Bioscientist: Jurnal Ilmiah Biologi
https://e-journal.undikma.ac.id/index.php/bioscientist

March 2026 Vol. 14, No. 1
e-ISSN: 2654-4571
pp. 225-238

Purple Yam (*Dioscorea alata*) Tuber Improves the Histological Appearance of the Ampulla of the Uterine Tube in a Mouse Model of Endometriosis

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Received: February 2026; Revised: March 2026; Accepted: March 2026; Published: March 2026

Abstract: This study aimed to examine the effect of *Dioscorea alata* ethanol extract (EEDA) on the histological features of the ampulla of the uterine tube in a mouse model of endometriosis. This was a true experimental study with a posttest-only control group design using 30 mice divided into six groups: a normal control group (K), a negative control group (KN) induced with endometriosis, a positive control group (KP) induced with endometriosis and treated with letrozole, and three treatment groups induced with endometriosis and administered EEDA at doses of 50, 250, and 500 mg/kg body weight. The observed parameters included inflammatory cell infiltration, epithelial damage, and fibrosis. Data were analyzed using the Kolmogorov–Smirnov test for normality, which showed that the data were not normally distributed; therefore, the nonparametric Kruskal–Wallis test followed by the Mann–Whitney post hoc test was applied. The results showed that the KN group had the highest scores for inflammatory cell infiltration, epithelial damage, and fibrosis ($p < 0.05$). Administration of EEDA significantly reduced all three parameters compared with the KN group ($p < 0.05$), with histological improvement increasing in a dose-dependent manner and the most optimal dose observed at 500 mg/kg body weight. It can be concluded that *Dioscorea alata* ethanol extract may improve the histological features of the ampulla of the uterine tube through anti-inflammatory and antifibrotic mechanisms at an optimal dose of 500 mg/kg body weight; however, the specific molecular mechanisms still require further verification. These findings indicate the potential of *Dioscorea alata* ethanol extract as a candidate herbal-based alternative therapy in an experimental model of endometriosis.
Keywords: Endometriosis; *Dioscorea alata*; histopathology; anti-inflammatory; antifibrotic

How to Cite: Makiyah, S. N. N., Usman, S., & Adawiyah, R. (2026). Purple Yam (Dioscorea alata) Tuber Improves the Histological Appearance of the Ampulla of the Uterine Tube in a Mouse Model of Endometriosis. *Bioscientist: Jurnal Ilmiah Biologi*, *14*(1), 225–238. https://doi.org/10.33394/bioscientist.v14i1.20007

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INTRODUCTION

Endometriosis is a chronic gynecological disorder characterized by the growth of endometrium-like tissue outside the uterine cavity. This condition is associated with persistent inflammation, chronic pelvic pain, and reproductive disorders such as infertility. Globally, the prevalence of endometriosis is estimated to be approximately 10% among women of reproductive age, affecting around 176 million women worldwide (Czubak et al., 2025). In addition, the prevalence of endometriosis has been reported to reach 20–50% among women undergoing infertility evaluation and 30–70% among women with chronic pelvic pain (Králíčková et al., 2020). The pathogenesis of endometriosis involves complex hormonal interactions, genetic factors, and immune dysfunction, including macrophage activation, reduced Natural Killer (NK) cell cytotoxicity, and increased levels of pro-inflammatory cytokines such as IL-1β, IL-6, and TNF-α (Shifon et al., 2025; Zhang et al., 2024). This persistent inflammatory environment triggers oxidative stress and activates pro-fibrotic pathways such as transforming growth factor-β (TGF-β), which contributes to collagen deposition and tissue remodeling (Allaire et al., 2023). These chronic inflammatory processes lead to fibrogenesis and structural remodeling in reproductive organs, including the ovaries and uterine tubes. The uterine tube, particularly the ampullary segment, plays a crucial role as the primary site of fertilization. Damage to the ampulla of the uterine tube may impair epithelial ciliary function, oocyte transport, and fertilization, thereby reducing the likelihood of pregnancy (Nassir et al., 2024; Park et al., 2025). These findings indicate that endometriosis not only causes chronic pain but may also specifically compromise uterine tubal function, especially in the ampullary region, which is essential for fertilization.

Nevertheless, the persistence of inflammation and fibrogenesis leads to progressive tissue damage, making this condition a major challenge in the treatment of endometriosis. Current therapies are largely symptomatic, including hormonal treatment and surgery, which aim to relieve symptoms and reduce lesion volume. However, these approaches have not been able to comprehensively prevent disease progression and are associated with risks of long-term side effects and high recurrence rates (Allaire et al., 2023; Czubak et al., 2025). Molecular studies have shown that activation of inflammatory pathways such as NF-κB contributes to increased expression of pro-inflammatory cytokines in endometriotic lesions, while modulation of pro-fibrotic pathways such as TGF-β plays a role in tissue adhesion and fibrogenesis, making these pathways potential targets for therapeutic strategies aimed at suppressing inflammation and fibrosis formation (Chen & Li, 2025; Liu et al., 2022). Most previous studies have focused on ovarian tissue or endometrial lesions and have emphasized molecular analyses, whereas studies specifically evaluating histological changes in the ampulla of the uterine tube, a key site for fertilization, in endometriosis models remain limited. Therefore, there is a need to develop therapeutic approaches that are not merely symptomatic but also target the underlying mechanisms of endometriosis pathogenesis, particularly inflammation and fibrogenesis. In this context, compounds with anti-inflammatory and antioxidant activities represent promising candidates, as they may suppress oxidative stress and modulate immune responses within the endometriotic lesion microenvironment. Accordingly, natural compound-based approaches constitute a potential strategy for further investigation.

One natural candidate with considerable potential is purple yam tuber (*Dioscorea alata*). *D. alata* is known to contain flavonoids, saponins, and anthocyanins, which exhibit strong anti-inflammatory and antioxidant activities (Lebot et al., 2023; Qiu et al., 2023). These compounds contribute to reducing reactive oxygen species (ROS) production, enhancing endogenous antioxidant enzyme activity, and suppressing pro-inflammatory mediators. Furthermore, its bioactive compounds may inhibit inflammatory pathways such as NF-κB as well as pro-fibrotic pathways that contribute to tissue damage caused by chronic inflammation (Feng et al., 2023). Although numerous studies have reported the anti-inflammatory and antioxidant effects of *Dioscorea alata*, research specifically evaluating its effects on the histological features of the ampulla of the uterine tube in endometriosis models remains scarce. Most previous studies have focused on ovarian tissue or endometrial lesions and have placed greater emphasis on molecular aspects than on organ-specific histological evaluation of the reproductive tract.

Based on these considerations, the novelty of this study lies in its focus on the ampulla of the uterine tube as a key site of fertilization and in its evaluation of histological alterations as direct indicators of tissue damage. This study aimed to investigate the effect of ethanolic extract of purple yam tuber (*Dioscorea alata*) on the improvement of the histological features of the ampulla of the uterine tube in a mouse model of endometriosis. The evaluated parameters included inflammatory cell infiltration as an indicator of the inflammatory response, the degree of epithelial damage as a marker of the structural integrity of the tubal mucosa, and the extent of fibrosis as a manifestation of pro-fibrotic pathway activation associated with collagen deposition and tissue remodeling (Liu et al., 2022; Xu et al., 2025). Alterations in epithelial structure and increased fibrosis may disrupt ciliary motility, tubal lumen integrity, and the microenvironment required for successful conception (Xu et al., 2025). Therefore, this study is expected to contribute scientifically in three aspects: empirically, by providing histological evidence of tissue repair; mechanistically, by indicating potential anti-inflammatory and anti-fibrotic effects; and applicatively, by serving as a basis for the development of natural compound-based adjuvant therapies for endometriosis management.

METHOD

This study was conducted from January to July 2025. Animal maintenance and experimental treatments were carried out at the Animal House, Laboratory of Pharmacology and Clinical Pharmacy, Faculty of Pharmacy, Universitas Gadjah Mada. Preparation of the ethanol extract of purple yam tuber (*Dioscorea alata*) was performed at the Laboratory of Pharmaceutical Technology, Faculty of Medicine and Health Sciences, Universitas Muhammadiyah Yogyakarta. Histological preparation of the ampulla of the uterine tube in mice was conducted at the Microanatomy Laboratory, Faculty of Veterinary Medicine, Universitas Gadjah Mada, whereas histological observations and data analysis were performed at the Histology Laboratory, Faculty of Medicine and Health Sciences, Universitas Muhammadiyah Yogyakarta.

This study employed a true experimental design with a posttest-only control group design. A total of 30 female BALB/c mice (*Mus musculus*) were used and randomly allocated into six groups: normal control (K), negative control (KN), positive control (KP), and three treatment groups receiving ethanol extract of *D. alata* at doses of 50, 250, and 500 mg/kg body weight (P1, P2, and P3, respectively). Each group consisted of five mice, with the sample size determined using the Federer formula.

The animals were acclimatized for 7 days before treatment. Endometriosis was induced using chocolate cyst slurry at a dose of 0.1 mL/20 g body weight (Brahmana et al., 2025), along with the administration of cyclosporine and ethinyl estradiol. The induction protocol in this study referred to the method reported by Brahmana et al. (2025), in which the material was inoculated intraperitoneally in mice, with ethinyl estradiol administration to support lesion growth. This approach is consistent with experimental models using suspensions or fragments of endometrial tissue injected into the peritoneal cavity to induce endometriotic lesions (Burns et al., 2022). This model is widely used because it can reproduce inflammatory conditions and lesion formation resembling human endometriosis. Endometriosis induction was performed on day 1, and ethinyl estradiol administration was repeated on day 5. After induction, the animals were left untreated for 14 days to allow the development of endometriotic lesions. Subsequently, the mice were assigned to six treatment groups. The normal control group (K) received only 0.5% CMC-Na. The negative control group (KN) was induced with endometriosis and administered 0.5% CMC-Na. The positive control group (KP) was induced with endometriosis and treated with letrozole at a dose of 0.2 mg/kg body weight. The treatment groups (P1, P2, and P3) were induced with endometriosis and administered ethanol extract of *D. alata* at doses of 50, 250, and 500 mg/kg body weight, respectively. All treatments were administered orally using a gastric gavage at a volume of 0.5 mL per animal, once daily in the morning, for 14 days, from day 15 to day 29.

The ethanol extract of *D. alata* was prepared by maceration using 70% ethanol as the solvent. Purple yam tuber simplicia was dried and then ground into powder. The powder was extracted with 70% ethanol for 7 days, after which the filtrate was evaporated using a vacuum evaporator at 50°C to obtain a viscous extract.

Histological preparations were made using the paraffin block method. The mice were euthanized by cervical dislocation and dissected to collect the ampulla of the uterine tube. The tissues were washed with 0.9% physiological NaCl solution and fixed in 10% buffered formalin for approximately 24 hours. The tissues were then processed through graded alcohol dehydration, xylene clearing, paraffin infiltration, and embedding in paraffin blocks. The paraffin blocks were sectioned using a microtome at a thickness of approximately 4–5 µm and mounted on glass slides. The sections then underwent deparaffinization, rehydration, and Hematoxylin–Eosin (HE) staining. The slides were examined under a binocular light microscope at 400× magnification in 10 fields of view.

The observed parameters were inflammatory cell infiltration, epithelial damage, and fibrosis in the ampulla of the uterine tube, as presented in Table 1. Scoring was performed using a semi-quantitative scoring system modified from Erben et al. (2014) and Hoorsan et al. (2022).

Table 1. Scoring criteria for the degree of damage in the ampulla of the uterine tube in the endometriosis model

Category	Definition	Score
Inflammatory Cell Infiltration	No inflammatory cell infiltration observed	0
	Infiltration limited to the mucosal layer	1
	Infiltration extending to the mucosa and muscularis	2
	Infiltration reaching the mucosa, muscularis, and serosa	3
Fibrosis	No fibrosis	0
	Minimal fibrotic tissue growth	1
	Irregular fibrotic tissue growth	2
	Fibrotic accumulation and hyalinization	3
Epithelium	Epithelial layer well preserved and intact	0
	Epithelial layer showing minimal damage (desquamation)	1
	Epithelial layer showing inflammatory cell infiltration	2
	Absence of epithelial layer	3

The data were presented in the form of tables and figures. Normality was assessed using the Kolmogorov–Smirnov test, and homogeneity was evaluated using Levene's test. The results showed that the data were not normally distributed ($p < 0.05$); therefore, the analysis was continued using the non-parametric Kruskal–Wallis test followed by the Mann–Whitney post hoc test. The level of significance was set at 95% ($p < 0.05$).

RESULTS AND DISCUSSION

Inflammatory Cell Infiltration

Based on the histological observations of the ampulla of the uterine tube, differences in the degree of inflammatory cell infiltration were observed among the treatment groups. The highest mean inflammatory cell infiltration score was found in the negative control group, with a value of 2.74 ± 0.56, whereas the lowest value was observed in treatment group P3, which received *D. alata* ethanol extract at a dose of 500 mg/kg body weight, with a value of 0.18 ± 0.39. The positive control group showed a value of 1.86 ± 0.97, while treatment group P1 showed a value of 1.55 ± 0.60. The mean inflammatory cell infiltration score for each group is presented in Table 2.

Table 2. Mean inflammatory cell infiltration scores in the ampulla of the uterine tube in a mouse model of endometriosis

Group	Inflammatory cell infiltration score (Mean ± SD)
Normal Control (K)	0 ± 0^{d}
Negative Control (KN)	1,28 ± 0,50^{a}
Positive Control (KP)	0,92 ± 0,78^{b}
Treatment 1 (P1)	0,38 ± 0,54^{c}
Treatment 2 (P2)	0,06 ± 0,24^{d}
Treatment 3 (P3)	0,07 ± 0,36^{d}

Note: SD = standard deviation. Superscript letters indicate the results of intergroup comparisons: **a** = group with the highest value and significantly different from the other groups; **b** = group significantly different from group **a**, but not different from groups sharing the same letter; **c** = group significantly different from groups **a** and **b**, but not different from groups sharing the same letter; **d** = group with the lowest value and significantly different from the other groups. Groups with the same letter are not significantly different ($p < 0.05$).

Statistical analysis using the Kruskal-Wallis test showed a significant difference among treatment groups ($p < 0.05$). Further analysis using the Mann-Whitney test indicated that the negative control group differed significantly from the KP, P2, and P3 groups. Histological observations showed that the negative control group exhibited denser inflammatory cell infiltration, whereas the treatment groups showed lower levels of infiltration, particularly group P3. The histological appearance of each group is presented in Figure 1.

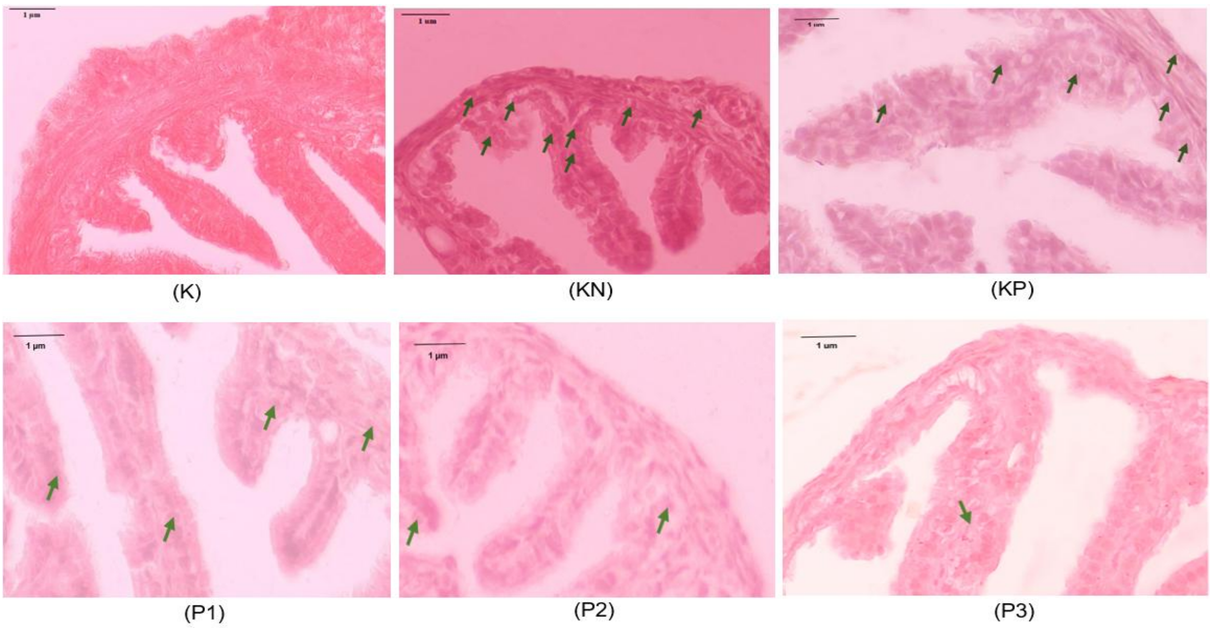

Figure 1. Inflammatory cell infiltration in the ampulla of the uterine tube in a mouse model of endometriosis. (Note: K = normal control; KN = negative control (endometriosis-induced); KP = positive control (endometriosis-induced + letrozole 0.2 mg/kg body weight); P1 = Treatment 1 (endometriosis-induced + EEDA 50 mg/kg body weight); P2 = Treatment 2 (endometriosis-induced + EEDA 250 mg/kg body weight); P3 = Treatment 3 (endometriosis-induced + EEDA 500 mg/kg body weight). Green arrows indicate inflammatory cell infiltration in the ampulla of the uterine tube (hematoxylin-eosin staining)).

In this study, the normal control group showed no inflammatory cell infiltration in the ampulla of the uterine tube, with an intact epithelial structure and no pathological changes. This finding is attributable to the fact that the normal control group received only 0.5% CMC-Na without endometriosis induction, thereby reflecting normal physiological conditions. CMC-Na acts as an inert vehicle for extract administration and does not induce inflammatory reactions in tissues. This finding is consistent with the studies of K. Chen et al. (2023) and Arifin et al. (2020), which reported that CMC-Na administration in experimental animals did not cause tissue alterations or immune responses.

In contrast, the negative control group showed the highest inflammatory cell infiltration score (2.74 ± 0.56), indicating that the endometriosis model used was capable of triggering a local inflammatory response. This condition is in accordance with the pathophysiological mechanism of endometriosis, in which implantation of ectopic endometrial tissue induces the release of proinflammatory cytokines that act as chemokines to recruit neutrophils to the lesion site (Wang et al., 2023). Activated neutrophils subsequently release reactive oxygen species (ROS), proteolytic enzymes, and neutrophil extracellular traps (NETs), all of which contribute to the maintenance of chronic inflammation (Wilson et al., 2025). These findings are consistent with previous studies showing that a chronic inflammatory environment is a hallmark of endometriotic lesions.

In the positive control group, inflammatory cell infiltration was still observed, although at a lower level than in the negative control group. This finding indicates that letrozole, which acts by inhibiting the aromatase enzyme and reducing estrogen levels, does not directly suppress inflammatory pathways. Under endometriotic conditions, immune cells such as macrophages, T lymphocytes, and natural killer (NK) cells remain active and continue to produce proinflammatory cytokines such as IL-1β, IL-6, and TNF-α despite reduced estrogen levels (Sapmaz et al., 2022). This result is in line with the study by Shi et al. (2023), which reported that aromatase inhibitors are effective in suppressing the proliferation of endometriotic lesions but exert limited anti-inflammatory effects.

In the treatment groups, administration of *Dioscorea alata* ethanol extract showed a decreasing trend in inflammatory cell infiltration with increasing dose. This effect is likely associated with the presence of bioactive compounds such as flavonoids, saponins, and anthocyanins, which possess anti-inflammatory and antioxidant activities. These compounds act by suppressing activation of the nuclear factor-kappa B (NF-κB) pathway and reducing the production of proinflammatory mediators such as IL-1β and IL-6, thereby decreasing inflammatory cell infiltration in the tissue (Feng et al., 2023). The reduction in inflammatory cell infiltration was more pronounced at the dose of 500 mg/kg body weight, suggesting a dose-response trend. This finding is also consistent with the study by Makiyah & Zahra (2025), which reported that *D. alata* ethanol extract exerts immunomodulatory effects capable of reducing tissue inflammatory responses.

Fibrosis

Histological observations showed differences in the degree of fibrosis in the ampulla of the uterine tube in the mouse model of endometriosis. The highest mean fibrosis score was found in the negative control group (KN), at 1.28 ± 0.50, whereas the lowest score was observed in the normal control group (K), at 0 ± 0. The positive control group (KP) showed a value of 0.92 ± 0.78, while treatment group P1 had a value of 0.38 ± 0.54. A clearer reduction in fibrosis score was observed in groups P2 and P3, with values of 0.06 ± 0.24 and 0.07 ± 0.36, respectively. The mean fibrosis score for each group is presented in Table 3.

Table 3. Mean fibrosis scores in the ampulla of the uterine tube in a mouse model of endometriosis

Group	Fibrosis (Mean ± SD)
Normal Control (K)	0 ± 0[d]
Negative Control (KN)	1,28 ± 0,50[a]
Positive Control (KP)	0,92 ± 0,78[b]
Treatment 1 (P1)	0,38 ± 0,54[c]
Treatment 2 (P2)	0,06 ± 0,24[d]
Treatment 3 (P3)	0,07 ± 0,36[d]

Note: SD = standard deviation. Superscript letters indicate the results of intergroup comparisons: **a** = group with the highest value and significantly different from the other groups; **b** = group significantly different from group **a**, but not different from groups sharing the same letter; **c** = group significantly different from groups **a** and **b**, but not different from groups sharing the same letter; **d** = group with a lower value and not significantly different from groups sharing the same letter, including the normal control group. Groups with the same letter are not significantly different (p < 0.05).

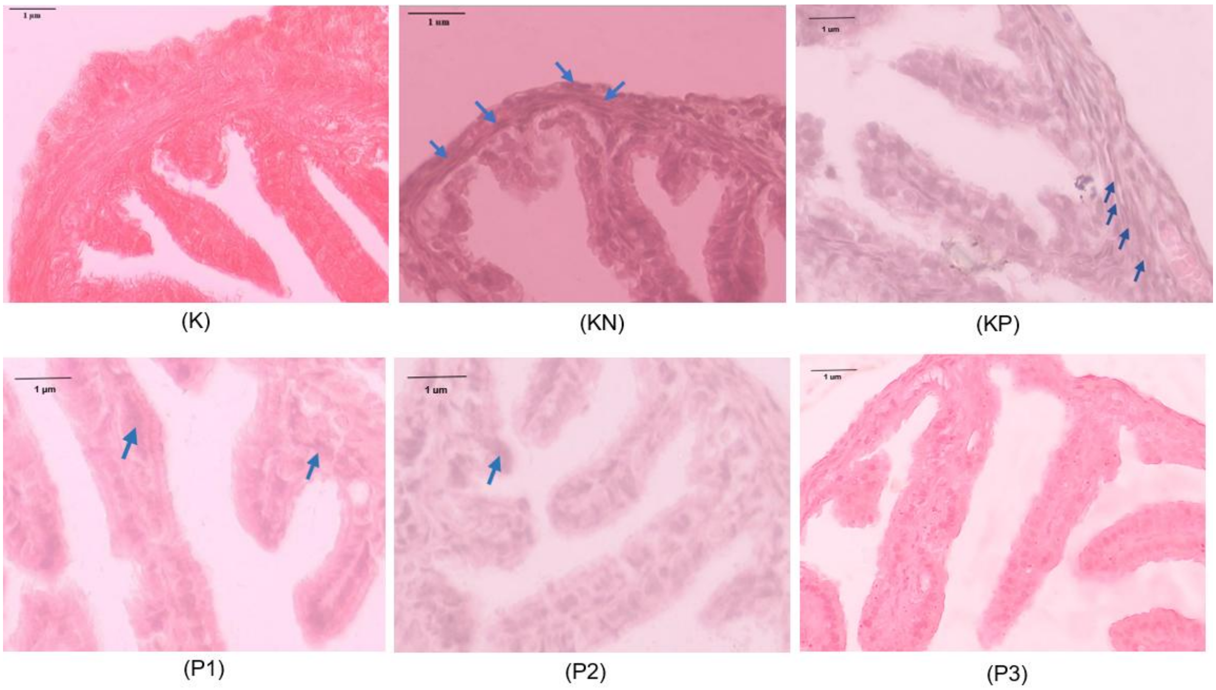

Figure 2. Fibrosis in the ampulla of the uterine tube in a mouse model of endometriosis. (Note: K = normal control; KN = negative control (endometriosis-induced); KP = positive control (endometriosis-induced + letrozole 0.2 mg/kg body weight); P1 = Treatment 1 (endometriosis-induced + EEDA 50 mg/kg body weight); P2 = Treatment 2 (endometriosis-induced + EEDA 250 mg/kg body weight); P3 = Treatment 3 (endometriosis-induced + EEDA 500 mg/kg body weight). Blue arrows indicate fibrotic areas in the ampulla of the uterine tube (hematoxylin-eosin staining)).

Statistical analysis using the Kruskal-Wallis test revealed significant differences among groups (p < 0.05). Histological observations showed that the negative control group exhibited more marked tissue thickening due to collagen deposition than the other groups. In contrast, the treatment groups showed lower collagen deposition and tissue structures more closely resembling normal conditions. The histological appearance of each group is presented in Figure 2.

The increased fibrosis score in the negative control group indicates that the endometriosis model used was capable of inducing fibrogenesis in the ampulla of the uterine tube. This finding is consistent with the pathophysiology of endometriosis, in which oxidative stress and activation of inflammatory cells trigger the release of profibrotic cytokines, particularly transforming growth factor-β1 (TGF-β1). This cytokine stimulates the differentiation of fibroblasts into myofibroblasts, which actively produce collagen and extracellular matrix (ECM) components, thereby leading to fibrotic tissue formation (Vissers et al., 2024). This finding is in line with previous studies showing that the chronic inflammatory environment in endometriosis contributes to tissue remodeling and fibrosis (Anchan et al., 2025).

In the positive control group, fibrosis was still observed, although at a lower level than in the negative control group. This suggests that letrozole, which acts by reducing estrogen levels, does not directly suppress profibrotic pathways. Signaling pathways such as TGF-β/Smad and Wnt/β-catenin may remain active through autocrine and paracrine mechanisms, thereby allowing fibrogenesis to continue (Garcia et al., 2023; Vissers et al., 2024). This finding is consistent with the report by Sapmaz et al. (2022), which showed that aromatase inhibitors are effective in suppressing the proliferation of endometriotic lesions but have limited effects on tissue fibrosis.

In the treatment groups, administration of *Dioscorea alata* ethanol extract showed a clearer tendency to reduce fibrosis scores compared with the negative control group. This effect is likely related to the presence of active compounds such as diosgenin, which has antifibrotic activity. Diosgenin has been reported to inhibit profibrotic pathways, including TGF-β-induced epithelial-mesenchymal transition (EMT), and to reduce the expression of α-SMA and inflammatory mediators such as IL-1β and TGF-β (Dinesh Babu et al., 2022). This mechanism is consistent with reports indicating that activation of the TGF-β pathway plays a central role in fibrogenesis in endometriotic lesions (Liu et al., 2022; Vissers et al., 2024). The reduction in fibrosis was more evident at higher doses, suggesting a dose-response trend.

Epithelial Damage

Based on histological observations of the ampulla of the uterine tube in the mouse model of endometriosis, differences in the degree of epithelial damage were observed among the treatment groups. The highest mean epithelial damage score was found in the negative control group (KN), at 1.84 ± 0.37, whereas the lowest score was observed in the normal control group (K), at 0 ± 0. The positive control group (KP) showed a value of 1.30 ± 0.61, while treatment group P1 had a value of 1.20 ± 0.65. A more pronounced reduction in epithelial damage score was observed in groups P2 and P3, with values of 0.76 ± 0.56 and 0.70 ± 0.46, respectively. The mean epithelial damage score for each group is presented in Table 4.

Table 4. Mean epithelial damage scores in the ampulla of the uterine tube in a mouse model of endometriosis

Group	Epithelium (Mean ± SD)
Normal Control (K)	0 ± 0^{d}
Negative Control (KN)	$1,84 \pm 0,37^{a}$
Positive Control (KP)	$1,30 \pm 0,61^{b}$
Treatment 1 (P1)	$1,20 \pm 0,65^{b}$
Treatment 2 (P2)	$0,76 \pm 0,56^{c}$
Treatment 3 (P3)	$0,70 \pm 0,46^{c}$

Note: SD = standard deviation. Superscript letters indicate the results of intergroup comparisons: **a** = group with the highest value and significantly different from the other groups; **b** = group significantly different from group **a**, but not different from groups sharing the same letter; **c** = group significantly different from groups **a** and **b**, but not different from groups sharing the same letter; **d** = group with the lowest value and significantly different from the other groups. Groups with the same letter are not significantly different ($p < 0.05$).

Statistical analysis using the Kruskal-Wallis test showed significant differences among treatment groups ($p < 0.05$). Further analysis using the Mann-Whitney test indicated that the negative control group differed significantly from the higher-dose treatment groups. Histological observations showed differences in epithelial morphology among groups, with the negative control group exhibiting epithelial damage in the form of desquamation and irregular epithelial layering. In contrast, the treatment groups showed a more organized epithelial structure, particularly group P3, which exhibited a more intact epithelial lining. The histological appearance of each group is presented in Figure 3.

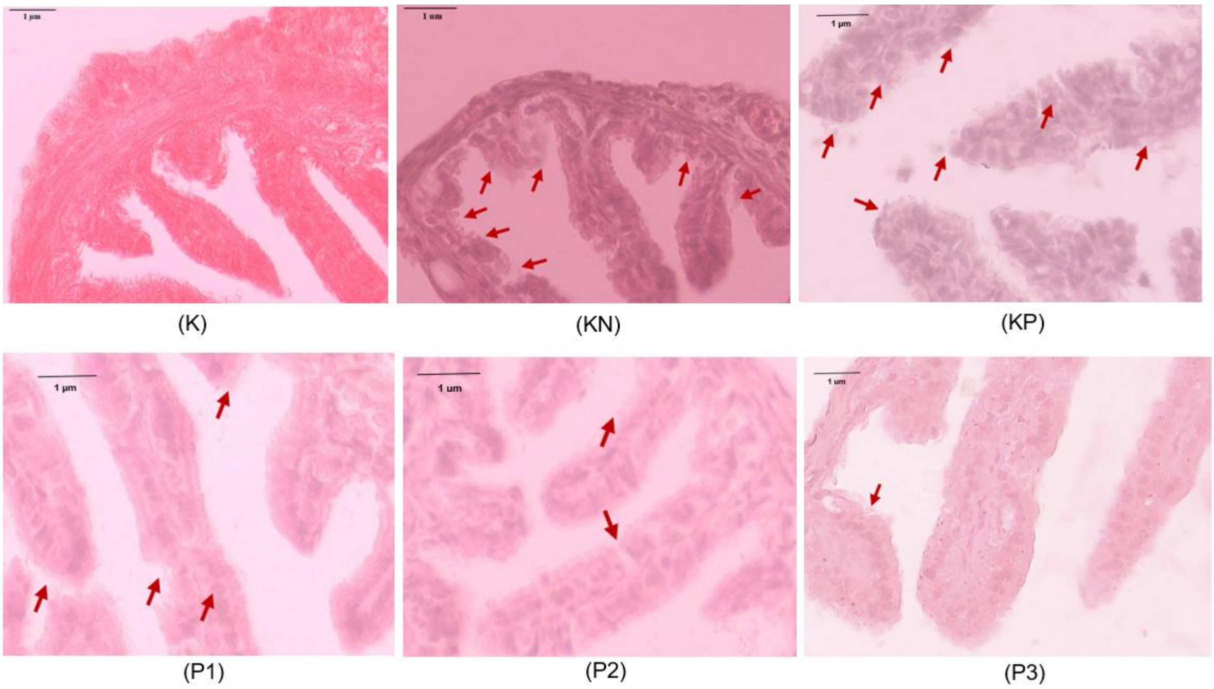

Figure 3. Histological appearance of epithelial damage severity in the ampulla of the uterine tube in a mouse model of endometriosis. (Note: K = normal control; KN = negative control (endometriosis-induced); KP = positive control (endometriosis-induced + letrozole 0.2 mg/kg body weight); P1 = Treatment 1 (endometriosis-induced + EEDA 50 mg/kg body weight); P2 = Treatment 2 (endometriosis-induced + EEDA 250 mg/kg body weight); P3 = Treatment 3 (endometriosis-induced + EEDA 500 mg/kg body weight). Red arrows indicate epithelial damage in the ampulla of the uterine tube (hematoxylin-eosin staining)).

The epithelial damage parameter in this study also showed differences among groups. The negative control group had the highest epithelial damage score (1.84 ± 0.37). This finding is consistent with the pathophysiology of endometriosis, in which increased reactive oxygen species (ROS) and proinflammatory cytokines induce oxidative stress and epithelial cell apoptosis. This condition leads to decreased expression of junctional proteins such as claudin, occludin, and E-cadherin, thereby compromising the integrity of the epithelial lining (Guo et al., 2023; Ni & Li, 2024; Oală et al., 2024).

In addition, epithelial damage is also influenced by activation of the epithelial-to-mesenchymal transition (EMT) process. This process causes a reduction in epithelial markers such as E-cadherin and an increase in mesenchymal markers such as N-cadherin and vimentin, which contribute to cell migration and invasion. EMT activation is regulated by transcription factors such as SNAIL (Snail Family Transcriptional Repressor 1/SNAI1), SLUG (Snail Family Transcriptional Repressor 2/SNAI2), and TWIST (Twist Family bHLH Transcription Factor 1/TWIST1), as well as by the TGF-β/Smad, Wnt/β-catenin, and NF-κB signaling pathways (Adamyan et al., 2025; Wang et al., 2020). Furthermore, an imbalance between matrix metalloproteinases (MMPs) and tissue inhibitors of metalloproteinases (TIMPs) also accelerates extracellular matrix degradation, thereby exacerbating epithelial damage (Barbe et al., 2020; Wu et al., 2020).

In the treatment groups, administration of *D. alata* ethanol extract showed a decreasing trend in epithelial damage scores with increasing extract dose. This effect is likely associated with flavonoid and anthocyanin contents, which can reduce oxidative stress and increase the expression of epithelial junctional proteins such as E-cadherin and claudin, thereby strengthening epithelial integrity (Feng et al., 2023; Yun et al., 2023). In addition, diosgenin is also capable of suppressing ROS formation and inhibiting MMP-9 activity, which plays an important role in extracellular matrix degradation (Hao & Gao, 2022). This finding is consistent with the study by Chen et al. (2017), which showed that administration of *D. alata* extract improved tissue histological structure and increased tight junction expression in the epithelium.

However, compared with that study, epithelial improvement in the present study appears to have been quantified more systematically through a semi-quantitative histological scoring system, although it was not supported by direct molecular expression analysis. This difference may be influenced by variations in the animal model, extract dose, and assessment parameters used. Nevertheless, this study did not directly evaluate fertility-related outcomes such as ovulation, fertilization success, or pregnancy; therefore, the relationship between improved epithelial histology and enhanced reproductive function still requires further investigation.

CONCLUSION

Administration of purple yam (*Dioscorea alata*) tuber ethanol extract showed a tendency to improve the histological features of the ampulla of the uterine tube in a mouse model of endometriosis. The administration of *D. alata* ethanol extract was presumed to be associated with reduced inflammatory cell infiltration, decreased fibrosis severity, and improved epithelial damage. Improvements in these three parameters appeared to increase with escalating extract doses, with the most optimal effect observed at a dose of 500 mg/kg body weight. These findings suggest that *D. alata* ethanol extract has potential as a natural anti-inflammatory and antifibrotic agent that may contribute to the repair of tissue damage in endometriosis.

RECOMMENDATION

Future studies are recommended to use a wider range of extract doses to determine the minimum effective dose while also evaluating the potential toxic effects of higher-dose administration. In addition, further investigations should be conducted using a molecular biomarker analysis approach, such as transforming growth factor-β (TGF-β), nuclear factor kappa-B (NF-κB), alpha-smooth muscle actin (α-SMA), interleukin-6 (IL-6), and interleukin-1β (IL-1β). The use of these biomarkers is expected to provide a more comprehensive explanation of the anti-inflammatory and antifibrotic mechanisms of *D. alata* extract in repairing tissue damage associated with endometriosis.

ACKNOWLEDGMENT

The authors would like to thank the Institute for Research and Innovation, Universitas Muhammadiyah Yogyakarta, for partially funding this study. The authors also express their gratitude to all parties who provided facilities and assistance throughout the research and data analysis processes, which enabled this study to be completed successfully.

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