 *beta*), two inflammatory biomarkers that contribute to systemic inflammation.[9] Elevated CRP levels reflect systemic inflammation, which is known to impair insulin sensitivity and increase the risk of metabolic disorders.[10] IL-1*β*, a pro-inflammatory cytokine, plays a role in further exacerbating insulin resistance by damaging pancreatic beta cells and inducing additional inflammation.[11] Therefore, reducing CRP and IL-1*β* levels may serve as an effective strategy for improving metabolic function and managing obesity-related conditions.[12]

A. altilis (breadfruit) has shown promise as a therapeutic agent for metabolic disturbances associated with obesity. Previous studies have demonstrated that *A. altilis* extract can lower blood glucose levels in high-fat diet-induced obese rats, suggesting its potential for modulating glucose metabolism.[13] For instance, it has been shown that *A. altilis* extract improve insulin sensitivity and reduced blood glucose in obese rats.[14] Additionally, *A. altilis* extract has been shown to reduce DPP4 levels, thus potentially enhancing GLP-1 activity and improving insulin regulation.[15] By inhibiting DPP4 activity, *A. altilis* extract could increase GLP-1 levels, which would improve insulin secretion and reduce insulin resistance in obesity.

Moreover, *A. altilis* has the potential to reduce CRP and IL-1*β* levels, which can alleviate systemic inflammation associated with obesity. By reducing inflammation, *A. altilis* extract may not only improve insulin sensitivity but also promote overall metabolic health. As a result, *A.*

altilis extract may play a key role in reducing the risk of metabolic complications commonly observed in obesity, offering a promising natural therapeutic strategy for managing obesity and its associated metabolic disturbances.

This study aims to evaluate the effects of *A. altilis* extract on key metabolic and inflammatory parameters in obese rats subjected to a high-fat diet. Specifically, we measured the impact of *A. altilis* extract on insulin levels, DPP4 activity, GLP-1 activity, and the levels of CRP and IL-1*β*. It is expected that the findings of this research will provide further evidence of the therapeutic potential of *A. altilis* extract in improving insulin sensitivity, reducing inflammation, and enhancing glucose metabolism in the context of obesity.

Materials and Methods

Study Design

This study employs a quasi-experimental, post-test only control group design to assess the impact of an ethanol extract derived from *A. altilis* on biomarkers associated with obesity. The investigation specifically quantifies changes in Insulin, DPP4, GLP-1, IL-1*β*, and CRP levels. This methods facilitates a direct comparison of the effects of varying extract dosages against an untreated control, thereby enabling a robust evaluation of the extract's therapeutic potential.

Animals

Twenty-five (25) male Sprague Dawley rats, aged 2-3 months and weighing between 150-250 grams were used for this study. These rats were randomly assigned to five treatment groups: (1) obese rats (NC), (2) obese rats treated with metformin doses 45 mg/kg (PC), (3) obese rats treated with *A. altilis* extract at 200 mg/kg (EA1), (4) obese rats treated with *A. altilis* extract at 300 mg/kg (EA2), and (5) obeserats treated with *A. altilis* extract at 400 mg/kg (EA3).

Plant Collection and Identification

The primary material used in this study was the leaves of *Artocarpus altilis*, from which the extract was prepared. The plant material was collected in February 2024 from Dusun II (7.4267° S, 109.2875° E), Sokaraja Subdistrict, Banyumas Regency, Central Java Province, Indonesia. Botanical identification was conducted by Prof. Dr. Pudji Widodo, M.Sc., a botanist from the Faculty of Biology, Universitas Jenderal Soedirman. A voucher specimen (Voucher No. B/034/UN23.6.10/TA.00.01/2024) was authenticated and deposited at the Pharmacology Laboratory, Faculty of Medicine, Universitas Jenderal Soedirman, for future reference.

Research Procedure

Ethical Approval

This study was conducted after obtaining ethical clearance from the Research Ethics Committee of Universitas Jenderal Soedirman (Dossier No. 091/KEPK/PE/X/2024). All experimental procedures involving animals were carried out in accordance with institutional and international guidelines for the care and use of laboratory animals (https://kepk.si.fk.unsoed.ac.id/).

Extraction of Plant Materials

The ethanol extract was prepared from dried leaves of *A. altilis*. Total of 250 g of dried leaf powder was macerated in 2.5 L of 90% ethanol (1:10 w/v ratio) for 72 hours at room temperature with occasional stirring. The mixture was then filtered, and the solvent was removed under reduced pressure using a rotary evaporator. The resulting crude extract was further dried and weighed prior to administration.

Experimental Animals and Obesity Induction

After an acclimatization period, the rats were randomly assigned into experimental groups. To induce obesity, all rats were fed a high-fat diet (HFD) for 10–12 weeks. The HFD consisted of standard laboratory chow supplemented with quail egg yolk (2 mL) and palm oil (2 mL) per 100 g of feed, in order to increase the total lipid content.

Animal Grouping and Administration of Extracts

Following obesity induction, animals were treated according to their respective group assignments. The ethanol extract of *A. altilis* was administered at predetermined doses for the specified treatment period.

Euthanasia Procedure

At the end of the experimental period, animals were humanely euthanized using sevoflurane anesthesia (5–6% for induction and 2–4% for maintenance, with an oxygen flow rate of 1–3 L/min) until complete cessation of respiration and cardiac activity was confirmed.

Measurement of Biomarkers

The study measured the levels of insulin, *dipeptidyl peptidase*-4 (DPP-4), *glucagon-like peptide*-1 (GLP-1), *interleukin*-1 *beta* (IL-1*β*), and C-reactive protein (CRP) using the enzyme-linked immunosorbent assay (ELISA) method with commercially available sandwich ELISA kits (BT Lab Bioassay Technology Laboratory, Shanghai, China). Blood was collected from the retro-orbital plexus under deep anesthesia and allowed to clot at room temperature for 20–30 minutes. Samples were centrifuged at 3,000 rpm for 10 minutes to obtain serum, which was then aliquoted and stored at −20 °C until analysis. All assays were performed in duplicate according to the manufacturer's instructions, and optical density was read using a microplate reader (Model ELx800, BioTek Instruments, United States) at 450 nm. Biomarker concentrations were calculated from standard curves and expressed as ng/mL.

Statistical Analysis

The collected data were first checked for normality using the Shapiro-Wilk test and for homogeneity using Levene's test. If the data met these conditions, a One-Way ANOVA was performed. To pinpoint which specific groups were significantly different from each other, a Tukey HSD post hoc test was then conducted. A p-value of less than 0.05 was considered the threshold for statistical significance. All statistical computations were performed using the R programming language (version 4.5.0).[16] (R Foundation for Statistical Computing, Vienna, Austria).

Results and Discussion

Effect of A. altilis Extract on Insulin, DPP4, and GLP-1 Levels in HFD-induced obese Rats

The results of the ANOVA test revealed significant differences in insulin, DPP4, and GLP-1 levels among the experimental groups of obese rats ($p < 0.001$) as shown in Fig 1. The negative control group (NC) exhibited the lowest mean insulin level at 4.28 ± 0.381 ng/L, while the positive control group (PC), treated with metformin (45 mg/kg) showed a markedly higher level at 8.07 ± 0.612 ng/L. Among the groups treated with *A. altilis* extract, the insulin levels increased progressively with higher doses. The EA1 group (200 mg/kg) recorded a mean insulin level of 5.16 ± 0.564 ng/L, the EA2 group (300 mg/kg) showed 6.14 ± 0.581 ng/L, and the EA3 group (400 mg/kg) displayed the highest level among the extract-treated groups at 7.55 ± 0.654 ng/L.

The negative control group (NC) exhibited a mean DPP4 concentration of 130.09 ± 5.29 ng/mL, while the positive control group (PC), treated with metformin (45 mg/kg) showed a slightly lower level of 127.94 ± 7.35 ng/mL. In the groups treated with *A. altilis* extract, DPP4 levels decreased progressively with increasing doses. The EA1 group (200 mg/kg) had a mean DPP4 level of 103.18 ± 10.20 ng/mL, while the EA2 group (300 mg/kg) showed a more pronounced reduction to 66.74 ± 6.32 ng/mL. The most significant decrease was observed in the EA3 group (400 mg/kg), with DPP4 levels dropping to 37.82 ± 4.73 ng/mL.

The negative control group (NC) showed the lowest GLP-1 levels (407.71 ± 61.34 ng/mL), while the metformin-treated positive control group (PC) exhibited the highest levels (633.06 ± 91.69 ng/mL). Treatment with *A. altilis* extract demonstrated a dose-dependent increase in GLP-1 levels, with the 200 mg/kg dose (EA1) producing levels (432.72 ± 45.07 ng/mL) slightly above NC but below PC.

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Notably, the 300 mg/kg (EA2) and 400 mg/kg (EA3) doses yielded comparable GLP-1 levels (590.41 ± 64.30 ng/mL and 595.74 ± 35.91 ng/mL, respectively) to the metformin group.

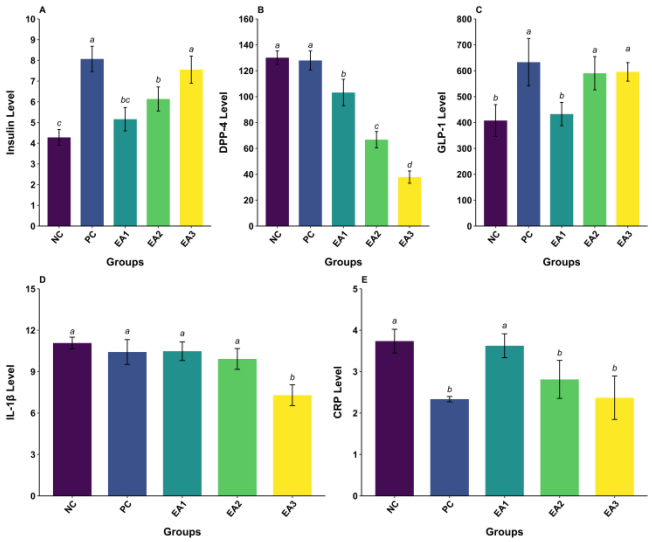

Figure 1: Post hoc analysis among insulin, DPP4, GLP-1, IL-1*β*, and CRP level in obesity-induced rats (NC), rats with metformin doses 45 mg/kg-induced obesity (PC), and obesity rats treated with extract of *A. altilis* 200 mg/kg (EA1), 300 mg/kg (EA2), 400 mg/kg (EA3).

Effect of A. altilis Extract on IL-1β and CRP Levels in Obesity-Induced Rats

The ANOVA test demonstrated significant differences in both IL-1β and CRP ($p<0.001$) levels among obese rat groups treated with *A. altilis* extract, as shown in Fig 1. For IL-1*β* levels, the negative control group (NC) showed a mean of 11.1±0.43 ng/mL. The positive control group (PC), treated with metformin (45 mg/kg) exhibited a slightly higher mean level of 10.4±0.90 ng/mL Treatment with *Artocarpus altilis* leaf extract resulted in a significant reduction in IL-1*β* levels, which was most pronounced at the highest dose. The lowest dose, the EA1 group (200 mg/kg), recorded the highest mean IL-1*β* level at 10.5 ± 0.67 ng/mL. In contrast, the highest dose, the EA3 group (400 mg/kg), had the lowest mean IL-1*β* level of all groups, at 7.29 ± 0.75 ng/mL. The EA2 group (300 mg/kg) showed a mean level of 10.1 ± 0.78 ng/mL, which was lower than the EA1 group. These results indicate that the reduction in IL-1β levels was evident primarily at the highest dose of *A. altilis* extract. Instead, IL-1β levels decreased progressively with increasing doses of the extract, with the most pronounced reduction observed at the highest dose.

Regarding CRP levels, the negative control group (NC) had a mean of 3.74±0.29 ng/mL. The positive control group (PC) showed a lower mean level of 2.33±0.06 ng/mL. Among the groups treated with *A. altilis* extract, the EA1 group showed a higher mean CRP level of 3.62±0.29 ng/mL. However, CRP levels then progressively decreased with increasing extract doses. The EA2 group exhibited a mean of 2.81±0.46 ng/mL. The most notable reduction was observed in the EA3 group, where CRP levels dropped to 2.37±0.52 ng/mL, closely approaching the levels seen in the metformin-treated PC group.

Post Hoc Analysis of Biomarker Levels in Treatment Groups

To further clarify the specific group-to-group differences underlying the significant ANOVA findings, post hoc pairwise comparisons were performed.

Insulin Levels

The post hoc analysis of insulin levels demonstrated differences among the treatment groups, reflecting significant differences in insulin secretion (Fig. 1). The negative control (NC) group had significantly lower insulin levels compared to all other groups. In contrast, the metformin-treated i.e. the positive control (PC) group showed the highest insulin levels. Among the *A. altilis* extract-treated groups, EA1 did not differ significantly from the NC group but showed markedly lower levels than both PC and EA3. The EA2 group had intermediate insulin levels that differed significantly from NC, PC, and EA3. Notably, the EA3 group did not differ significantly from the positive control group, suggesting that the highest dose of *A. altilis* extract gave an insulin-elevating effect comparable to metformin. These results demonstrate a clear dose-dependent response, with higher extract doses more closely mimicking metformin's pharmacological impact on insulin secretion.

DPP4 Levels

The post hoc analysis of DPP4 levels revealed significant differences among the treatment groups ($p < 0.05$) (Fig. 1). The negative control (NC) group and the positive control (PC) group had no significant difference. The *A. altilis* extract-treated groups showed a remarkable dose-dependent reduction in DPP4 activity. EA1 demonstrated significantly lower DPP4 levels compared to NC and PC groups. EA2 showed further reduction, while EA3 exhibited the strongest inhibitory effect. These results clearly demonstrate that higher doses of *A. altilis* extract progressively and significantly suppress DPP4 activity, with the 400 mg/kg dose showing the most potent effect, far exceeding the impact of metformin treatment.

GLP-1 Levels

The post hoc analysis of GLP-1 levels revealed distinct patterns among treatment groups ($p < 0.05$) (Fig. 1). There were no significant difference between the negative control (NC) and EA1 group, and they had significantly lower GLP-1 levels compared to the other groups. In contrast, the positive control (PC) group, EA2, and EA3 demonstrated significantly elevated GLP-1 levels that were statistically equivalent.. These results indicate that while the lowest dose of *A. altilis extract* (EA1) showed minimal effect on GLP-1 secretion, both medium and high doses (EA2 and EA3) were equally effective as metformin in significantly enhancing GLP-1 levels.

IL-1β Levels

The post hoc analysis of IL-1*β* levels revealed significant differences among the treatment groups ($p=<0.001$) (Fig. 1). The negative control (NC) group and the positive control (PC) group showed no significant difference in IL-1*β* levels between them. The groups treated with *A. altilis* extract exhibited varied effects. The EA1 group had the highest mean IL-1*β* level and was statistically different from EA3. The EA2 group was not significantly different from either the control groups or the EA1 group. Contrary to a dose-dependent increase, the highest dose of extract (EA3, 400 mg/kg) was associated with the lowest mean IL-1*β* levels, and this level was significantly lower than the EA1 group. These results demonstrate a dose-dependent reduction in IL-1β levels, with significantly lower values observed at the highest extract dose (EA3) compared with lower-dose groups. This pattern reflects an inverse dose-response relationship, in which increasing extract doses corresponded to decreasing IL-1*β* concentrations.

CRP Levels

The post hoc analysis of CRP levels demonstrated significant differences among the treatment groups ($p<0.001$) (Fig. 1). The positive control (PC) group exhibited the lowest CRP levels, significantly lower than the negative control (NC) group. Interestingly, the EA1 group (200 mg/kg) showed the highest CRP levels, significantly greater than all other groups treated with *A. altilis* extract. However, a dose-dependent reduction was observed with higher extract doses. The EA2 group (300 mg/kg) had CRP levels that were significantly lower than EA1 but not significantly different from the EA3 group. Most notably, the EA3 group (400 mg/kg) demonstrated a significant reduction in CRP levels, reaching levels statistically equivalent to the metformin-treated PC group and significantly lower than both NC and EA1. These findings indicate that higher doses effectively suppress CRP levels to an extent comparable to metformin.

The findings of this study provide compelling evidence regarding the therapeutic potential of *A. altilis* extract in modulating key biomarkers

associated with obesity and metabolic dysfunction, namely insulin, DPP4, GLP-1, IL-1*β*, and CRP levels. The results demonstrate a clear dose-dependent effect of the extract on these biomarkers, suggesting its potential as a natural alternative or complementary treatment for obesity-related metabolic disorders. The significant increase in insulin levels observed with doses of *A. altilis* extract aligns with its potential to enhance insulin secretion or improve pancreatic *β*-cell function. The EA3 group exhibited insulin levels comparable to those of the metformin-treated group, reflecting enhanced pancreatic *β*-cell function or increased insulin secretion. This finding is consistent with previous studies reporting the antidiabetic properties of plant-derived compounds, such as flavonoids and phenolic acids, which are abundant in *A. altilis*.[17] These bioactive compounds may enhance glucose uptake and insulin sensitivity by activating insulin signaling pathways such as the PI3K/Akt pathway and reducing oxidative stress.[18] However, the lower doses (EA1 and EA2) showed intermediate effects, emphasizing the importance of dose optimization in therapeutic applications. The dose-dependent increase in insulin levels suggests stimulation of insulin secretory capacity, although the precise mechanism remains unclear. Further mechanistic studies are warranted to elucidate the exact pathways through which *A. altilis* exerts its insulinotropic effects.

The dose-dependent reduction in DPP4 levels observed in the *A. altilis*-treated groups highlights its potential as a DPP4 inhibitor. DPP4 is a key enzyme involved in the degradation of GLP-1, an incretin hormone that plays a crucial role in glucose homeostasis.[19] By inhibiting DPP4 activity, *A. altilis* may prolong the half-life of GLP-1, thereby enhancing its insulinotropic and appetite-suppressing effects. Notably, the EA3 group exhibited the most pronounced reduction in DPP4 levels, surpassing the inhibitory effect of metformin. The reduction in DPP4 levels observed in the metformin-treated group is consistent with previous reports demonstrating that metformin can downregulate DPP4 expression and activity.[20] This finding underscores the superior efficacy of high-dose of *A. altilis* extract in targeting DPP4 activity, potentially making it a promising candidate for the development of novel antidiabetic therapies. The observed DPP4-inhibitory effect may be attributed to the presence of bioactive compounds such as prenylated flavonoids and stilbenoids, which have been previously reported to exhibit enzyme-modulating properties.[21] These compounds may interact with the active site of DPP4, thereby preventing its enzymatic activity. Future studies should focus on isolating and characterizing the specific compounds responsible for this effect.

The dose-dependent increase in GLP-1 levels observed in the *A. altilis* -treated groups further supports its potential as a therapeutic agent for obesity and diabetes. GLP-1 is a well-established target for the treatment of metabolic disorders due to its ability to stimulate insulin secretion, suppress glucagon release, and promote satiety.[22] The EA2 and EA3 groups demonstrated GLP-1 levels comparable to those of the metformin-treated group, indicating that medium to high doses of the extract can effectively enhance GLP-1 secretion. This effect may be mediated through the inhibition of DPP4, as discussed earlier, or via direct stimulation of GLP-1-producing cells in the gut. Interestingly, the lowest dose (EA1) showed minimal effects on GLP-1 levels, suggesting a threshold concentration required for the extract to exert its GLP-1-enhancing effects. This observation underscores the importance of optimizing the dosage of *A. altilis* extract to achieve maximal therapeutic benefits. Furthermore, the comparable efficacy of EA2 and EA3 with metformin highlights the potential of *A. altilis* as a natural alternative to conventional antidiabetic drugs.

The study revealed a more complex, non-linear dose-response relationship in the modulation of inflammatory biomarkers. At the highest dose (400 mg/kg), the *A. altilis* extract demonstrated potent anti-inflammatory activity, significantly reducing levels of the pro-inflammatory cytokine Interleukin-1β (IL-1*β*) and the systemic acute-phase reactant C-reactive protein (CRP) to levels comparable with the metformin group. IL-1*β* is a pivotal cytokine in the pathogenesis of obesity-induced inflammation and insulin resistance, promoting a vicious cycle of immune cell infiltration into adipose tissue and disrupting insulin signaling cascades.[23] The subsequent reduction in CRP, which is synthesized by the liver primarily in response to circulating IL-1*β* and IL-6, confirms that the extract's effect at this high dose translates to a systemic anti-inflammatory benefit.[24] This potent suppression is likely attributable to the rich phytochemical profile of *A. altilis*, which includes flavonoids, triterpenoids, and phenolic compounds known to inhibit key inflammatory signaling pathways such as Nuclear Factor-kappa B (NF-*κ*B) and the NOD-like receptor family pyrin domain containing 3 (NLRP3) inflammasome, which are responsible for IL-1*β* transcription and processing.[25]

Intriguingly, the lower dose of the extract (200 mg/kg) did not suppress, and in the case of CRP, appeared to transiently elevate, these inflammatory markers. This biphasic or U-shaped dose-response is a recognized phenomenon in pharmacology known as hormesis, which has been increasingly documented for various phytochemicals, including flavonoids.[26] It is plausible that at low concentrations, certain compounds within the extract exert a mild pro-inflammatory or immune-stimulatory effect, potentially inducing a minor cellular stress response. Although NF-*κ*B and COX-2 suppression may contribute to this response, the present findings do not allow confirmation of specific molecular mechanisms at these higher doses. These findings are consistent with a hormetic dose–response pattern, in which anti-inflammatory effects become evident only at higher extract concentrations. This complex dose-response underscores the importance of dose optimization in the development of phytopharmaceuticals and suggests that a therapeutic threshold must be achieved to engage the plant's full anti-inflammatory potential.[27] Collectively, these findings highlight that subtherapeutic dosing may yield unintended immunomodulatory effects, emphasizing the necessity of precise dose selection to ensure both efficacy, and safety in translational applications.[28] Interestingly, the lower extract dose (EA1, 200 mg/kg) did not suppress inflammatory markers, and CRP was transiently elevated at this level. This biphasic trend is consistent with a hormetic dose–response pattern, in which low concentrations may exert mild stimulatory or adaptive effects. At higher doses (EA2 and EA3), however, a marked reduction in IL-1*β* and CRP was observed, indicating a shift toward anti-inflammatory activity. Although NF-*κ*B and COX-2 suppression may contribute to this response, the present findings do not allow confirmation of specific molecular mechanisms at these higher doses.

Conclusion

This study provides compelling evidence of the therapeutic potential of *A. altilis* extract in managing obesity and metabolic dysfunction, as supported by changes in biochemical markers related to glucose metabolism (insulin, GLP-1, DPP4) and systemic inflammation (IL-1*β*, CRP). Our findings demonstrate that the extract effectively modulates several key biomarkers such as increasing insulin and GLP-1 levels while simultaneously decreasing DPP4, IL-1*β*, and CRP in a clear, dose-dependent manner. The consistent efficacy of the extract, particularly at its highest dose (EA3), is a significant finding, as it often exhibited effects comparable to or even superior to the standard antidiabetic drug, metformin. This multifaceted action suggests that the extract's rich array of bioactive compounds can simultaneously address several aspects of metabolic syndrome, including insulin resistance, glucose dysregulation, and chronic inflammation. Overall, this research positions *A. altilis* extract as a promising natural alternative for managing obesity and its associated metabolic complications. Future studies should focus on isolating the specific compounds responsible for these powerful effects and fully elucidating their underlying molecular mechanisms.

Conflict of Interest

The authors declare no conflict of interest.

Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

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