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Original Article

Anti-inflammatory and hepatoprotective effects of *Moringa oleifera* fruit in obesity-induced liver injury

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A B S T R A C T

Background: Hepatic metabolic disorders are closely associated with obesity and are characterized by systemic inflammation and liver injury. *Moringa oleifera* fruit contains various bioactive compounds with potential anti-inflammatory and hepatoprotective properties. However, evidence regarding its effects on obesity-induced liver injury remains limited.

Objective: This study aimed to evaluate the anti-inflammatory and hepatoprotective effects of *Moringa oleifera* fruit extract in an obesity-induced rat model.

Methods: This experimental study used 30 male Sprague-Dawley rats divided into five groups: normal control (N), obese control (O), obese rats treated with *Moringa oleifera* fruit extract at 500 mg/kg body weight once daily (OEMO1), twice daily (OEMO2), and obese rats treated with vitamin C (OC). Systemic inflammation was assessed by measuring serum C-reactive protein (CRP) levels using ELISA, while hepatic changes were evaluated through biochemical markers and histopathological analysis. Data were analyzed using one-way ANOVA followed by post hoc testing.

Results: Obese rats exhibited significantly elevated serum CRP levels and marked hepatic alterations compared to normal controls ($p < 0.05$). Administration of *Moringa oleifera* fruit extract significantly reduced CRP levels and improved hepatic histoarchitecture in obese rats, with the greatest effect observed in the twice-daily treatment group (OEMO2) ($p < 0.05$). The effects were comparable to or greater than those observed with vitamin C.

Conclusions: *Moringa oleifera* fruit extract demonstrates significant anti-inflammatory and hepatoprotective effects in an obesity-induced rat model, suggesting its potential as a natural therapeutic agent for obesity-related liver injury.

INTRODUCTION

Overweight and obesity are defined by the World Health Organization (WHO) as abnormal or excessive fat accumulation, with obesity classified as a body mass index (BMI) ≥ 30 kg/m², resulting from an imbalance between energy intake and expenditure. Globally, obesity has reached epidemic proportions, affecting more than 650 million adults.[1,2] In Indonesia, obesity prevalence has increased significantly, reaching 15.4% among adults, highlighting a growing public health concern. Obesity is a major risk factor for various non-communicable diseases, including type 2 diabetes mellitus, cardiovascular disease, and metabolic dysfunction-associated steatotic liver disease (MASLD), a recently updated term emphasizing the role of metabolic dysfunction in liver pathology.[3,4]

At the pathophysiological level, chronic caloric excess leads to excessive adipose tissue expansion beyond its physiological capacity, resulting in adipocyte hypertrophy, cellular stress, and adipose tissue inflammation. This condition is characterized by chronic low-grade systemic inflammation, marked by increased circulating inflammatory biomarkers such as C-reactive protein (CRP).[5-7] Adipose tissue dysfunction and systemic inflammation contribute to hepatic lipid accumulation, oxidative stress, and insulin resistance, ultimately leading to hepatocellular injury and progression of MASLD. Although CRP is widely used as a marker of systemic inflammation, its role in reflecting the severity of obesity-related liver injury remains under debate.[8]

Previous studies have explored the potential of natural antioxidants in reducing obesity-related inflammation and

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metabolic disturbances. *Moringa oleifera* has been widely investigated for its antioxidant, anti-inflammatory, and hepatoprotective effects, particularly its leaves, which have been shown to improve lipid metabolism and reduce inflammatory markers.[9,10] Emerging evidence suggests that Moringa oleifera fruit contains higher concentrations of bioactive compounds, such as polyphenols, flavonoids, and isothiocyanates, which may provide stronger biological activity. However, studies specifically evaluating the effects of *M. oleifera* fruit on obesity-induced liver injury and systemic inflammation remain limited.

Moreover, the potential superiority of *M. oleifera* fruit compared to its leaves, as well as its role in modulating key inflammatory pathways associated with hepatic injury, has not been well established. Therefore, a clear research gap exists regarding the hepatoprotective and anti-inflammatory effects of *M. oleifera* fruit in obesity-related liver injury. This study aims to evaluate the anti-inflammatory and hepatoprotective effects of Moringa oleifera fruit extract on systemic inflammation, as indicated by CRP levels, and on liver injury in an obesity-induced experimental model.

METHOD

Study Design

This study was a randomized controlled experimental laboratory study.[11]

Study Site

The study was conducted from June to December 2025 at the Animal Experimentation Laboratory and the Stem Cell Laboratory, Faculty of Medicine, Universitas Pembangunan Nasional "Veteran" Jakarta, Indonesia.

In Vivo Procedure

Animal Preparation

Thirty male Sprague-Dawley rats, aged 2–3 months and weighing 150–200 g, were used in this study. The animals were acclimatized for 7 days under standard laboratory conditions, housed in cages, and provided with BR II pellets and distilled water ad libitum. Obesity was induced using a high-fat diet administered for a defined experimental period. Rats were randomly assigned using a simple randomization method into five groups (n = 6 per group): normal control (N), obese control (O), obese rats treated with *M. oleifera* fruit extract once daily (OEMO1), obese rats treated with *M. oleifera* fruit extract twice daily (OEMO2), and obese rats treated with vitamin C (OC).

Preparation and Administration of M. oleifera Fruit Extract

M. oleifera fruits were processed and extracted using an ethanolic extraction method. The extract was administered orally at a dose of 500 mg/kg body weight once and twice daily according to the treatment protocol.

Experimental procedure of Systemic Inflammation and Hepatic Changes

Systemic inflammation was assessed by measuring serum C-reactive protein (CRP) levels using an enzyme-linked immunosorbent assay (ELISA) with the Elabscience® Rat CRP Kit (Catalog No. E-EL-R0506). Hepatic changes were evaluated through biochemical markers and histopathological examination. Liver tissues were stained using Hematoxylin–Eosin (HE) and examined under light microscopy to assess inflammatory infiltration and cellular morphology.

Statistical Analysis

Data distribution was assessed using the Shapiro–Wilk test. Differences among groups were analyzed using one-way ANOVA, followed by Tukey's post hoc test. A p-value < 0.05 was considered statistically significant.

Ethical Consideration

This study received ethical approval from the Health Research Ethics Committee of the Faculty of Medicine, Universitas Muhammadiyah Prof. Dr. HAMKA (UHAMKA), Indonesia (No. KEPKK/FK/068/06/2025).

RESULTS

Effect of M. oleifera Fruit Extract on CRP Levels

Administration of Moringa oleifera fruit extract significantly affected serum CRP levels among experimental groups (Figure 1). Obese control rats (O) exhibited markedly elevated CRP levels compared to normal controls (N) ($p < 0.05$), indicating systemic inflammation associated with obesity. Treatment with M. oleifera extract resulted in a significant reduction in CRP levels, with the greatest reduction observed in the twice-daily treatment group (OEMO2). The CRP levels in the OEMO2 group (1.600 ± 0.067) were lower than those in the normal control group (1.925 ± 0.077), suggesting a strong anti-inflammatory effect. Statistical analysis demonstrated significant differences among groups ($p < 0.0001$), while no significant difference was observed between the OEMO1 and OEMO2 groups.

Histopathological Changes in Liver Tissue

Histopathological examination of liver tissue using Hematoxylin–Eosin (HE) staining revealed distinct morphological differences among groups (Figure 2). The obese control group (O) showed marked hepatic alterations, including inflammatory cell infiltration and disrupted cellular architecture, consistent with obesity-induced liver injury. In contrast, rats treated with *M. oleifera* extract demonstrated improved hepatic morphology. The OEMO2 group exhibited reduced inflammatory infiltration, decreased cellular damage, and more organized hepatic structure, approaching normal histological features. The group treated with vitamin C (OC) showed moderate improvement compared to the obese control group but was less pronounced than that observed in the *M. oleifera* treatment groups.

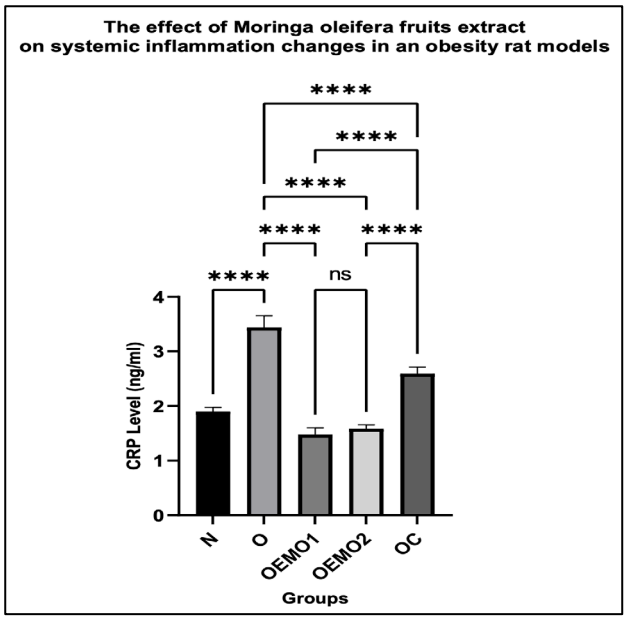

Figure 1. Effect of *M. oleifera* fruit extract on serum CRP levels in an obesity-induced rat model..

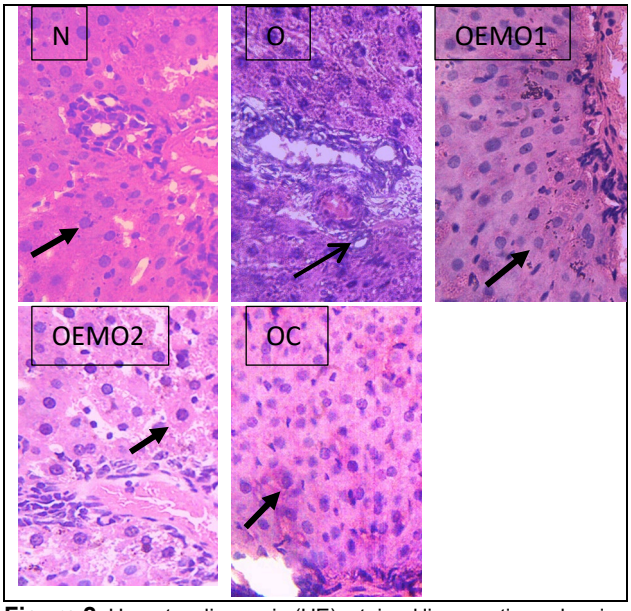

Figure 2. Hematoxylin–eosin (HE)–stained liver sections showing histopathological changes among experimental groups (N: normal control; O: obese control; OEMO1: once-daily extract; OEMO2: twice-daily extract; OC: vitamin C-treated group).

DISCUSSION

This study demonstrates that *M. oleifera* fruit extract exerts significant anti-inflammatory and hepatoprotective effects in an obesity-induced rat model, as evidenced by reduced serum CRP levels and improved hepatic histopathology. The most pronounced effect was observed in the twice-daily treatment group, indicating a dose-frequency-dependent response.

Obesity-induced adipose tissue expansion is associated with chronic low-grade systemic inflammation, characterized by increased secretion of proinflammatory cytokines such as TNF-α, IL-6, and IL-1β.[12,13] Among these mediators, IL-6 plays a central role in stimulating hepatic acute-phase responses, including CRP synthesis. Elevated CRP levels observed in the obese control group in this study reflect this inflammatory state.

CRP is synthesized by hepatocytes under IL-6–mediated activation of the JAK/STAT3 signaling pathway. Persistent elevation of IL-6 in obesity enhances CRP production, while oxidative stress and lipid accumulation further amplify inflammatory signaling within the liver.[14-17] These processes contribute to hepatocellular injury and progression of obesity-related liver disease.

The reduction of CRP levels following administration of M. oleifera fruit extract observed in this study suggests effective attenuation of systemic inflammation. This effect is likely mediated by the high content of bioactive compounds, including polyphenols, flavonoids, and isothiocyanates. These compounds exert antioxidant effects by scavenging reactive oxygen species and enhancing endogenous antioxidant defenses, thereby suppressing NF-κB activation and reducing proinflammatory cytokine production upstream of CRP synthesis.[18-22]

The observed effect of *M. oleifera* fruit extract, which appeared greater than that of vitamin C, may reflect the synergistic action of multiple bioactive constituents. Unlike vitamin C, which primarily acts as a single antioxidant molecule, *M. oleifera* fruit exhibits pleiotropic effects by targeting oxidative stress, inflammatory pathways, and metabolic dysfunction simultaneously. This multimodal action is particularly relevant in obesity-related inflammation, which involves complex interactions between adipose tissue, liver, and systemic metabolism.[23,24]

Histopathological findings further support these results. Treatment with *M. oleifera* fruit extract reduced inflammatory cell infiltration, decreased steatosis and hepatocellular ballooning, and improved hepatic architecture. These changes indicate reduced hepatic injury and improved cellular integrity. Activation of AMP-activated protein kinase by polyphenolic compounds may contribute to improved lipid metabolism and reduced hepatic triglyceride accumulation, thereby mitigating lipotoxic stress and oxidative damage.[25,26]

These findings are consistent with previous studies demonstrating the anti-inflammatory and hepatoprotective effects of *M. oleifera*, particularly its leaves. However, evidence regarding the fruit remains limited. The present study supports the hypothesis that M. oleifera fruit may provide comparable or even enhanced biological effects due to its bioactive composition.

Despite these promising findings, this study has several limitations. First, the use of an animal model may limit the direct generalizability of the results to humans. Second, the study primarily assessed CRP as a marker of systemic inflammation without evaluating other key inflammatory cytokines or molecular signaling pathways. Third, the relatively small sample size may affect the robustness of the findings. Overall, this study highlights the potential of *M.*

oleifera fruit as a natural therapeutic agent targeting both systemic inflammation and liver injury in obesity, warranting further investigation in clinical studies.

CONCLUSIONS AND RECOMMENDATION

M. oleifera fruit extract demonstrates significant anti-inflammatory and hepatoprotective effects in an obesity-induced model, as evidenced by reduced systemic inflammation and improved hepatic histopathological features. The most pronounced effect observed in the twice-daily administration group suggests a potential dose-frequency-dependent response.

These findings highlight the potential of *M. oleifera* fruit as a natural therapeutic agent targeting metabolic and inflammatory pathways in obesity-related liver injury. Future studies should focus on elucidating the underlying molecular mechanisms and validating these findings in clinical settings.

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