Journal Homepage: -www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI: 10.21474/IJAR01/23538
DOI URL: http://dx.doi.org/10.21474/IJAR01/23538

ISSN (O): 2320-5407
ISSN (P): 3107-4928

RESEARCH ARTICLE

HISTOPATHOLOGICAL TOXICITY EVALUATION OF DELTAMETHRIN ON THE INTEGRITY OF OVARIAN FOLLICLES ON MICE (*Mus musculus* L.)

Susantin Fajariyah[1], Eva Tyas Utami[1], Asmoro Lelono[1], Husnatun Nihayah[1], Purwatiningsih[1] and Rosidatus FitriaYulianti[2]

1. Lecturers of Biology Departement, The Faculty of Mathematics and Natural Sciences, University of Jember Univ ersity of Jember, Jember, Indonesia.
2. Biology undergraduate student at the Faculty of Mathematics and Natural Sciences, University of Jember.Univers ity of Jember, Jember, Indonesia.

Manuscript Info

Manuscript History
Received: 14 March 2026
Final Accepted: 16 April 2026
Published: May 2026

Key words:-
deltametrin, insecticide, follicle, ovary, mice

Abstract

Deltamethrin, a widely used pyrethroid insecticide,can induce oxidative stress through the production of reactive oxygen species (ROS), leading to cellular damage and affecting ovarian function. This study investigat ed the effects of deltamethrin exposure on the ovarian structure of female mice (*Mus musculus* L.). Fifteen mice were divided into three groups: a control group, and two treatment groups receiving deltamethr in at doses of 18 mg/kgBW and 36 mg/kgBW for 14 days. Ovarian folli cle data were analyzed using one-way ANOVA followed by Duncan's Multiple Range Test (DMRT). The results showed that deltamethrin ex posure caused ovarian structural damage, characterized by a reduction in secondary and Graafian follicles and an increase in atretic follicles. These findings indicate that deltamethrin adversely affects ovarian health in mice.

Introduction:-

Deltamethrin is a widely used pyrethroid insecticide. Exposure to deltamethrin not only affects insects but can also negatively impact non-target organisms, such as mammals. Toxic effects caused by deltamethrin exposure on non-target organisms include disruption of the nervous system and other organs. Direct contact with the skin can cause irritation, itching, rashes, and inflammation. Contact with the eyes can cause irritation, inflammation, and redness. Inhalation of deltamethrin can irritate the respiratory tract, causing coughing and difficulty breathing. Ingestion can cause digestive problems, nausea, vomiting, and diarrhea (Tomassoni et al., 2015).

Deltamethrin, once ingested, is metabolized by microsomal enzymes in the liver and broken down into metabolites. Deltamethrin metabolites can trigger the formation of reactive oxygen species (ROS). Continuous exposure to deltamethrin, when the amount of ROS in the body is too high, can lead to oxidative stress. This oxidative stress can cause damage to lipids, DNA, and proteins, and can further lead to cell death and apoptosis (Sharma et al., 2014).

Corresponding Author:-Susantin Fajariyah
Address:-Lecturers of Biology Departement, The Faculty of Mathematics and Natural Sciences, University of JemberUniversity of Jember, Jember, Indonesia.

Rehman et al. (2006) stated that oral administration of deltamethrin at doses of 5, 6, and 18 mg/kgBW for 15 days in Swiss strain mice significantly induced lipid peroxidation (LPO) in the liver. In line with this, there was a decrease in the activity of antioxidant enzymes such as glutathione peroxidase (GPx), glutathione S-transferase (GST), and catalase. Research by Otçu et al. (2023) showed that intraperitoneal administration of deltamethrin at a dose of 30 mg/kgBW in Wistar rats during the 6-21 day gestation period caused follicular degeneration, pyknotic nuclei, and hyperplasia cells in the mother rats. Another study conducted by Ali and Farzaneh (2014) showed the effect of deltamethrin at doses of 2.5, 5, and 10 mg/kgBW, causing a decrease in the number of primary and secondary follicles, an increase in the number of atretic follicles, and a significant decrease in the corpus luteum. Previous research used pure deltamethrin, so further research is needed on the effect of administering the insecticide deltamethrin on the ovarian structure of mice (*Mus musculus* L.).

Materials and Methods:-

Research materials:-

The test animals used in this study were 15 female mice (*Mus musculus*L.), aged 12 weeks with an average body weight 26.7 grams. The mice were acclimatized for 7 days (1 week) and given food and water ad libitum. The test material used was the insecticide deltamethrin® in packaging with a deltamethrin content of 25 grams/liter.

Research procedures:-

Mice were treated with deltamethrin at doses of 18 mg/kgBW, 36 mg/kgBW, and controls were given corn oil or no deltamethrin. Treatment was carried out daily for 14 days intraperitoneally with a dose of 1 ml/day. On the 15th day, the mice were anesthetized and dissected, then the ovaries were removed for histological preparations using the paraffin method and Hematoxylin-Eosin staining. The parameters observed in this study included the number of primordial, primary, secondary, Graafian, and atretic follicles. Ovarian histology slides were observed using a binocular microscope at 400x magnification.

Statistical Analysis:-

The research data was analyzed quantitatively using a One-Way ANOVA test with a 95% significance level ($\alpha = 0.05$) to evaluate the effect of the dose treatment. Duncan's test was performed to identify significant differences between treatment groups.

Results and Discussion:-

In this study, we observed the number of follicles in mice (*Mus musculus* L.) after administration of the insecticide deltamethrin. The observed follicles included primordial, primary, secondary, Graafian, and atretic follicles. The results of the calculation of the number of follicles in each treatment group are shown in Table 1. Based on one-way ANOVA analysis, the p value>0.05 was shown for the number of primordial and primary follicles, but the p value<0.05 was shown for the number of secondary, Graafian, and atretic follicles. This indicates that the treatment of deltamethrin insecticide did not significantly affect the average number of primordial and primary follicles but significantly affected the average number of secondary, Graafian, and atretic follicles. The results of further tests using DMRT (Table 1) showed that the number of secondary and atretic follicles in treatment K was not significantly different from treatment D1, but significantly different from treatment D2 and the number of Graafian follicles in treatment K was significantly different from treatments D1 and D2. The research results can also be seen in Figure 1.

Table 1 Average number of primordial, primary, secondary, Graafian and atretic follicles in mice after administration of deltamethrin insecticide

Follicle type	Average number of follicles ($\bar{x}$±SD)		
	Control (K)	6 mg/kgBW (D1)	36 mg/kg BB (D2)
Primordial	22.20±17.25[a]	13.66±12.89[a]	20.00 ±15.77[a]
Primary	39.80 ± 28.39[a]	34.33±26.86[a]	42.75±7.32[a]
Secondary	9.40 ± 2.30[a]	9.00 ± 2.00[a]	4.00 ± 1.83[b]
Graaf	3.80 ± 1.30[a]	2.00 ± 1.00[b]	1.00 ± 0.82[b]
Atretic	2.20 ± 1.48[a]	8.00 ± 8.89[a]	37.50±11.09[b]

Description: The same letter notation behind the numbers in the same row indicates no significant difference between treatment groups.

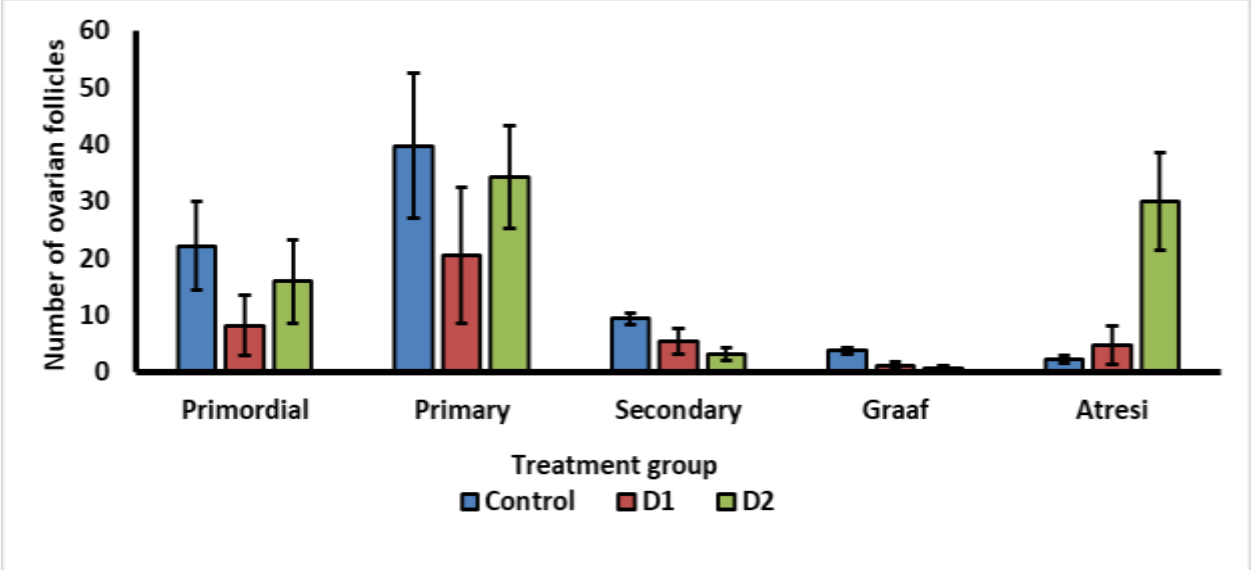

Figure 1. Number of ovarian follicle types after administration of deltamethrin insecticide

Deltamethrin that enters the body of an organism will be metabolized by the body. The main metabolic results of deltamethrin are oxidative metabolites (2', 4'- and 5-OH-deltamethrin) and metabolites of trans-methyl and ester groups (3-phenoxybenzoic acid (3-PBA) and 4'- and 2'-OH-PBA) (Lu et al., 2018). Previous research in rodents showed that deltamethrin is rapidly metabolized by esterase, which is then widely distributed by liver microsomal enzymes (Rehman et al., 2014). Deltamethrin metabolism in mice produces the main metabolites in the form of 3-PBA, 4'- and 5'-OH-deltamethrin (Shono et al., 1979). Other research added that 4-OH-deltamethrin is more toxic than deltamethrin in SH-SY5Y cells. The results of the study by Romero et al. (2012) showed that deltamethrin and its metabolites cause oxidative stress.

Oxidative stress is a condition of imbalance between oxidants and antioxidants in the body, through the excessive formation of free radicals and/or ROS, such as hydroxyl (OH), superoxide (O2-), and hydrogen peroxide (H2O2) (Lu et al., 2018). Research by Rehman et al. (2006) states that deltamethrin causes oxidative stress in the body through the formation of ROS. The results of other studies support this statement, which show that deltamethrin significantly increases ROS production in PC12 cells (Li et al., 2007).

The presence of ROS in the ovaries is found in follicular fluid. Follicular fluid contains macrophages, leukocytes, and cytokines, which are known sources of ROS. ROS present in this follicular fluid plays a role in oocyte maturation and development. This suggests that ROS at certain levels are necessary for ovarian physiological processes. However, when ROS accumulates beyond a certain level or even too high in the ovaries, it can cause a decrease in follicular fluid, inhibit meiosis, disrupt oocyte maturation, cause direct damage to the oocyte, and even lead to infertility (Ali and Farzaneh, 2014).

Several types of pyrethroids and their metabolites can disrupt the function of several hormone receptors, further affecting the endocrine system and reproductive organs. Several studies have identified deltamethrin and its metabolites as endocrine disruptors (Marettova et al., 2017). Deltamethrin is considered a compound similar to estrogen. Consequently, deltamethrin can inhibit estrogen action through direct interaction with estrogen receptors and may function as an endocrine modulator (Kim et al., 2004).

Estrogen is a steroid hormone that plays a crucial role in regulating the female reproductive system. In the ovaries, estrogen is produced by follicle cells or granulosa cells. Estrogen production in granulosa cells occurs when Luteinizing Hormone (LH) stimulates theca cells, resulting in the production of androgens.

The aromatase enzyme found in granulosa cells, along with Follicle Stimulating Hormone (FSH) stimulation, converts androgens into estrogen. Estrogen binds to estrogen receptors in target cells, such as granulosa cells and the endometrium. Activation of these receptors regulates the production of gonadotropin hormones, FSH and LH, by the anterior pituitary, and induces follicle proliferation and maturation. When deltamethrin binds to estrogen receptors, it can disrupt the regulation of FSH and LH production, as well as disrupt follicle proliferation and maturation (Marettova et al., 2017).

Based on research by Ali and Farzaneh (2014), it was shown that administration of deltamethrin at doses of 2.5, 5, and 10 mg/kgBW to mice resulted in a significant decrease in the number of primary and secondary follicles, and a significant increase in the number of atretic follicles. In this study, it was found that administration of deltamethrin at doses of 18 and 36 mg/kgBW to mice resulted in a significant decrease in the number of secondary and Graafian follicles, and a significant increase in the number of atretic follicles. This indicates that administration of deltamethrin to rodents (in this case, rats and mice) can cause a decrease in the number of follicles at several stages of development and an increase in the number of atretic follicles. The results of observations of mouse ovarian follicles after administration of deltamethrin can be seen in Figure 1.

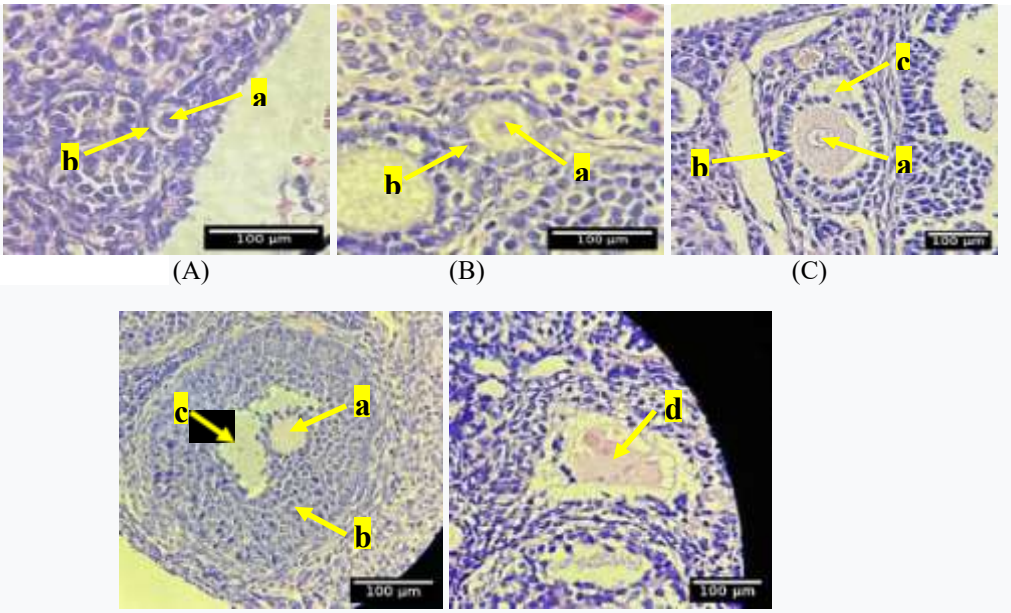

Figure 2. Mouse ovarian follicles at various stages of development (Magnification 400x)

Description: (A) Primordial follicle, (B) Primary follicle, (C) Secondary follicle, (D) Graafian follicle, (E) Atretic follicle; (a) Oocyte; (b) Follicular cell; (c) Antrum; (d) Connective tissue. Folikel ovarium mencit setelah pemberian deltametrin dapat dilihat pada Gambar 1.

The results showed that the number of secondary and Graafian follicles decreased significantly. Furthermore, follicles in the mouse ovaries experienced degeneration (atretic) at various stages of development, as indicated by a significant increase in their number. The higher the deltamethrin dose given to the mice, the more the number of secondary and Graafian follicles decreased, while conversely, the number of atretic follicles increased. The increasing number of atretic follicles with increasing deltamethrin dose can be seen in Figure 2.

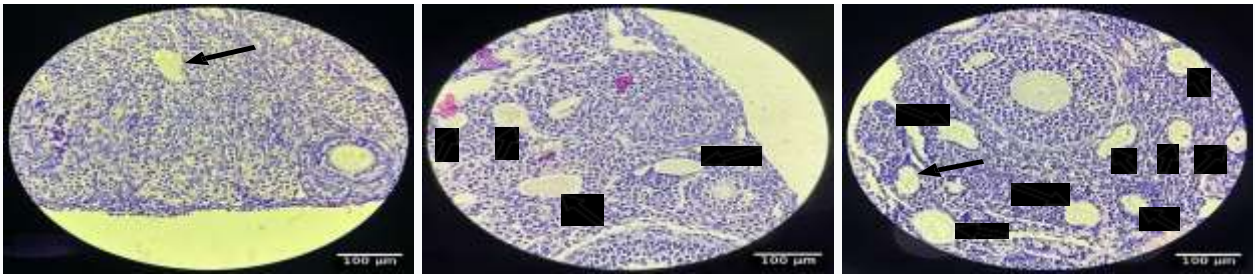

Figure 3. Atretic follicles in each treatment group (400x magnification)

Description: (A) Control; (B) 18 mg/kgBW; (C) 36 mg/kgBW; arrows indicate atretic follicles

Conclution:-

Administration of the insecticide deltamethrin at doses of 18 and 36 mg/kgBW to mice (*Mus musculus* L.) caused damage to the ovarian structure, including a decrease in the number of secondary and Graafian follicles, as well as an increase in the number of atretic follicles.

References:-

1. Ali, P.M., &Farzaneh, R. (2014). The effect of vitamin C as antioxidant on the toxic effects due to deltamethrin pesticide on morphometric and histopathological parameters of ovary in the rats. Biosci. Biotechnol. Res. Asia, 11, 959–964.
2. Kim, S.S., Kwack, S.J., Lee, R.D., Lim, K.J., Rhee, G.S., Seok, J.H., Kim, B.H.,
3. Won, Y.H., Kojima, H., Katsura, E., Takeuchi, S., Niiyama, K., & Kobayashi,
4. K. (2004). Screening for estrogen and androgen receptor activities in 200 pesticides by in vitro reporter gene assays using Chinese hamster ovary cells. Environ. Health Perspect, 112, 524–531.
5. Li, H.Y., Zhong, Y.F., Wu, S.Y., Shi, N. (2007). NF-E2 related factor 2 activation and heme oxygenase-1 induction by tert-butylhydroquinone protect against deltamethrin- mediated oxidative stress in PC12 cells. Chem. Res. Toxicol. 20, 1242-1251.
6. Lu, Q., Sun, Y., Ares, I., Anadón, A., Martínez, M., Martínez-Larrañaga, M. R., Yuan, Z., Wang, X., &Martínez, M. A. (2018). Deltamethrin toxicity: a review of oxidative stress and metabolism. Environmental Research, 1–86. https://doi.org/10.1016/j.envres.2018.12.045
7. Marettova, E., Maretta, M., &Legáth, J. (2017). Effect of pyrethroids on female genital system: Review. Animal Reproduction Science, 2017, 184, 132-138.
8. Otçu, S., Deveci, E., Özgökçe, Ç.,Gürsoy, G. T., &Tuncer, M. C. (2023). Protective effect of nebivolol on rat ovary exposed to deltamethrin toxicity. ActaCirurgicaBrasileira, 38, 1–10. https://doi.org/10.1590/acb385423
9. Rehman, H., Ali, M., Atif, F., Kaur, M., Bhatia, K., &Raisuddin, S. (2006). The modulatory effect of deltamethrin on \antioxidants in mice. ClinicaChimicaActa, 369, 61–65. https://doi.org/10.1016/j.cca.2006.01.010
10. Rehman, H., Aziz, A. T., Saggu, S., Abbas, Z. K., Mohan, A., & Ansari, A. A. (2014). Systematic review on pyrethroid toxicity with special reference to deltamethrin. Journal of Entomology and Zoology Studies, 2(6), 60–70.
11. Rehman, H., Aziz, A. T., Saggu, S., Vanwert, A. L., Zidan, N., &Saggu, S. (2017). Additive toxic effect of deltamethrin and cadmium on hepatic, hematological, and immunological parameters in mice. Toxicology and Industrial Health, 1–8. https://doi.org/10.1177/0748233716684710
12. Romero, A., Ramos, E., Castellano, V., Martinez, M.A., Ares, I., Martinez, M., Martinez- Larranaga, M.R., &Anadón, A. (2012). Cytotoxicity induced bdeltamethrin and its metabolites in SH-SY5Y cells can be differentially prevented by selected antioxidants. Toxicol. In Vitro, 26, 823-830.
13. Sharma, P., R.Singh dan M.Jan. 2014. Dose-dependent effect of deltamethrin in testis, liver and kidney of wistar rat. Toxicology International. 21(2), 131-139.
14. Shono, T., Ohsawa, K., Casida, J.E.. (1979). Metabolism of trans-permethrin and cis- permethrin, trans-cypermethrin, and cis-cypermethrin, and decamethrin by microsomal-enzymes. J. Agric. Food Chem, 27, 316-325.
15. Tomassoni, A.J., French, R.N., & Walter, F.G. (2015). Toxic industrial chemicals and chemical weapons: exposure, identification, and management by syndrome. Emergency Medicine Clinics, 33(1), 13-36.