Available online on 15.11.2026 at http://jddtonline.info

Journal of Drug Delivery and Therapeutics

Open Access to Pharmaceutical and Medical Research

Copyright © 2026 The Author(s): This is an open-access article distributed under the terms of the CC BY-NC 4.0 which permits unrestricted use, distribution, and reproduction in any medium for non-commercial use provided the original author and source are credited

Open Access Full Text Article

Research Article

Aloe vera Attenuates Cisplatin-Induced Histological Injury in Rat Ovaries

Ceren Erantepli [1], Cenap Ekinci *[1], Fırat Aşır [1]

[1] Department of Histology and Embryology, Medical Faculty, Dicle University, Diyarbakır, Turkey

Article Info:

Article History:

Received 13 Aug 2026
Reviewed 19 Sep 2026
Accepted 15 Oct 2026
Published 15 Nov 2026

Cite this article as:

Erantepli C, Ekinci C, Aşır F, Aloe vera Attenuates Cisplatin-Induced Histological Injury in Rat Ovaries, Journal of Drug Delivery and Therapeutics. 2026; 16(11):14-18 *DOI:* https://doi.org/10.22270/jddt.v16i11.8046

For Correspondence:

Cenap Ekinci, Department of Histology and Embryology, Medical Faculty, Dicle University, Diyarbakır, Turkey

Abstract

Objective: To evaluate the histological effects of Aloe vera on cisplatin-induced ovarian injury in rats. **Materials and Methods:** Thirty-two female Sprague–Dawley rats were randomly allocated to four groups of eight: sham control, cisplatin, Aloe vera, and cisplatin plus Aloe vera. Cisplatin was administered as a single intraperitoneal dose of 7.5 mg/kg, while Aloe vera was administered orally at 300 mg/kg/day for seven days. At the end of the experimental period, ovarian tissues were collected, processed for paraffin embedding, and stained with hematoxylin and eosin. Ovarian architecture, follicular and oocyte morphology, surface epithelial integrity, and stromal and vascular changes were evaluated qualitatively. **Results:** The sham control and Aloe vera groups exhibited generally preserved ovarian architecture, with normal follicular morphology and a regular surface epithelium. Cisplatin administration was associated with marked follicular degeneration, epithelial irregularity and focal cell loss, oocyte nuclear pyknosis and cytoplasmic vacuolization, stromal edema, vascular congestion, and perifollicular hemorrhage. The cisplatin plus Aloe vera group showed better preserved epithelial, follicular, and oocyte morphology, with less pronounced stromal edema and vascular congestion. However, degenerative changes persisted in some follicles. **Conclusion:** Aloe vera administration was associated with partial attenuation of cisplatin-induced ovarian histological injury in this short-term rat model. These qualitative findings suggest a potential tissue-protective effect; quantitative histological, molecular, and functional assessments are needed to establish the extent of protection and its relevance to reproductive function.

Keywords: Aloe vera; cisplatin; ovarian injury; histopathology; rat.

INTRODUCTION

Cisplatin is widely used in cancer treatment, but its effects on healthy tissues remain a concern. For patients of reproductive age, ovarian injury is particularly relevant because damage to developing follicles and their supporting cells may affect future ovarian function[1]. Experimental studies have shown that cisplatin exposure can cause follicular loss and granulosa cell apoptosis[2, 3]. These findings have prompted investigation of interventions that might reduce ovarian injury during treatment.

Cisplatin-induced ovarian damage involves more than one cellular process. Alongside its DNA-damaging action, experimental work has implicated oxidative stress, disturbances in cellular stress responses, and apoptosis in follicular injury[4]. Histological examination provides a means of assessing the resulting changes in ovarian structure, including follicular degeneration, oocyte abnormalities, and alterations in the stroma and vasculature[5, 6]. However, tissue morphology alone cannot identify which molecular pathways are responsible for the observed damage.

Aloe vera has attracted interest as a potential tissue protective agent because its preparations contain a range of biologically active compounds[7]. In rat models of cisplatin toxicity affecting the testis and hippocampus, *Aloe vera* administration has been associated with improvements in tissue morphology and measures related to oxidative stress or apoptosis[8]. These findings provide a rationale for examining its effects in the ovary, while differences between organs and experimental protocols limit direct extrapolation.

Previous research has also examined the effects of *Aloe vera* on rat ovarian morphology[9]. Nevertheless, whether *Aloe vera* is associated with preservation of ovarian architecture after cisplatin exposure requires assessment within a cisplatin-induced injury model. Comparing untreated, *Aloe vera*-treated, cisplatin-treated, and combined-treatment groups allows changes associated with cisplatin exposure to be considered alongside the appearance of ovarian tissue after *Aloe vera* administration alone.

This study aimed to evaluate the histological effects of *Aloe vera* in rats with cisplatin-induced ovarian injury. Hematoxylin and eosin-stained ovarian sections were examined for changes in follicular and oocyte morphology, the ovarian surface epithelium, stroma, and blood vessels. We hypothesized that ovarian tissue from rats receiving both cisplatin and *Aloe vera* would show less conspicuous structural injury than tissue from rats receiving cisplatin alone.

MATERIALS AND METHODS

Animals and experimental design

The study protocol specified 32 female Sprague–Dawley rats, aged 10–12 weeks and weighing 240–270 g. Following a seven day acclimatization period, the animals were randomly allocated to four groups of eight. They were housed at 23 ± 2 °C under a 12 h light/12 h dark cycle, with free access to food and water. The experimental period was seven days. The protocol also specified monitoring of the estrous cycle by vaginal cytology.

The groups were defined as follows: (1) sham control, receiving standard care without an experimental agent; (2) cisplatin, receiving a single intraperitoneal dose of 7.5 mg/kg; (3) *Aloe vera*, receiving 300 mg/kg/day orally for seven days; and (4) cisplatin plus *Aloe vera*, receiving a single intraperitoneal dose of cisplatin at 7.5 mg/kg followed by oral *Aloe vera* at 300 mg/kg/day for seven days. The protocol described preparation of an ethanolic extract from *Aloe vera* leaf gel, followed by dissolution in sterile water before administration.

Tissue collection and histological examination

At the end of the experimental period, the protocol specified anesthesia with ketamine hydrochloride (90 mg/kg) and xylazine (8 mg/kg), followed by exsanguination and ovarian tissue collection. Ovarian specimens were fixed in zinc formalin, dehydrated through graded alcohols, embedded in paraffin, and sectioned at 5 µm [10, 11]. Sections were stained with hematoxylin and eosin and examined using a Zeiss Imager A2 light microscope [12].

The present report describes the available qualitative histological findings. Ovarian architecture, follicular and oocyte morphology, the ovarian surface epithelium, stromal edema, vascular congestion, and hemorrhage were assessed descriptively. No quantitative histopathological scores or follicle counts were available for analysis in the supplied results.

RESULTS

Control group findings

Ovarian tissue from the sham group exhibited normal histological architecture. The cortex and medulla were preserved, and follicles at different stages of development showed normal morphology. The ovarian surface epithelium was regular, with an intact basement membrane. Healthy follicles (f), morphologically normal oocytes (ok), distinct corpora lutea (cl), and normal stromal tissue (★) containing capillaries (*) were observed.

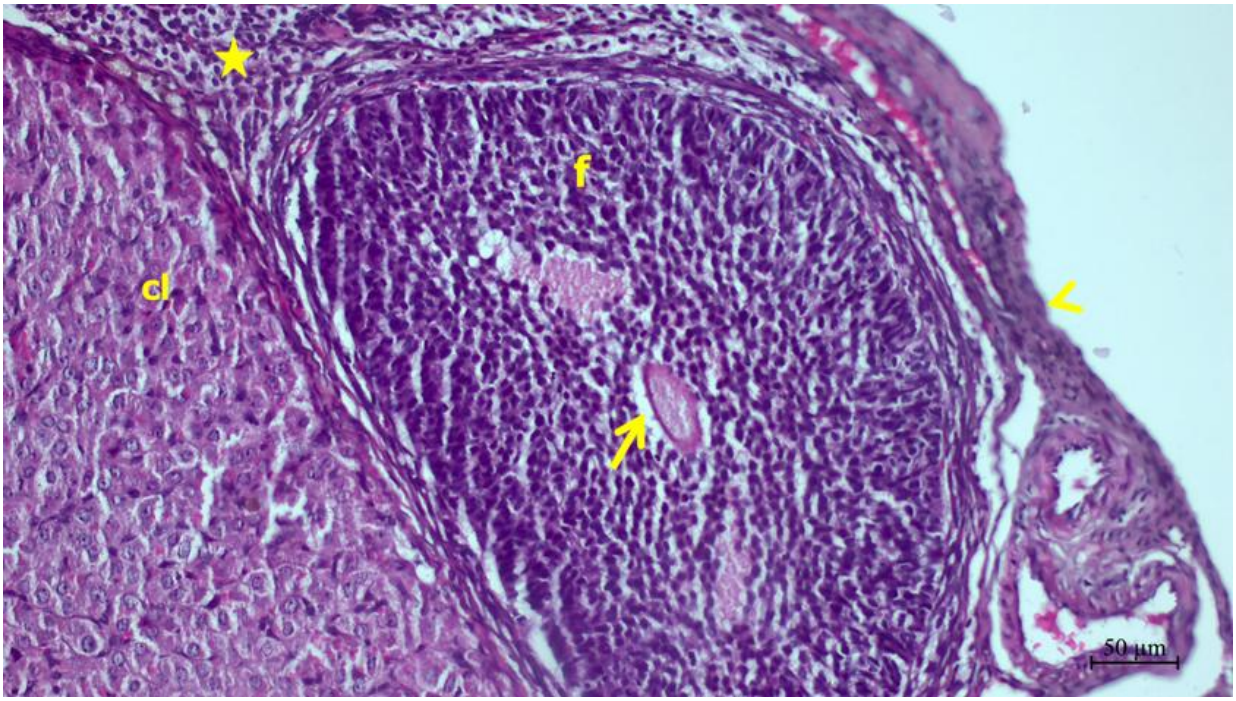


Figure 1. Light micrograph of hematoxylin and eosin (H&E)-stained ovarian tissue from the sham group. Normal ovarian architecture is evident, including a regular ovarian surface epithelium (arrowhead), healthy follicles (f), an oocyte (ok), a corpus luteum (cl), and normal stroma (★) with capillaries (*). Scale bar = 50 µm.

Aloe vera group findings

In the *Aloe vera* group, overall tissue integrity was preserved, as in the sham group. The ovarian surface epithelium was regular, and the follicles retained normal morphology. Corpora lutea appeared slightly more numerous, with more prominent stromal vascularity and well-preserved cellular morphology. Overall, the ovarian tissue maintained a physiological appearance, with no evident histological signs of injury associated with *Aloe vera* administration.

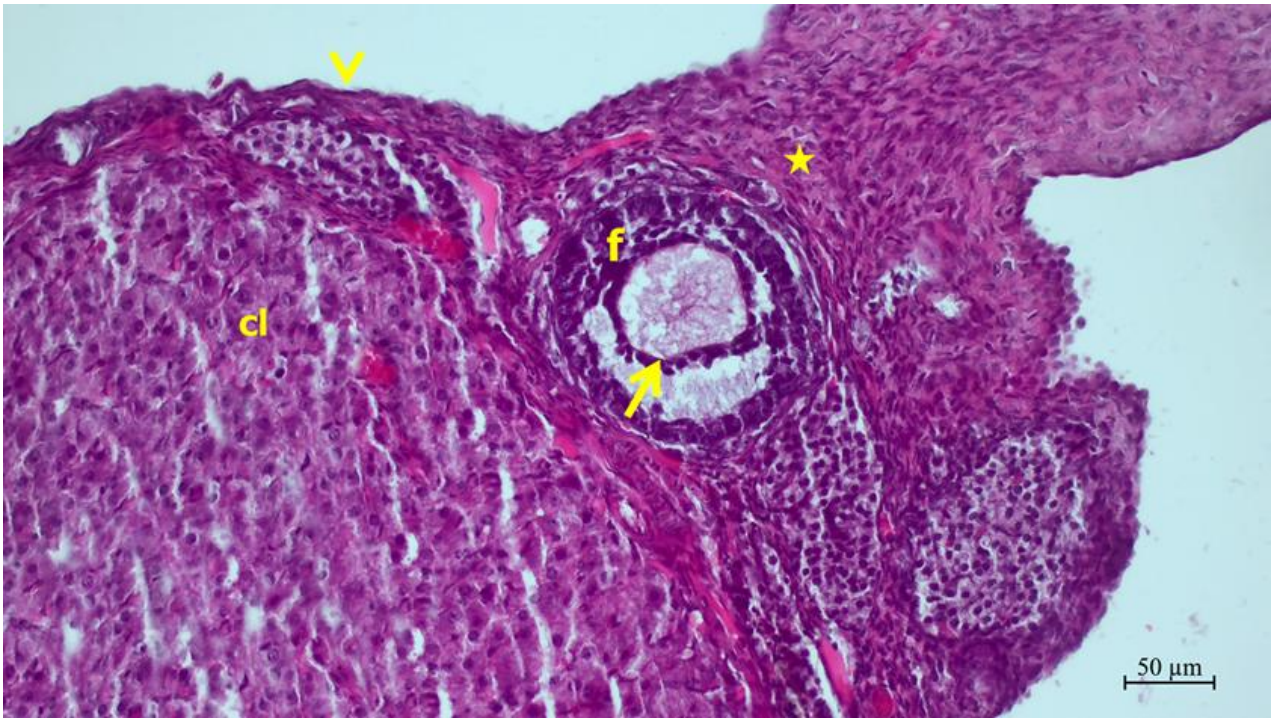


Figure 2. Light micrograph of hematoxylin and eosin (H&E)-stained ovarian tissue from the *Aloe vera* group. Tissue integrity is preserved, and the follicles and corpora lutea retain a physiological appearance. Scale bar = 50 µm.

Cisplatin group findings

Marked histopathological injury was observed in the cisplatin group. The follicles showed degenerative changes, while the ovarian surface epithelium exhibited irregularity and focal cell loss (arrowhead). Pronounced edema and congestion were present in the stroma (★). Oocytes (ok) showed pyknotic nuclei and cytoplasmic vacuolization, and areas of hemorrhage were observed around the follicles. Stromal capillaries (*) were dilated and congested. Together, these findings indicate follicular, vascular, and stromal injury following cisplatin administration

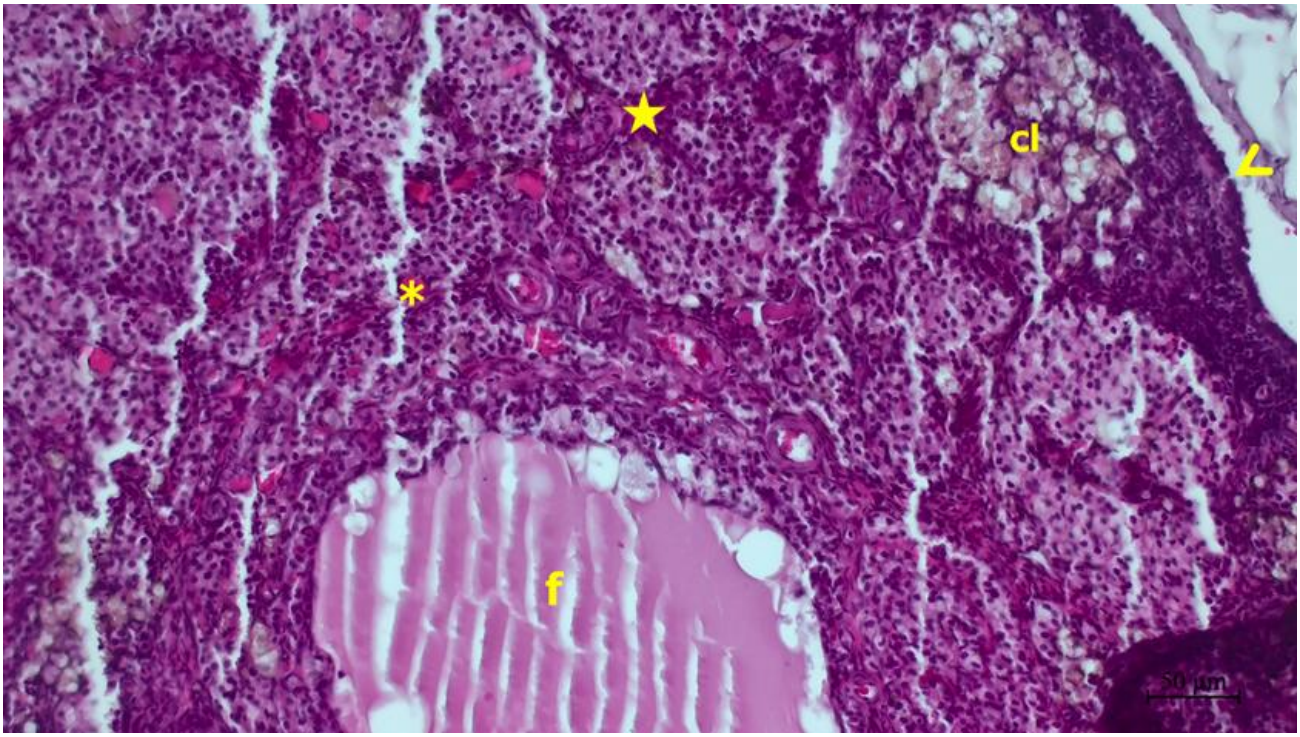


Figure 3. Light micrograph of hematoxylin and eosin (H&E)-stained ovarian tissue from the cisplatin group. Follicular degeneration (f), irregularity of the ovarian surface epithelium (arrowhead), oocytes (ok) with pyknotic nuclei and cytoplasmic vacuolization, stromal edema (★), vascular congestion (*), and hemorrhage are observed. Scale bar = 50 µm.

Cisplatin + *Aloe vera* group findings

Ovarian tissue from the cisplatin + *Aloe vera* group showed less histological injury than tissue from the cisplatin group. The ovarian surface epithelium appeared more regular. Although degeneration persisted in some follicles, most retained their normal morphology. Stromal edema and vascular congestion were less pronounced. The corpora lutea (cl) and oocytes (ok) showed better preserved morphology, while capillaries (*) appeared more regular and inflammatory cell infiltration in the surrounding tissue was minimal. These observations suggest that *Aloe vera* attenuated cisplatin-induced ovarian injury at the histological level.

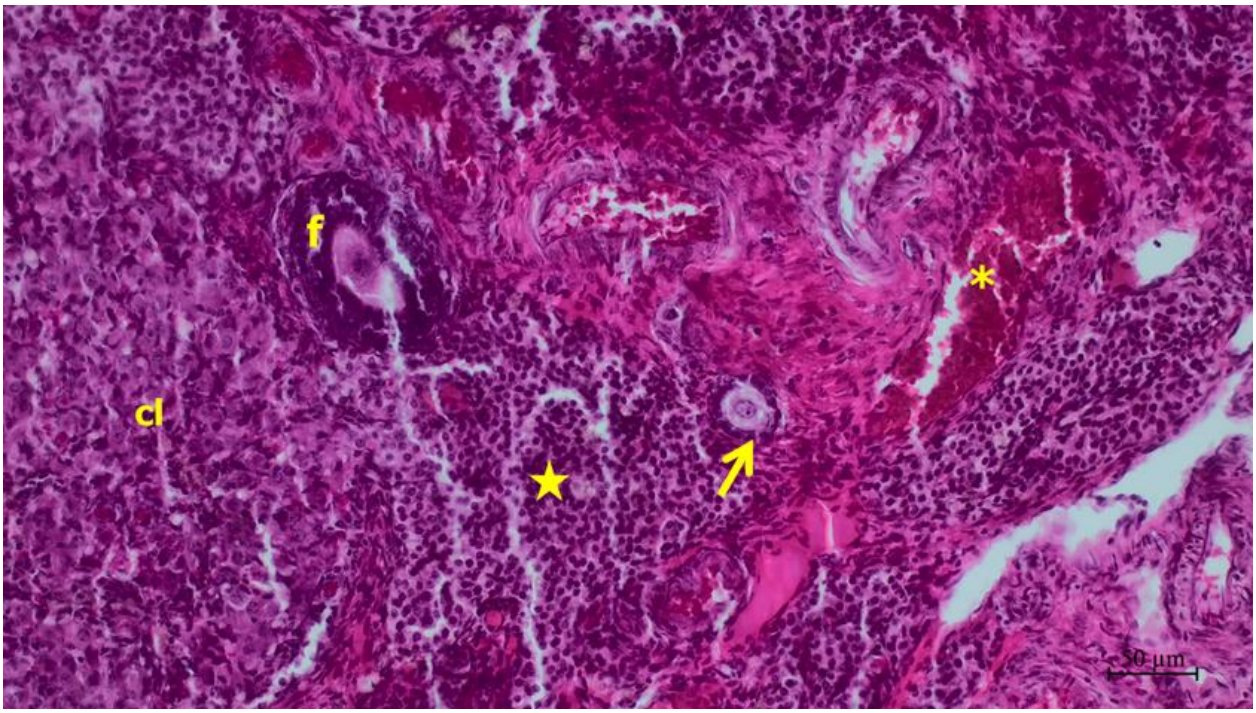


Figure 4. Light micrograph of hematoxylin and eosin (H&E)-stained ovarian tissue from the cisplatin + *Aloe vera* group. Cisplatin-associated tissue injury appears reduced, with partial preservation of the ovarian surface epithelium and better preserved follicular and corpus luteum (cl) morphology. Scale bar = 50 µm.

DISCUSSION

The principal finding of this study is that ovarian sections from the cisplatin plus *Aloe vera* group showed less conspicuous structural injury than those from the cisplatin group. Cisplatin exposure was associated with follicular degeneration, oocyte abnormalities, stromal edema, congestion, and hemorrhage. In the combined treatment group, much of the ovarian architecture appeared preserved, although some follicular degeneration persisted. The findings therefore support a **partial histological attenuation** of injury within this seven day experimental model, rather than complete restoration of normal ovarian morphology[13].

The changes observed after cisplatin exposure are broadly consistent with experimental evidence that cisplatin can injure ovarian follicles and promote granulosa cell death[14]. A previous rat study likewise reported ovarian inflammation, congestion, and hemorrhage following cisplatin administration. These comparisons provide context for the present morphological observations; the underlying cellular events cannot be determined from H&E staining alone.

The appearance of the combined treatment group is also compatible with the possibility that *Aloe vera* limits some consequences of cisplatin exposure. Experimental studies in rat testicular and hippocampal tissues have reported protective effects of *Aloe vera* alongside changes in oxidative stress or apoptosis related measures[8, 9]. Those findings offer possible directions for further investigation, but they do not demonstrate that the same mechanisms operated in the ovaries examined here. The planned malondialdehyde, caspase-3, and BCL-2 assessments cannot be interpreted until their results are available.

The *Aloe vera* only group retained generally normal ovarian architecture. Although corpora lutea and stromal vessels appeared prominent in the supplied description, their number or density was not quantified. Moreover, ovarian morphology varies across the estrous cycle[15]. The available qualitative findings therefore do not establish that *Aloe vera* increased corpus luteum formation, stimulated follicular development, or altered ovarian function.

This study has several limitations. The supplied results consist of qualitative observations from a single endpoint; they do not include blinded histological scores, follicle counts, hormone measurements, fertility outcomes, or numerical comparisons. Consequently, the magnitude and statistical certainty of the apparent

improvement cannot be assessed. The short observation period also prevents conclusions about sustained preservation of follicles or reproductive capacity. Finally, protection of ovarian tissue in a rat model would not, by itself, establish the safety or effectiveness of *Aloe vera* during anticancer treatment.

CONCLUSION

In this experimental model, cisplatin exposure was associated with substantial ovarian histological injury, whereas the cisplatin plus *Aloe vera* group showed better preserved tissue architecture and less apparent stromal and vascular damage. These qualitative findings suggest that *Aloe vera* may attenuate cisplatin associated ovarian injury. Quantitative histological, molecular, and functional results are needed before a protective mechanism or benefit for fertility can be established.

Acknowledgements: This study was part of doctoral thesis of Ceren Erantepli at department of Histology and Embryology, Dicle University.

Ethical Approval: This study was approved by the Dicle University Faculty, Animal Experimentation Center, Local Ethics Committee (DÜSAM)(Approval date: 31/07/2025; Approval number: 2025/13). All procedures were conducted in accordance with the ethical standards of the institutional and national research committees.

Informed Consent: N/A

Conflict of Interest: The author declares that there is no conflict of interest regarding the publication of this thesis.

Funding: This research wasn't received any financial support.

REFERENCES

1. Spears N, Lopes F, Stefansdottir A, Rossi V, De Felici M, Anderson RA, Klinger FG. Ovarian damage from chemotherapy and current approaches to its protection. Hum Reprod Update. 2019;25(6):673-93. https://doi.org/10.1093/humupd/dmz027 PMid:31600388 PMCid:PMC6847836
2. Chatterjee R, Helal M, Mobberley M, Ryder T, Bajoria R. Impaired steroidogenesis and apoptosis of granulosa-luteal cells in primary culture induced by cis-platinum. Am J Obstet Gynecol. 2014;210(3):252.e1-7. https://doi.org/10.1016/j.ajog.2013.11.014 PMid:24215857
3. Morgan S, Lopes F, Gourley C, Anderson RA, Spears N. Cisplatin and doxorubicin induce distinct mechanisms of ovarian follicle loss; imatinib provides selective protection only against cisplatin. PLoS One. 2013;8(7):e70117. https://doi.org/10.1371/journal.pone.0070117 PMid:23922929 PMCid:PMC3726485
4. Trujillo M, Odle AK, Aykin-Burns N, Allen AR. Chemotherapy induced oxidative stress in the ovary: drug-dependent mechanisms and potential interventions. Biology of Reproduction. 2023;108(4):522-37. https://doi.org/10.1093/biolre/ioac222 PMid:36539327 PMCid:PMC10106837
5. Ayazoglu Demir E, Mentese A, Livaoglu A, Turkmen Alemdar N, Demir S. Ameliorative effect of gallic acid on cisplatin-induced ovarian toxicity in rats. Drug Chem Toxicol. 2023;46(1):97-103. https://doi.org/10.1080/01480545.2021.2011312 PMid:34886721
6. Ayazoglu Demir E, Mentese A, Kucuk H, Turkmen Alemdar N, Demir S. p-Coumaric acid alleviates cisplatin-induced ovarian toxicity in rats. J Obstet Gynaecol Res. 2022;48(2):411-9. https://doi.org/10.1111/jog.15119 PMid:34877753
7. Sánchez M, González-Burgos E, Iglesias I, Gómez-Serranillos MP. Pharmacological Update Properties of Aloe Vera and its Major Active Constituents. Molecules. 2020;25(6). https://doi.org/10.3390/molecules25061324 PMid:32183224 PMCid:PMC7144722
8. Erfani Majd N, Tabandeh MR, Hosseinifar SH, Sadeghi M. Protective Effect of Aloe vera Gel against Cisplatin-Induced Testicular Damage, Sperm Alteration and Oxidative stress in Rats. Int J Fertil Steril. 2021;15(3):210-8.
9. Erfani Majd N, Shahraki R, Tabandeh MR, Hosseinifar S. Protective effects of Aloe vera gel on cisplatin-induced oxidative stress, apoptosis and neurons structure in rat hippocampus. Vet Res Forum. 2022;13(1):111-9.
10. Yıldırım E, Aydeniz Acar GE, Türe Z, Aşır A, Aşır F, Korak T, Ege S. Investigation of M3 muscarinic acetylcholine receptor expression in placentas of smoking women. Perinatal Journal. 2025;33(2):1-8. https://doi.org/10.57239/prn.25.0332001
11. Acar GEA, Akdeniz AS, Türe Z, Aşır A, Acar M, Aşır F, et al. HOXA1 expression in placentas of woman with fetal growth restriction. Perinatal Journal. 2024;32(2):166-72.
12. Türe Z, Akdeniz AS, Acar GEA, Aşır F, Korak T, Ege S. HOXA1 Expression in preeclampsia: immunohistochemical and bioinformatic analyses. Perinatal Journal. 2025;33(1):11-7.
13. Pandir D, Kara O, Kara M. Protective effect of bilberry (Vaccinium myrtillus L.) on cisplatin induced ovarian damage in rat. Cytotechnology. 2014;66(4):677-85. https://doi.org/10.1007/s10616-013-9621-z PMid:23959170 PMCid:PMC4082771
14. Yuksel A, Bildik G, Senbabaoglu F, Akin N, Arvas M, Unal F, et al. The magnitude of gonadotoxicity of chemotherapy drugs on ovarian follicles and granulosa cells varies depending upon the category of the drugs and the type of granulosa cells. Hum Reprod. 2015;30(12):2926-35. https://doi.org/10.1093/humrep/dev256 PMid:26466914
15. Westwood FR. The Female Rat Reproductive Cycle: A Practical Histological Guide to Staging. Toxicologic Pathology. 2008;36(3):375-84. https://doi.org/10.1177/0192623308315665 PMid:18441260