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Dioscorea alata enhances on the corpus luteum histology in an endometriosis mouse model

Sri Nabawiyati Nurul Makiyah[1], Suci Nur Rahmawati[2]

[1]Department of Histology, Faculty Medicine and Health Sciences, Universitas Muhammadiyah Yogyakarta, Indonesia

[2]Faculty of Medicine and Health Sciences, Universitas Muhammadiyah Yogyakarta, Indonesia

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ABSTRACT

Endometriosis is a chronic inflammatory disease that causes ovarian damage and infertility. *Dioscorea alata* contains anti-inflammatory and antioxidant agents. This study examined the effect of ethanol extract of *Dioscorea alata* (EEDA) on the histology of corpus luteum in an endometriosis mouse model. This research is a quasi-experimental with a post-test-only controlled group design. Twenty-four mice were divided into six groups: control (C), negative control (NC) induced endometriosis model, positive control (PC) induced endometriosis model and letrozole, and three treatment groups induced endometriosis model and EEDA 50, 250, and 500 mg/kg body weight (T1, T2, T3). The number and diameter of corpus luteum analyzed with Kruskal-Wallis test, One-way ANOVA, and Duncan's test. The number of corpus luteum decreased in negative control group and increased significantly in the treatment groups (P = 0.038). The diameter of corpus luteum decreased in the negative control group and increased non-significantly in the treatment groups (P = 0.206). The conclusions of this research prove that EEDA has a positive effect both the number and diameter of corpus luteum in an endometriosis mouse model.

Corresponding Author:

Sri Nabawiyati Nurul Makiyah,
Department of Histology,
Universitas Muhammadiyah Yogyakarta,
Jl. Brawijaya, Geblangan, Tamantirto, Kasihan, Bantul, Yogyakarta, 55183, Indonesia
Email: nurul.makiyah@umy.ac.id

INTRODUCTION

Endometriosis is an estrogen dependent disease that characterized by abnormal endometrial tissue outside uterus (Herrera et al., 2024). Endometriosis affects 10% of women of reproductive age (World Health Organization (WHO), 2025). Infertility affects fifty percent of women (Shah et al., 2024). Endometriosis impacts work productivity and quality of life (Brahmana et al., 2023). Chronic inflammation in endometriosis can cause ovarian damage and affects corpus luteum (Hestianah et al., 2024). A reduction both the quantity and size of corpus luteum leads to a deficiency in progesterone, ultimately resulting in infertility (Ali et al., 2024). Analgesics, hormone therapy, and surgery are employed to manage endometriosis (Herrera et al., 2024; Momenimovahed et al., 2024; Peitsidis et al., 2023). Long-term treatment of endometriosis presents new challenges in terms of

complications, recurrence, adverse effects, and high cost of treatment (Barnard et al., 2023; Brahmana et al., 2023). Research has indicated the potential efficacy of medical plants in the treatment of endometriosis.

Silambarasan et al. (2025) exploring the molecular mechanism of *Dioscorea alata* for the treatment of menstrual disorders using network pharmacology and molecular docking. *Dioscorea alata* has anti-inflamatory and antioxidant agent that can be potentially treatment for endometriosis. Research by Wang et al. (2023) shows that *Dioscorea alata* contains diosgenin as anti-inflammatories. Diosgenin can inhibit inflammation by suppressing nuclear factor kappaB (NF kB) pathway, proinflammatory cytokines such as tumor necrosis factor alpha (TNF-α), and cyclooxygenase 2 (COX-2) (Cong et al., 2024). Research by Makiyah & Zahra (2025) shows that *Dioscorea alata* contains flavonoids as antioxidants. Flavonoids may repair ovarian damage associated with endometriosis (Latief et al., 2021). This study examined the effect of ethanol extract of *Dioscorea alata* (EEDA) on the histology of corpus luteum in endometriosis model mouse.

RESEARCH METHOD

The study was a quasi-experimental with a post-test only controlled group design.This study utilized female BaLB/c mouse (*Mus musculus*), aged 2 months, weighing 20-40 grams, and healthy. The mice were acclimatized for seven days before treatment to adapt laboratory conditions. The number of research subject was calculated using the Federer formula, resulting in 6 each groups with a total of 24 mouse. There are six groups in this study. The control group (C) was only given 0.5% CMC-Na. The negative control group (NC) was induced with 0.1 ml/20 gBW of chocolate cyst pulp. The positive control group (PC) was induced with 0.1 ml/20 gBW of chocolate cyst pulp and given 0.2 mg/kgBW of letrozole. There are 3 treatment groups, namely treatment group 1 (T1), treatment group 2 (T2), and treatment group 3 (T3) were induced with 0.1 ml/20 gBW of chocolate cyst pulp and then given EEDA at doses of 50 mg/kg, 250 mg/kg, and 500 mg/kg.

The choice of dosage was based on a study by Makiyah *et al*. (2026) which demonstrated that EEDA at doses of 50 mg/kg, 250 mg/kg, and 500 mg/kg improves the histological appearance of the ampulla of the uterine tubeina mouse model of endometriosis.

Mouse were induced endometriosis models with 0.1 ml/20 gBW of chocolate cyst pulp on day 1 and left for 14 days (Brahmana et al., 2025). Synchronization of the estrous cycle is performed by administering an injection of ethinyl estradiol 0.05 ml/40 g of body weight on the fifth day. On day 16-29, the mouse were given the appropiate tretament group. On day 30, the mouse were termination with ketamine 0.3 mg/kgBW. Surgery was performed and the ovarium was removed. Ovarian preparations were made using paraffin block and Hematoxylin and Eosin (HE) staining.

Observation were made of the histology corpus luteum. This was indicated by number and diameter of corpus luteum (Batubara et al., 2020; Essono et al., 2020). The number of corpus luteum in mouse was performed using a binocular microscope in one field of view at 40x magnification. The diameter of corpus luteum in mouse was performed using a binocular microscope in five field of view at 100x magnification. The number of corpus luteum analyzed using Shapiro-Wilk test, Levene test, one-way ANOVA, and Duncan test. The diameter of corpus luteum analyzed using Shapiro Wilk test, Levene test, and Kruskal Wallis test. The Research Ethics Committee of the Faculty of Medicine and Health Sciences at Muhammadiyah University of Yogyakarta has approved this study by letter number 47/PSK/Akd.2024.2025/241116/FKIKUMY.

RESULTS AND DISCUSSIONS

This study examined the positive effect of ethanol extract of *Dioscorea alata* (EEDA) on the number and diameter corpus luteum in endometriosis mouse mouse. The number of corpus luteum can observed in the Figure 1.

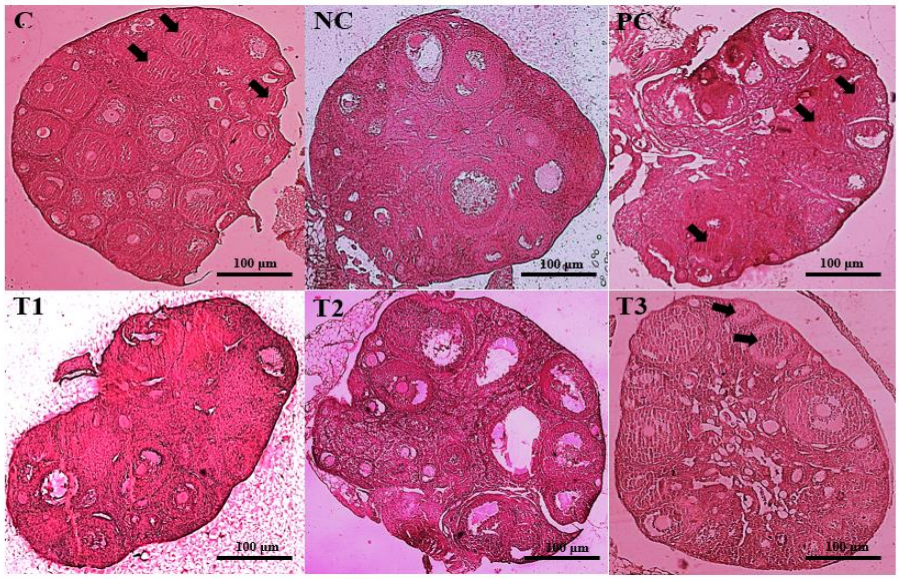

Figure 1. Histological number of corpus luteum endometriosis mouse model with HE staining at 10x magnification in the control group (C), negative control group (NC), and treatment group of EEDA at a dose of 50 mg/kg (T1), 250 mg/kg (T2), 500 mg/kg (T3). → : corpus luteum

The average number of corpus luteum are seen in Figure 2.

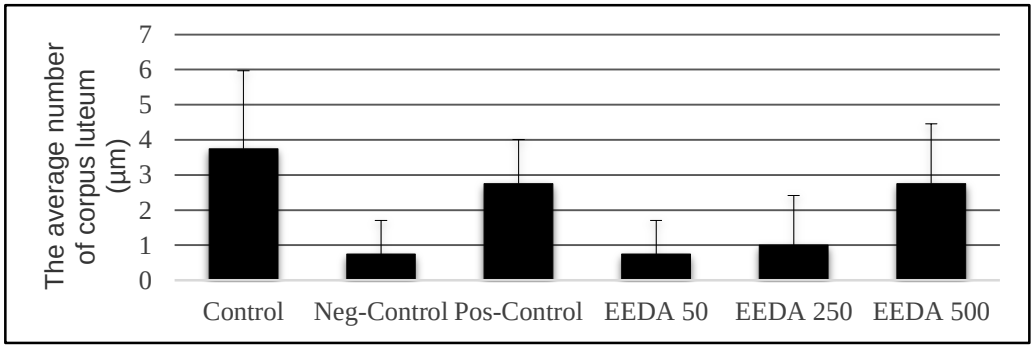

Figure 2. The number of corpus luteum endometriosis mouse model. Control group (C), negative control group (NC), and treatment group of EEDA at a dose of 50 mg/kg (T1), 250 mg/kg (T2), 500 mg/kg (T3)

Control group without any treatment had the highest number of corpus luteum. The negative control group induced endometriosis model had a number of corpus luteum comparable to EEDA 50 mg/kgBW. The positive control induced endometriosis model and lerozole had a number of corpus luteum comparable to EEDA 500 mg/kgBW. This indicate that the number of corpus luteum increased with increasing doses of EEDA.

Data analyzed using SPSS. The Shapiro-Wilk normality test showed that all groups had a normal distribution ($P > 0.05$). Levene's test showed that all groups had homogeneous variance ($P = 0.393$; $P > 0.05$). Analysis data was continued with a parametric One-way ANOVA test that showed a significant difference between groups ($P = 0.038$; $P < 0.05$). This result proved that EEDA has a positive effect on the number of corpus luteum of endometriosis model mouse.

This study in line with Essono et al. (2020) which proved that avocado seed ethanol extract increasing the number of corpus luteum in mouse with endometriosis. An increased number of corpus luteum indicates improvement in the processes of folliculogenesis and ovulation that

reducing the risk of infertility. Avocado seed ethanol extract contains diosgenin and flavonoids (Bangar et al., 2022). These bioactive compounds are also found in EEDA (Makiyah et al., 2022).

Endometriosis influenced by a number of factors including interactions between hormones, genetics, the immune system, the activation of macrophages, the action of natural killer (NK) cells and pro-inflammatory cytokines such as tumor necrosis factor alpha (TNF-α) (Shifon et al., 2025; Zhang et al., 2025). The persistent inflammation has been shown to induce oxidative stress and activate profibrotic pathways, including transforming growth factor-β (TGF-β), which has been identified as a key mediator in the deposition of collagen and the remodelling of tissue (Allaire et al., 2023). The process of chronic inflammation is the underlying cause of fibrogenesis and the remodelling of the structural composition of the reproductive organs, including the ovary.

The inflammation associated with endometriosis can affect ovarian function, thereby disrupting folliculogenesis and ovulation (Bonavina & Taylor, 2022). Disrupted ovulation results in the failure to form the corpus luteum, which plays a role in regulating hormones essential for fertilization, implantation, and pregnancy (Przygrodzka et al., 2021).

Diosgenin targets proinflammatory cytokines such as TNF-α (Cong et al., 2024). In addition, diosgenin can inhibit inflammation by suppressing the nuclear factor-kappaB (NF-kB) pathway and inhibiting the activation of cyclooxygenase 2 (COX-2) (Feng et al., 2023; Parama et al., 2020). The decreased of COX-2 expression leads to inhibition prostaglandin formation and a decrease in inflammatory response. Flavonoid has strong antioxidant activity (>70%) (Jamaludin et al., 2023). These compounds function as electron donors to neutralize reactive oxygen species (ROS). Flavonoids can increase glutathione levels and decrease malondialdehyde, which is a parameter for measuring oxidative stress. The decrease of ROS leads to improvement in the processes of folliculogenesis, ovulation, and corpus luteum formation in ovary. The histological feature diameter of corpus luteum can observed in the Figure 3.

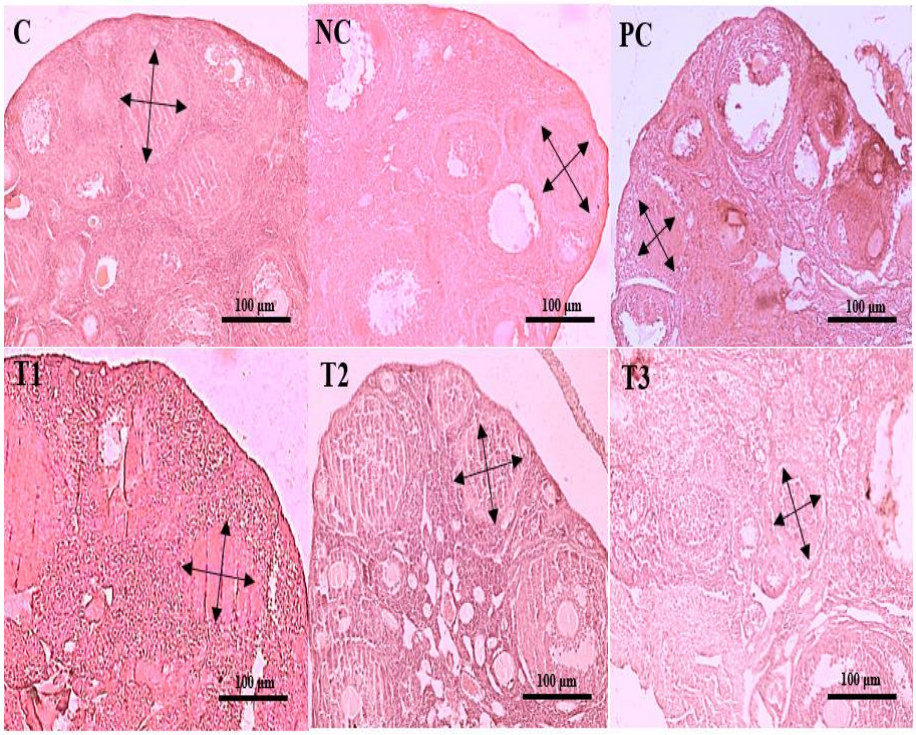

Figure 3. Histological diameter of corpus luteum endometriosis mouse model with HE staining at 10x magnification in the control group (C), negative control group (NC), and treatment group EEDA at a dose of 50 mg/kg (T1), 250 mg/kg (T2), 500 mg/kg (T3). ↔ : diameter corpus luteum

The average diameter of corpus luteum are seen in Figure 4.

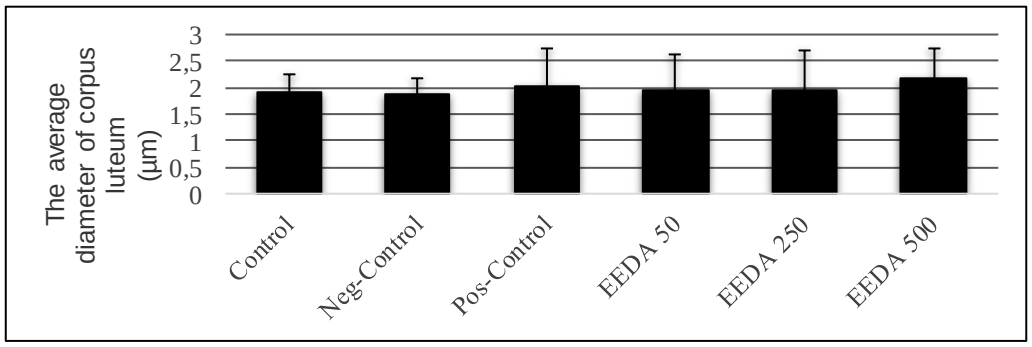

Figure 4. The diameter of corpus luteum endometriosis mouse model. Control group (C), negative control group (NC), and treatment group of EEDA at a dose of 50 mg/kg (T1), 250 mg/kg (T2), 500 mg/kg (T3).

Endometriosis mouse model that given 500 mg/kg of EEDA had the highest diameter corpus luteum. Positive control group induced endometriosis mouse model and letrozole equal with control group without any treatment. Negative control group induced endometriosis model had the lowest diameter corpus luteum. This indicate that the diameter of corpus luteum increased with increasing doses of EEDA in endometriosis mouse model.

Data analyzed using SPSS. The Shapiro-Wilk normality test showed that all groups have a normal distribution ($P > 0.05$). Levene's test shows that all groups had non-homogeneous variance ($P = 0.020$; $P < 0.05$). Kruskal–Wallis test showed no significant difference diameter of corpus luteum between groups ($P = 0.847$; $P > 0.05$). This result indicates that EEDA had no significant positive effect on the diameter corpus luteum of endometriosis mouse model.

The results of this study different from Sitepu et al. (2024) that proved nanochitosan extract of mimba leaves which contain diosgenin and flavonoid compounds, affects the diameter of the corpus luteum. The factor influencing the difference in research results is estrous cycle of mouse and differences dose of EEDA. Mouse have an estrous cycle of 4–5 days (Maulina et al., 2023). Estrous cycle have an impact on ovarian structure. Setiawan et al. (2022) stated that the relatively short estrous cycle in mouse can accelerate ovulation. Shorter duration of the estrous cycle is concomitant with a more rapid degradation of corpus luteum.

Differences dose of EEDA affect the diameter of the corpus luteum in endometriosis mouse model. Research by Batubara et al. (2020) proves that the diameter of the corpus luteum fluctuates with increasing doses of andaliman leaves which contain diosgenin and flavonoids. The dose of EEDA is directly proportional to the effectiveness of the bioactive compound. The administration of EEDA has not reached an effective dose that unable to maintain the corpus luteum has been formed. The regression of corpus luteum resulting smalest diameter of corpus luteum.

CONCLUSION

The research findings that ethanol extract of *Dioscorea alata* (EEDA) has a positive effect on the corpus luteum of endometriosis model mouse. The number of corpus luteum increased with increasing doses of EEDA. The diameter of the corpus luteum increased with high doses of EEDA.

The findings of this study suggest that *Dioscorea alata* possesses potential as an endometriosis treatment. However, the optimal dose of Dioscorea alata must be adjusted for human use to ensure greater effectiveness and avoid toxicity. The next step of this research involves evaluating the efficacy of *Dioscorea alata* in more intricate animal models, specifically non-

human primates to analyze responses closer to human. Further research is needed to observe the histological picture of the right and left ovaries in mouse with endometriosis.

Additional investigations should employ a molecular biomarker analysis technique, including nuclear factor kappa-B (NF-κB), transforming growth factor-β (TGF-β), and tumor necrosis factor alpha (TNF-α). The application of these biomarkers is anticipated to offer a more thorough elucidation of the anti-inflammatory mechanisms of EEDA in the restoration of tissue damage relating to endometriosis.

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