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THE EFFECT OF ALOIN ADMINISTRATION ON FOAM CELL FORMATION IN THE KIDNEYS OF MALE MICE (*MUS MUSCULUS*) WITH DYSLIPIDEMIA-INDUCED OBESITY

Nadya Mukhti[1], Ade Teti Vani[2*], Khomeini[3], Nadia Purnama Dewi[4], Dessy Abdullah[5], Rosmaini[6]

[1,2,3,4,5,6]Universitas Baiturrahmah, Indonesia

[1]Email: 2110070100121@student.unbrah.ac.id
[2*]Email: adetativani@fk.unbrah.ac.id
[3]Email: khomeini@fk.unbrah.ac.id
[4]Email: nadiapurnamadewi@fk.unbrah.ac.id
[5]Email: dessyabdullah@fk.unbrah.ac.id
[6]Email: rosmaini@fk.unbrah.ac.id

Abstract
Dyslipidemia and obesity are major metabolic disorders characterized by abnormal lipid metabolism, chronic inflammation, and oxidative stress, all of which contribute to progressive renal injury. Excessive accumulation of oxidized low-density lipoprotein (ox-LDL) promotes macrophage infiltration and foam cell formation within renal tissue, accelerating glomerular damage and increasing the risk of chronic kidney disease. Aloin, the principal anthraquinone glycoside isolated from Aloe vera, *possesses potent antioxidant and anti-inflammatory properties that may attenuate oxidative injury and inhibit foam cell formation. This study aimed to investigate the effect of oral aloin administration on renal foam cell formation in male* Mus musculus *with dyslipidemia-induced obesity. A true experimental study employing a posttest-only control group design was conducted using male mice with experimentally induced dyslipidemia and obesity. Animals were randomly allocated into control and treatment groups. The treatment group received oral aloin for 28 consecutive days following dyslipidemia induction. Kidney tissues were collected for histopathological examination using Hematoxylin–Eosin staining. Foam cell formation was evaluated microscopically, and differences between groups were analyzed using the Independent Samples* t*-test with a significance level of* $p < 0.05$*. Histopathological analysis demonstrated that aloin administration reduced renal foam cell formation compared with the untreated control group. The treatment group exhibited approximately 25% foam cell formation, whereas the control group demonstrated approximately 93.8%. These findings suggest that aloin suppresses lipid accumulation and inflammatory responses within renal tissue through its antioxidant activity. Nevertheless, the therapeutic effect remained lower than that reported for atorvastatin, indicating that aloin is more appropriately considered a complementary rather than a replacement therapy. Oral administration of aloin effectively reduced foam cell formation in the kidneys of dyslipidemia-induced obese male mice. The protective effect is likely mediated through antioxidant activity, inhibition of lipid peroxidation, and attenuation of inflammatory processes.*

Keywords: *Aloin; Aloe vera; dyslipidemia; obesity; foam cells; kidney; oxidative stress; histopathology.*

INTRODUCTION

Dyslipidemia and obesity have become major public health concerns worldwide due to their rapidly increasing prevalence and their substantial

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contribution to the development of chronic non-communicable diseases. Both conditions are characterized by disturbances in lipid metabolism, including elevated levels of total cholesterol, triglycerides, and low-density lipoprotein cholesterol (LDL-C), accompanied by reduced high-density lipoprotein cholesterol (HDL-C). Persistent dyslipidemia promotes excessive lipid deposition in various tissues and is recognized as one of the principal risk factors for cardiovascular disease, metabolic syndrome, and chronic kidney disease (CKD). The coexistence of obesity further aggravates metabolic abnormalities by increasing systemic inflammation, insulin resistance, and oxidative stress, thereby accelerating tissue injury in multiple organs, including the kidneys(Aman *et al.*, 2021; Nussbaumerova and Rosolova, 2023; Malbos, 2025).

The kidneys play a pivotal role in maintaining metabolic homeostasis through the regulation of electrolyte balance, fluid volume, acid-base equilibrium, and the excretion of metabolic waste products. Under physiological conditions, renal function is preserved by the structural integrity of the glomeruli and renal tubules. However, prolonged exposure to metabolic disturbances associated with dyslipidemia and obesity progressively impairs renal architecture. Excess circulating lipids accumulate within renal tissue and induce lipotoxicity, ultimately leading to glomerular hypertrophy, mesangial expansion, tubular injury, and progressive renal fibrosis. These pathological alterations contribute significantly to the initiation and progression of chronic kidney disease(Bonilha *et al.*, 2021; Vekic *et al.*, 2023).

One of the most important pathological mechanisms underlying renal injury in dyslipidemia is the formation of foam cells. Elevated circulating LDL particles undergo oxidative modification to form oxidized LDL (ox-LDL), which is subsequently internalized by macrophages through scavenger receptors. Continuous lipid uptake transforms macrophages into lipid-laden foam cells that accumulate within renal tissue and produce excessive inflammatory mediators, including tumor necrosis factor-alpha (TNF-α), interleukin-1β (IL-1β), and interleukin-6 (IL-6). The persistent inflammatory response stimulates oxidative stress, extracellular matrix remodeling, and progressive glomerulosclerosis, thereby compromising renal function. Although foam cell formation has traditionally been associated with atherosclerosis, increasing evidence indicates that similar pathological processes also occur within the kidney during dyslipidemia and obesity (Santosa *et al.*, 2023; Vekic *et al.*, 2023; Xu *et al.*, 2024).

Oxidative stress represents a central mechanism linking dyslipidemia to renal tissue damage. Excessive production of Reactive Oxygen Species (ROS) overwhelms endogenous antioxidant defense systems, resulting in lipid peroxidation, mitochondrial dysfunction, DNA damage, and activation of pro-inflammatory signaling pathways. Activation of Nuclear Factor-kappa B (NF-κB) further amplifies inflammatory responses by increasing cytokine production and promoting macrophage infiltration into renal tissue. Consequently, oxidative stress and chronic inflammation establish a vicious cycle that accelerates foam cell formation and renal injury(Hua *et al.*, 2021; Saleh Al-Sowayan and Mohammad AL-Sallali, 2023a).

Given the limitations and adverse effects associated with long-term pharmacological lipid-lowering therapy, increasing attention has been directed toward natural compounds possessing antioxidant and anti-inflammatory

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properties. Among these, *Aloe vera* has attracted considerable scientific interest because of its diverse bioactive constituents, including polysaccharides, flavonoids, vitamins, phenolic compounds, and anthraquinones. One of its principal active constituents is aloin, an anthraquinone glycoside that exhibits antioxidant, anti-inflammatory, antimicrobial, antiviral, and cytoprotective activities. Experimental studies have demonstrated that aloin effectively scavenges reactive oxygen species, suppresses lipid peroxidation, inhibits pro-inflammatory cytokine production, and modulates lipid metabolism. These biological activities suggest that aloin may provide protection against oxidative tissue injury induced by metabolic disorders(Zhang *et al.*, 2020; Vani, 2022; Dewi *et al.*, 2024).

Previous investigations have primarily focused on the effects of aloin or *Aloe vera* on glycemic control, lipid metabolism, wound healing, hepatic injury, and cardiovascular protection. Several studies have reported that antioxidant compounds derived from medicinal plants reduce oxidative damage by enhancing endogenous antioxidant enzyme activity and attenuating inflammatory responses. However, evidence regarding the direct effect of aloin on renal foam cell formation under dyslipidemia-induced obesity remains limited. Most published studies have evaluated biochemical parameters or general histopathological alterations rather than specifically quantifying foam cell formation as an indicator of renal lipid accumulation. Consequently, the histopathological role of aloin in preventing renal foam cell development under dyslipidemic conditions has not been fully elucidated(Li *et al.*, 2017; Wang, Wang and Yang, 2020; Saleh Al-Sowayan and Mohammad AL-Sallali, 2023b).

The present study addresses this research gap by evaluating the effect of oral aloin administration on foam cell formation in the kidneys of male *Mus musculus* with experimentally induced dyslipidemia and obesity using histopathological examination. Unlike previous studies that primarily investigated systemic metabolic parameters, this study specifically focuses on renal histological alterations associated with lipid accumulation. The findings are expected to provide additional evidence regarding the nephroprotective potential of aloin and contribute to the development of complementary therapeutic strategies for preventing renal complications associated with dyslipidemia and obesity

METHODE

This study employed a true experimental design using a posttest-only control group design to evaluate the effect of oral aloin administration on renal foam cell formation in male *Mus musculus* with dyslipidemia-induced obesity. The experiment was conducted at the Biomedical Laboratory, Faculty of Medicine, Baiturrahmah University, Padang, Indonesia. Healthy male mice aged approximately 8–10 weeks with body weights ranging from 27–38 g were used as experimental animals. Before the intervention, all animals underwent a seven-day acclimatization period under standard laboratory conditions, including controlled temperature, a 12-hour light–dark cycle, and unrestricted access to food and drinking water. Dyslipidemia-induced obesity was established through the administration of a high-fat diet according to the experimental protocol.

Following successful induction, the animals were randomly assigned into two experimental groups using a simple random sampling technique. The control group

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received a high-fat diet without aloin administration, whereas the treatment group received oral aloin at a dose of 750 μg/kg body weight once daily by gastric gavage for 28 consecutive days. Throughout the intervention period, all animals were maintained under identical environmental conditions to minimize potential confounding variables, including housing conditions, dietary intake, and water availability. Animal welfare was monitored daily throughout the experiment.

At the end of the treatment period, all animals were euthanized humanely, and both kidneys were carefully excised for histopathological examination. Tissue specimens were immediately fixed in 10% neutral buffered formalin, processed routinely through dehydration, clearing, paraffin embedding, sectioning, and subsequently stained using the Hematoxylin–Eosin (H&E) method. Histopathological evaluation was performed under a light microscope at 400× magnification. Foam cell formation within renal tissue was identified based on the presence of lipid-laden macrophages exhibiting characteristic foamy cytoplasm, and quantitative assessment was conducted by examining representative microscopic fields from each specimen.

The primary outcome of this study was the percentage of renal foam cell formation following aloin administration. Data were presented as mean ± standard deviation (SD). Prior to hypothesis testing, data normality and homogeneity were assessed using the Shapiro–Wilk and Levene's tests, respectively. Differences between the control and treatment groups were analyzed using the Independent Samples *t*-test, with statistical significance established at $p < 0.05$. Ethical approval for this study was obtained from the Health Research Ethics Committee of the Faculty of Medicine, Baiturrahmah University, and all experimental procedures involving animals were conducted in accordance with internationally accepted principles for the ethical use of laboratory animals.

RESULT AND DISCUSSION

Histopathological examination was performed to evaluate the effect of oral aloin administration on foam cell formation in the kidneys of male *Mus musculus* with dyslipidemia-induced obesity. Foam cells were identified microscopically as lipid-laden macrophages characterized by abundant vacuolated cytoplasm within renal tissue. Quantitative analysis demonstrated a marked reduction in foam cell formation in the aloin-treated group compared with the untreated control group. The mean percentage of foam cell formation was 93.8% in the control group, whereas the aloin-treated group exhibited a substantially lower value of 25.0%, indicating that aloin administration effectively attenuated lipid accumulation within renal tissue.

Table 1. Foam Cell Formation in the Kidneys of Male *Mus musculus* with Dyslipidemia-Induced Obesity

Group	n	Foam Cell Formation (%)
Control	16	93.8
Aloin-treated	16	25.0

Statistical analysis using the Independent Samples *t*-test demonstrated a significant difference between the two groups ($p < 0.05$), indicating that oral administration of aloin significantly reduced renal foam cell formation in

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dyslipidemia-induced obese mice. These findings suggest that aloin possesses biological activity capable of limiting lipid deposition and attenuating the inflammatory processes associated with dyslipidemia-induced renal injury.

The reduction in foam cell formation observed in this study may be attributed to the antioxidant properties of aloin. Dyslipidemia and obesity are characterized by excessive production of reactive oxygen species (ROS), which promote oxidative modification of LDL into oxidized LDL (ox-LDL). Oxidized LDL is readily internalized by macrophages through scavenger receptors, leading to intracellular lipid accumulation and transformation into foam cells. Continuous foam cell formation amplifies inflammatory responses by stimulating the release of pro-inflammatory cytokines, including tumor necrosis factor-alpha (TNF-α), interleukin-1β (IL-1β), and interleukin-6 (IL-6), thereby accelerating glomerular injury and renal dysfunction. By scavenging reactive oxygen species and suppressing lipid peroxidation, aloin may reduce ox-LDL formation and interrupt this pathogenic cascade, ultimately limiting macrophage lipid accumulation within renal tissue(Wan *et al.*, 2017; Ma *et al.*, 2018; Zhang *et al.*, 2020; Abdel-Moniem *et al.*, 2022).

In addition to its antioxidant activity, aloin has been reported to exert anti-inflammatory and hypolipidemic effects that may further contribute to renal protection. Experimental evidence suggests that aloin modulates inflammatory signaling pathways, inhibits activation of Nuclear Factor-kappa B (NF-κB), and decreases the production of inflammatory mediators involved in chronic metabolic inflammation. Furthermore, aloin has been shown to improve lipid metabolism by reducing circulating total cholesterol, LDL cholesterol, and triglyceride concentrations while enhancing endogenous antioxidant defense mechanisms. These biological effects collectively decrease lipotoxicity and reduce the availability of oxidized lipids responsible for foam cell formation. The present findings are therefore biologically plausible and support previous reports describing the protective effects of *Aloe vera*-derived bioactive compounds against oxidative tissue injury(Burmistrova, Krivets and Monakhova, 2020; Jing *et al.*, 2020; Dewi *et al.*, 2024).

Although the present study demonstrated a significant reduction in renal foam cell formation following aloin administration, the protective effect should be interpreted cautiously. The study evaluated only histopathological changes in renal tissue without assessing biochemical markers of renal function such as serum creatinine, blood urea nitrogen, or oxidative stress biomarkers. Consequently, the observed reduction in foam cell formation cannot be directly interpreted as complete restoration of renal function. Furthermore, previous studies have consistently demonstrated that statins remain the most effective pharmacological agents for lipid lowering through inhibition of HMG-CoA reductase. Therefore, aloin should be considered a complementary therapeutic agent rather than a replacement for established lipid-lowering medications. Future investigations incorporating biochemical analyses, molecular inflammatory markers, and different dosage regimens are warranted to clarify the mechanisms underlying the nephroprotective effects of aloin and to determine its long-term therapeutic potential in dyslipidemia-associated renal disease.

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CONCLUSION

Oral administration of aloin significantly reduced foam cell formation in the kidneys of male *Mus musculus* with dyslipidemia-induced obesity. Histopathological findings demonstrated that aloin effectively attenuated lipid accumulation within renal tissue, suggesting a protective role against dyslipidemia-associated renal injury. The beneficial effects of aloin are likely mediated through its antioxidant and anti-inflammatory activities, which suppress oxidative stress, inhibit lipid peroxidation, and reduce macrophage transformation into foam cells.

Although aloin demonstrated promising nephroprotective effects, its therapeutic efficacy should be regarded as complementary rather than substitutive to conventional lipid-lowering therapy. Further investigations involving biochemical renal function parameters, oxidative stress biomarkers, inflammatory mediators, molecular signaling pathways, and dose-response analyses are recommended to better elucidate the mechanisms underlying the renoprotective effects of aloin and to determine its clinical applicability in dyslipidemia-related kidney disease.

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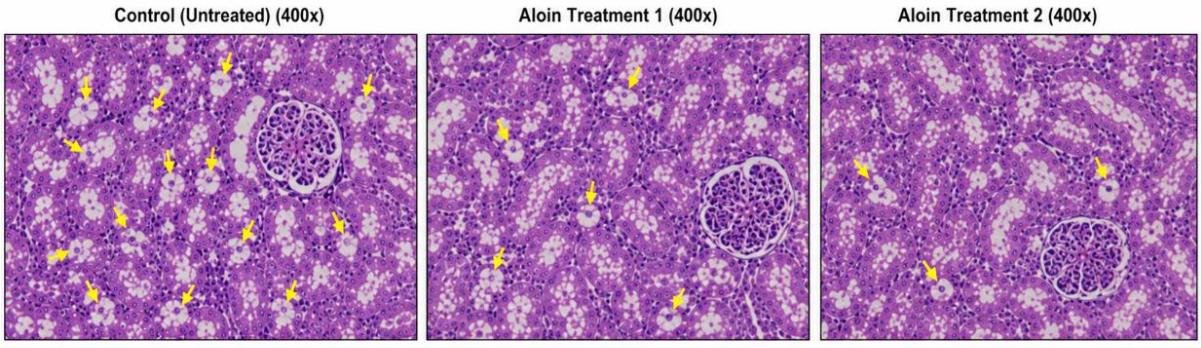
APPENDICES

APPENDIX Renal Histology of *Mus Musculus*



Group	Histopathological Features	Degree of Foam Cell Formation	Interpretation
Control (Untreated) n = 16	• Numerous foam cells are observed. • Abundant foamy cytoplasm with clear lipid vacuoles. • Predominantly located in the interstitium and around tubules. • Frequently seen near glomeruli.	HIGH (Severe accumulation of foam cells)	Marked lipid accumulation and macrophage infiltration indicating severe renal involvement.
Aloin Treatment 1 (750 µg/kg BW) n = 16	• Moderate number of foam cells. • Cytoplasm contains lipid vacuoles of various sizes. • Mainly located in the interstitium between tubules. • Some foam cells are observed near glomeruli.	HIGH–MODERATE (Moderate reduction)	Reduction of foam cell formation compared with control, indicating partial protective effect of aloin.
Aloin Treatment 2 (750 µg/kg BW) n = 16	• Few foam cells are observed. • Less prominent foamy cytoplasm. • Mostly located in the interstitium and near tubules. • Rarely observed around glomeruli.	MODERATE–LOW (Marked reduction)	Marked reduction of foam cell formation, suggesting stronger protective effect of aloin.

Yellow arrows indicate foam cells (lipid-laden macrophages) characterized by foamy / vacuolated cytoplasm.

Histopathological Findings

Figure Histopathology presents representative hematoxylin and eosin (H&E)-stained kidney sections from the control and aloin-treated groups at 400×

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magnification. Foam cells were identified based on their characteristic histomorphological features, including enlarged cells with abundant foamy or vacuolated cytoplasm resulting from intracellular lipid accumulation and eccentrically displaced nuclei. Yellow arrows indicate representative foam cells located predominantly within the renal interstitium and adjacent to renal tubules.

The control group exhibited extensive foam cell formation, characterized by numerous lipid-laden macrophages distributed throughout the renal interstitial tissue. The foam cells demonstrated prominent cytoplasmic vacuolation, indicating excessive intracellular lipid deposition associated with dyslipidemia-induced renal injury. The widespread distribution of these cells reflects enhanced macrophage infiltration and persistent lipid accumulation within the renal microenvironment.

In contrast, kidney sections from the aloin-treated group demonstrated a noticeable reduction in foam cell formation compared with the untreated control group. The extent of foam cell reduction varied among the treated specimens, with some sections showing only a few scattered foam cells, whereas others exhibited a moderate number of residual foam cells. Despite this histological variability, all aloin-treated specimens consistently displayed fewer foam cells than the control group, indicating an overall attenuation of lipid accumulation within renal tissue.

Collectively, these histopathological findings suggest that oral administration of aloin reduced foam cell formation in the kidneys of dyslipidemia-induced obese mice. Although the degree of reduction differed among individual specimens, the overall trend indicates that aloin effectively suppressed foam cell formation. This protective effect is likely attributable to the antioxidant and anti-inflammatory properties of aloin, which may reduce oxidative modification of low-density lipoprotein (LDL), inhibit macrophage lipid uptake, and consequently limit the formation of lipid-laden foam cells within the renal parenchyma.

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