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THE EFFECT OF ALOIN ADMINISTRATION ON DERMAL THICKNESS IN MALE MICE (*MUS MUSCULUS*) WITH DYSLIPIDEMIA-INDUCED OBESITY

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Abstract
Introduction: Dyslipidemia and obesity are major metabolic disorders associated with persistent oxidative stress and chronic low-grade inflammation. These pathological conditions impair dermal homeostasis by promoting collagen degradation, suppressing fibroblast activity, and disrupting extracellular matrix remodeling, ultimately resulting in dermal thinning and delayed tissue repair. Aloin, the principal anthraquinone glycoside isolated from Aloe vera, *possesses well-documented antioxidant and anti-inflammatory properties that may protect dermal tissue against oxidative injury. This study aimed to investigate the effect of aloin administration on dermal thickness in male Mus musculus with dyslipidemia-induced obesity. Methode: A true experimental study employing a posttest-only control group design was conducted using thirty-two male mice with experimentally induced dyslipidemia and obesity. Animals were randomly allocated into a control group (n = 16) and an aloin-treated group (n = 16). The treatment group received oral aloin at a dose of 750 µg/kg body weight once daily via gastric gavage for 28 consecutive days. Skin specimens were processed for histopathological examination using hematoxylin-eosin staining. Statistical comparisons between groups were performed using the Independent Samples t-test, with statistical significance established at* $p < 0.05$. *Result: The mean dermal thickness was 0.485 ± 0.090 mm in the control group and 0.465 ± 0.116 mm in the aloin-treated group. Statistical analysis demonstrated no significant difference in dermal thickness between the two experimental groups (*$p > 0.05$*). Conclusion: Oral administration of aloin at 750 µg/kg body weight for 28 days did not significantly increase dermal thickness in male mice with dyslipidemia-induced obesity*
Keywords: *Aloin; Aloe vera; dermal thickness; dyslipidemia; obesity; collagen*

INTRODUCTION

Dyslipidemia is a metabolic disorder characterized by abnormal plasma lipid profiles, including elevated concentrations of total cholesterol, Low-Density Lipoprotein (LDL), triglycerides, and/or reduced High-Density Lipoprotein (HDL). Together with the increasing prevalence of obesity, dyslipidemia has become one of the leading contributors to chronic non-communicable diseases, particularly cardiovascular and metabolic disorders. Beyond its well-established systemic consequences, accumulating evidence suggests that dyslipidemia also adversely affects skin physiology by altering the structural integrity and regenerative capacity of dermal tissue(Aman *et al.*, 2021; Seliem *et al.*, 2024).

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The skin serves as the body's largest organ and constitutes the primary barrier against environmental insults while maintaining physiological homeostasis. The dermis, composed predominantly of fibroblasts, collagen fibers, elastic fibers, vascular networks, and extracellular matrix components, provides the mechanical strength and elasticity required for normal skin function. Dermal integrity depends on the dynamic equilibrium between collagen synthesis and degradation. Disruption of this balance accelerates extracellular matrix breakdown, resulting in dermal thinning, impaired wound healing, and progressive deterioration of skin mechanical properties(Lintzeri *et al.*, 2022; Dudás, 2023).

Oxidative stress represents one of the principal mechanisms linking dyslipidemia and obesity to dermal injury. Excessive production of reactive oxygen species (ROS) activates intracellular inflammatory signaling pathways, particularly Nuclear Factor-kappa B (NF-κB), leading to increased secretion of pro-inflammatory cytokines such as Tumor Necrosis Factor-Alpha (TNF-α), Interleukin-1β (IL-1β), and Interleukin-6 (IL-6). These mediators subsequently stimulate the expression of Matrix Metalloproteinases (MMPs), especially MMP-1 and MMP-3, enzymes responsible for collagen degradation and extracellular matrix remodeling. Persistent activation of these pathways progressively compromises dermal architecture and delays tissue regeneration(Addis *et al.*, 2020; Wilkinson and Hardman, 2020).

Obesity further aggravates this pathological process through chronic low-grade inflammation originating from adipose tissue. Hypertrophic adipocytes recruit macrophages that continuously release inflammatory mediators, thereby suppressing fibroblast proliferation and collagen biosynthesis. Consequently, individuals with obesity and dyslipidemia exhibit impaired dermal repair capacity and increased susceptibility to structural skin abnormalities(Mohite *et al.*, 2021; Vani, 2022).

Natural antioxidants have gained considerable attention as potential therapeutic agents capable of attenuating oxidative stress and inflammatory tissue damage. Among these, *Aloe vera* has been extensively investigated because of its diverse bioactive constituents, including polysaccharides, flavonoids, vitamins, enzymes, and anthraquinones. Aloin, the major anthraquinone glycoside present in *Aloe vera*, exhibits potent antioxidant, anti-inflammatory, antimicrobial, and cytoprotective activities that may contribute to maintaining dermal integrity(Mohite *et al.*, 2021; Dewi *et al.*, 2023).

Experimental studies have demonstrated that aloin scavenges reactive oxygen species, inhibits lipid peroxidation, suppresses pro-inflammatory cytokine production, and preserves fibroblast viability. Furthermore, aloin has been reported to enhance collagen synthesis while reducing the expression of matrix metalloproteinases, suggesting a protective role against extracellular matrix degradation. These biological activities indicate that aloin may improve dermal architecture by preserving collagen integrity and promoting tissue remodeling(Marta Sánchez, Elena González-Burgos, 2020; Kong *et al.*, 2022).

Despite these promising findings, evidence regarding the histological effects of aloin on dermal thickness under dyslipidemic-obese conditions remains scarce. Most previous investigations have focused primarily on wound healing, antioxidant capacity, or the anti-inflammatory effects of *Aloe* vera, whereas studies specifically evaluating dermal thickness in experimental models of dyslipidemia

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and obesity are still limited. Moreover, inconsistencies among published findings—attributable to differences in dosage, treatment duration, disease induction protocols, and histological assessment methods—have hindered the establishment of a definitive conclusion regarding the therapeutic efficacy of aloin in metabolically compromised skin.

Accordingly, the present study addresses this research gap by evaluating the effect of oral aloin administration on dermal thickness in male mice with dyslipidemia-induced obesity using histopathological analysis. Unlike previous studies that primarily assessed wound healing outcomes, this investigation quantitatively evaluates dermal thickness as the principal histomorphometric endpoint. The findings are expected to provide additional evidence regarding the potential application of aloin as a natural therapeutic agent for preserving dermal integrity under chronic metabolic inflammatory conditions.

METHODE

This study employed a true experimental design with a posttest-only control group design to investigate the effect of aloin administration on dermal thickness in male *Mus musculus* with dyslipidemia-induced obesity. The experiment was conducted at the Biomedical Laboratory, Faculty of Medicine, Baiturrahmah University, Padang, Indonesia. A total of 32 healthy male mice, aged approximately 18 weeks and weighing 27–38 g, were included in the study. Following a seven-day acclimatization period under standard laboratory conditions, all animals were induced to develop dyslipidemia-induced obesity using a high-fat diet (HFD). The mice were then randomly assigned into two groups (n = 16/group): a control group and an aloin-treated group using a simple random sampling technique.

Following successful induction, the treatment group received aloin at a dose of 750 µg/kg body weight administered orally via gastric gavage once daily for 28 consecutive days, whereas the control group received no aloin treatment. Throughout the experimental period, all animals were maintained under identical environmental conditions, including housing, temperature, lighting cycle, dietary intake, and access to drinking water, in order to minimize potential confounding factors that might influence the study outcomes.

At the end of the intervention period, all animals were humanely euthanized, and skin specimens were collected from the same anatomical region for histopathological analysis. Tissue samples were fixed in 10% neutral buffered formalin, processed routinely through dehydration, clearing, paraffin embedding, sectioning, and stained with hematoxylin and eosin (H&E). Dermal thickness was subsequently evaluated under a light microscope at 400× magnification, and measurements were obtained from multiple representative microscopic fields to generate the mean dermal thickness for each specimen.

The primary outcome of this study was dermal thickness expressed in millimeters (mm). Data were analyzed using descriptive statistics and presented as mean ± standard deviation (SD). Data normality and homogeneity were assessed using the Shapiro–Wilk and Levene's tests, respectively. Differences in dermal thickness between the control and treatment groups were analyzed using the Independent Samples *t*-test, with statistical significance established at $p < 0.05$. Ethical approval was obtained from the Health Research Ethics Committee of the Faculty of Medicine, Baiturrahmah University, and all experimental procedures

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involving animals were conducted in accordance with the principles of Replacement, Reduction, and Refinement (3Rs).

RESULT AND DISCUSSION

All 32 male mice completed the experimental protocol and were included in the final analysis. Dermal thickness was evaluated after 28 days of intervention using histopathological examination. The mean dermal thickness in the control group was 0.485 ± 0.090 mm, whereas the aloin-treated group exhibited a mean dermal thickness of 0.465 ± 0.116 mm. Statistical analysis using the Independent Samples *t*-test demonstrated no significant difference between the two groups ($p > 0.05$), indicating that oral administration of aloin at a dose of 750 µg/kg body weight did not significantly influence dermal thickness in male mice with dyslipidemia-induced obesity under the experimental conditions employed in this study (Table 1).

Table 1. Dermal Thickness in Male *Mus musculus* with Dyslipidemia-Induced Obesity

Group	n	Dermal Thickness (mm) Mean ± SD	*p*-value
Control	16	0.485 ± 0.090	
Aloin-treated	16	0.465 ± 0.116	>0.05

The absence of a statistically significant increase in dermal thickness suggests that aloin, at the administered dose and treatment duration, was insufficient to reverse the structural alterations associated with dyslipidemia-induced obesity. Chronic metabolic disorders such as obesity and dyslipidemia are characterized by persistent oxidative stress and low-grade inflammation, both of which disrupt extracellular matrix homeostasis through excessive production of reactive oxygen species (ROS) and activation of inflammatory signaling pathways(Goddard *et al.*, 2022; Malbos, 2025). These mechanisms stimulate the expression of matrix metalloproteinases (MMPs), particularly MMP-1 and MMP-3, which accelerate collagen degradation while simultaneously impairing fibroblast proliferation and collagen synthesis. Consequently, the regenerative capacity of dermal tissue is compromised, resulting in reduced dermal integrity and delayed tissue remodeling. Although aloin has been reported to possess antioxidant and anti-inflammatory activities capable of attenuating oxidative damage, these biological effects may not be sufficient to overcome the extensive metabolic disturbances induced by prolonged exposure to a high-fat diet(Fu *et al.*, 2021; Ge *et al.*, 2023; López de Figueroa *et al.*, 2023).

Several factors may explain the lack of a significant histological response observed in the present study. First, the administered dose of 750 µg/kg body weight may not have reached the therapeutic threshold required to induce measurable changes in collagen deposition and dermal remodeling. Second, the 28-day treatment period may have been insufficient to promote substantial extracellular matrix regeneration, as collagen synthesis and tissue remodeling are complex biological processes that often require prolonged intervention. Third, chronic inflammation associated with dyslipidemia-induced obesity may have exceeded the protective capacity of aloin, thereby masking its potential therapeutic effects. Furthermore, previous experimental studies investigating *Aloe vera* and its

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bioactive constituents have produced inconsistent findings, likely due to differences in animal models, extraction methods, dosage regimens, treatment duration, and outcome measurements. Therefore, the absence of statistical significance in the present study should not be interpreted as evidence of biological inactivity but rather as an indication that the selected experimental conditions may not have been optimal to demonstrate the histological benefits of aloin.

Despite these findings, this study contributes valuable experimental evidence regarding the histological effects of aloin in a dyslipidemia-induced obesity model, an area that remains relatively underexplored. Unlike previous investigations that primarily focused on wound healing or antioxidant capacity, the present study quantitatively assessed dermal thickness as a histomorphometric indicator of tissue integrity. Future studies should investigate different dosage regimens, longer intervention periods, and additional molecular endpoints, including collagen type I and III expression, transforming growth factor-β (TGF-β), matrix metalloproteinases, oxidative stress biomarkers, and inflammatory cytokines(López-Otín *et al.*, 2023; Seliem *et al.*, 2024). Such comprehensive approaches would provide a deeper understanding of the mechanisms through which aloin may influence dermal remodeling under chronic metabolic conditions and help clarify its therapeutic potential in preventing skin structural deterioration associated with obesity and dyslipidemia.

Strengths of the Study

This study provides experimental evidence regarding the histological effect of aloin on dermal thickness in a dyslipidemia-induced obesity model, which remains relatively underexplored. The use of a controlled experimental design and quantitative histopathological assessment contributes to the growing body of evidence supporting the investigation of natural bioactive compounds for metabolic disease-associated skin alterations.

Limitations of the Study

Several limitations should be acknowledged. The study evaluated only a single aloin dose and one treatment duration, which may not have been sufficient to elicit detectable histological changes. In addition, dermal thickness was used as the sole outcome measure without assessing molecular biomarkers related to collagen remodeling, oxidative stress, or inflammation. These limitations should be considered when interpreting the findings and designing future studies.

CONCLUSION

The present study demonstrated that oral administration of aloin at a dose of 750 µg/kg body weight for 28 consecutive days did not produce a statistically significant effect on dermal thickness in male *Mus musculus* with dyslipidemia-induced obesity. These findings suggest that the selected dosage and treatment duration were insufficient to induce measurable histological improvement in dermal architecture under chronic metabolic stress. Nevertheless, considering the established antioxidant and anti-inflammatory properties of aloin, its therapeutic potential should not be disregarded. Further investigations employing different dosage regimens, extended treatment durations, and comprehensive molecular analyses, including collagen synthesis, matrix metalloproteinase activity, oxidative stress markers, and inflammatory mediators, are warranted to better elucidate the

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role of aloin in preserving dermal integrity and preventing skin structural deterioration associated with dyslipidemia and obesity.

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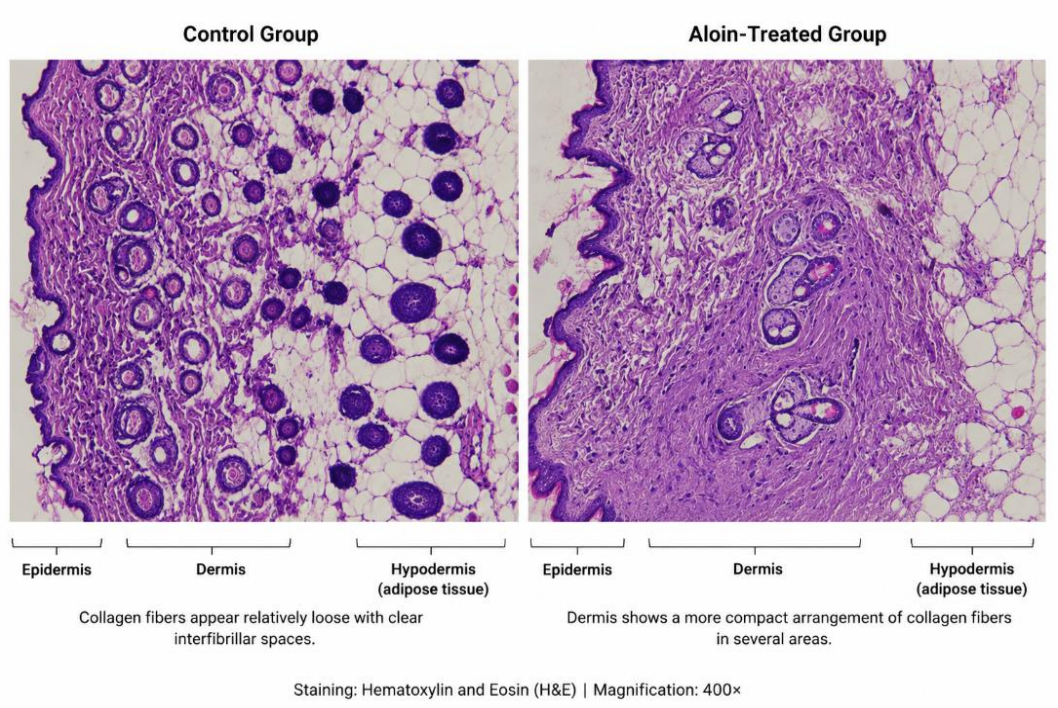
APPENDICES

APPENDIX A Skin Histology of *Mus Musculus*



Parameter	Control Group	Aloin-Treated Group
Epidermis	The epidermis appeared intact with a relatively smooth surface contour. Epidermal thickness was generally uniform, and the overall epithelial architecture remained well preserved.	The epidermis also remained intact without evidence of structural damage. Although the surface contour appeared slightly more undulated, no remarkable morphological differences were observed compared with the control group.
Dermis	The dermis exhibited relatively loose collagen fiber bundles with distinct interfibrillar spaces.	The dermis qualitatively appeared more compact, with collagen bundles showing a denser arrangement in several areas. The extracellular matrix surrounding the hair follicles

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	Hair follicles were evenly distributed throughout the connective tissue, while the extracellular matrix demonstrated moderate collagen density.	also appeared more condensed; however, these observations were not accompanied by an apparent increase in overall dermal thickness.
Hair Follicles and Skin Appendages	Hair follicles were evenly distributed and maintained normal morphological characteristics. No abnormalities in the associated skin appendages were identified.	Hair follicles and cutaneous appendages remained well preserved, exhibiting morphology comparable to that of the control group. No evidence of degenerative changes or structural damage was observed.
Hypodermis (Subcutaneous Adipose Tissue)	The hypodermis consisted predominantly of loosely arranged adipose tissue with relatively large adipocytes.	The hypodermis displayed adipocyte morphology and distribution similar to those observed in the control group, without appreciable structural alterations.
Overall Histological Appearance	The overall skin architecture was well preserved, although the connective tissue appeared relatively loose within the dermal layer.	The overall skin architecture remained preserved, with a qualitative tendency toward increased connective tissue compactness in certain dermal regions. Nevertheless, these subtle morphological differences were insufficient to indicate a clear histological distinction between the two groups.

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