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RESEARCH

Effects of carvacrol on hormonal, inflammatory, antioxidant changes, and ovarian reserve in polycystic ovary syndrome in Wistar rats

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Abstract

The study, which explored the effects of carvacrol on female reproductive health, particularly in terms of hormonal, inflammatory, antioxidant, and ovarian reserves in polycystic ovary syndrome, could significantly influence future treatments and clinical practice. The study, conducted on thirty-five female Wistar albino rats, was designed to mimic the conditions of polycystic ovary syndrome in humans. The rats were randomly assigned into five groups: control (C), vehicle (V), polycystic ovary syndrome (PCOS), carvacrol (CAR), and polycystic ovary syndrome + carvacrol (PCOS + CAR). The following practices were applied to the groups during the study. Normal saline was administered to the C group, DMSO to the V group, letrozole (1 mg/kg/day) to the PCOS group, carvacrol (20 mg/kg) to the CAR group, and letrozole and carvacrol together to the PCOS + CAR group for twenty-one days. At the end of the administration, blood, and ovarian samples were taken for hormone analysis (E_2, and AMH), inflammatory (TNF-α, IL-6), oxidant-antioxidant analysis (malondialdehyde (MDA), glutathione (GSH), glutathione peroxidase (GSH-Px), and catalase), and histopathological examinations. Ovary, and body weights were measured, and the ovary index was calculated. As a result, it was observed that carvacrol caused beneficial effects through inflammatory, and antioxidant mechanisms in PCOS.

Keywords PCOS · Carvacrol · Ovarian reserve · Antioxidant · Anti-inflammatory

Introduction

Polycystic ovary syndrome (PCOS) is a complex endocrine disorder affecting approximately 15% of women of reproductive age worldwide (March et al. 2010). Polycystic ovary syndrome is strongly associated with several health risks in women, including infertility, type 2 diabetes, psychiatric disorders, and gynaecological cancers (Xu et al. 2022). The prevalence, diagnosis, and treatment costs of PCOS place a significant economic burden on healthcare systems, with the annual healthcare costs of PCOS in the US estimated to be approximately $4.36 billion (Lizneva et al. 2016). This complexity underscores the need for further research and understanding of the disease. Although the precise cause of PCOS remains unclear, hyperandrogenism and peripheral insulin resistance, which are considered the primary clinical findings of this syndrome, provide essential clues to understanding the pathophysiology of the disease, and play a critical role in determining treatment strategies (Lizneva et al. 2016; Azziz et al. 2016). There are several different approaches to treating PCOS (Teede et al. 2011). For this purpose, lifestyle changes, pharmacological treatments, and surgical interventions can be applied when necessary (Moran et al. 2010). Pharmacological treatment of PCOS includes interventions such as oral contraceptive pills, and hormone therapy (Patel 2018; Sadeghi et al. 2022).

Carvacrol (5-isopropyl-2-methylphenol; CAR) is a phenolic monoterpene commonly found in the essential oils of the Laminaceae family, including plants from the Origanum, and Thymus genders (Somensi et al. 2019; Dinc et al. 2023). Carvacrol has various bioactive properties such as

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anti-inflammatory, antioxidant, antitumour, antibacterial, antifungal, spasmolytic, vasorelaxant, analgesic, antiparasitic, and antigenotoxic due to its rich hydroxyl groups (Suntres et al. 2015; Shoorei et al. 2019). This broad spectrum of action increases the pharmacological, and therapeutic potential of carvacrol. In the literature, carvacrol improves ovarian reserves, and functions by correcting oxidative stress, and restoring impaired inflammatory response in ovarian damage (Mahran et al. 2019; Dinc et al. 2023).

Considering the pathogenesis of PCOS, antioxidant, and anti-inflammatory therapies can be especially significant (Panti et al. 2018; Patel 2018). In this context, it was predicted that carvacrol's antioxidant, anti-inflammatory, and other bioactive properties may be effective in PCOS. For this purpose, this study investigated the effects of carvacrol treatment on oxidant-antioxidant, inflammatory, and hormonal mechanisms in PCOS.

Material and methods

Animals and study design

Animals used in the study were obtained from Hatay Mustafa Kemal University Experimental Research, and Application Centre. Animal care, and experimental protocols were performed according to the National Institutes of Health (NIH) Guide for the Care, and Use of Laboratory Animals.

Before starting the experimental practices, the animals were observed for eleven days, and then animals with regular estrous cycles were included in the study. Female Wistar albino, rats were divided into five groups with equal numbers of animals in each group randomly: Control (C), Vehicle (V), Polycystic ovary syndrome (PCOS), Carvacrol (CAR), and Polycystic ovary syndrome + Carvacrol (PCOS + CAR). The study lasted twenty-one days (Prajapati et al. 2022). A total of thirty-five animals (220–270 g) were used, with seven in each group. Normal saline was administered to the control group. Dimethyl sulphoxide (DMSO) was applied to the Vehicle group. To the PCOS group, letrozole (1 mg/kg/day/orally) was given to the animals by dissolving in DMSO. Carvacrol (20 mg/kg/day/orally) was administered to the CAR group by dissolving in DMSO. Letrozole, and carvacrol were administered to the PCOS + CAR group.

Collection of samples, ovarian weights and ovarian index

At the end of the administration, the body weights of the animals were weighed under xylazine ketamine anaesthesia. Blood samples were collected from the heart using the intracardiac method, and centrifuged at 3000 g for 5 min to collect blood serum. In addition, the ovary samples were thoroughly cleaned, and weighed (Daihan, SC210, South Korea) and expressed in mg. The ovary samples were stored at -20 °C until the relevant analyses were performed. Also, the body weight of each animal was measured, and the relative ratio of ovary weight to body weight was calculated (Prajapati et al. 2022; Peng et al. 2021).

AMH and E_2 analyses

AMH, and E_2 levels were measured in serum samples. E_2 levels were measured by electrochemuliminance immunoassay on a Siemens Health-branded device. AMH measurement was based on the antigen–antibody complex method specified by a commercial enzyme-linked immunosorbent assay (ELISA) kit (Finetest, China). The E_2 levels were expressed as pg/ml, and AMH as ng/ml.

Ovarian oxidative stress and inflammatory cytokine analyses

Ovarian samples were homogenised (IKA T18 Digital Ultra-Turrax, Germany) using Tris-buffered saline (pH 7.4), with two samples for each animal, both ovaries. The homogenate thus obtained was centrifuged at 4000 rpm for 60 min, and the supernatant was collected (Arkali et al. 2021). Malondialdehyde (MDA) was measured spectrometrically to determine the lipid peroxidation of ovarian tissue (Placer et al. 1966). Also, Glutathione (GSH), glutathione peroxidase (GSH-Px), and catalase were measured spectrometrically to analyse ovarian tissue's antioxidant systems (Sedlak & Lindsay 1968; Lawrence & Burk 1976; Aebi 1984). In addition, some of the ovarian tissue pieces were homogenised with phosphate-buffered saline (PBS), and centrifuged at 5000 g for 5 min at + 4 °C (IKA T18 Digital Ultra-Turrax, Germany) for inflammatory cytokine analysis. The supernatant was collected, and used in the related analyses. The tumor necrosis factor-alpha (TNF-α), and interleukin 6 (IL-6) were measured using the commercial enzyme-linked immunosorbent assay (ELISA) kits (Finetest, China).

Histological analysis

For histopathological analysis, ovarian tissues were fixed in 10% buffered formaldehyde solution for 72 h. The tissues were placed in cassettes, and washed in running water for 12 h. After washing, they were passed through serial alcohols (70%, 80%, 90%, 100%) for dehydration, and taken into the xylol series for transparency. After embedding in paraffin blocks, serial sections of 4–5 µm thickness were taken using a microtome (Leica RM 2125 RT). Crosman's modified triple staining technique was applied to reveal the general structure of the sections (Denk et al. 1989). The

tissue sections were analysed, evaluated, and photoed using an Olympus CX21 research microscope.

Statistical analyses

Data obtained from this study were expressed as mean ± standard error of the mean. One-way analysis of variance (ANOVA) was used to assess the difference between means followed by Turkey's multiple comparison test. Graph Pad Prism 8.01 was the statistical package used for the analysis, and p-values < 0.05 were considered statistically significant for differences in means.

Result

Ovary weight, body weight and ovarian index

The ovarian weights of all groups (C, V, PCOS, CAR, and PCOS + CAR) were 84.666 ± 1.929, 80.235 ± 1.358, 98.634 ± 1.395, 88.129 ± 1.606, 92.973 ± 2.687 mg, respectively. There was a significant difference in ovarian weights between the groups ($p < 0.001$). A statistically significant difference was observed when comparing the ovarian weights of the PCOS + CAR group with the PCOS group. The ovarian weights of the groups are shown in Fig. 1A.

The body weights of all groups (C, V, PCOS, CAR, and PCOS + CAR) were 240.000 ± 4.756, 233.571 ± 4.185, 255.000 ± 4.629, 238.571 ± 4.845, 246.429 ± 5.424 g, respectively. Compared to the vehicle group, body weight was higher in the PCOS group ($p < 0.035$). The body weights of the groups are shown in Fig. 1B.

The ovarian index (%) of all groups (C, V, PCOS, CAR, and PCOS + CAR) were 0.035 ± 0.001, 0.034 ± 0.001, 0.040 ± 0.000, 0.037 ± 0.001, 0.038 ± 0.001, respectively. There was a statistically significant difference in the ovarian indexes between the groups ($p < 0.001$). A statistically significant difference was observed when comparing the ovarian index of the PCOS + CAR group to that of the PCOS group. The ovarian index of the groups are shown in Fig. 1C.

Hormonal findings

The E_2 was 41.257 ± 0.988 in the C, 39.476 ± 1.421 in the V, 26.109 ± 1.435 in the PCOS, 43.446 ± 1.490 in the CAR, and 31.631 ± 2.314 pg/ml in the PCOS + CAR. There was a statistically significant difference in E_2 levels between the groups ($p < 0.001$). E_2 levels were found to be statistically lower in the PCOS + CAR and PCOS groups than in the C, CAR and V groups. E_2 levels are shown in Fig. 2A.

The AMH was 1.313 ± 0.058 in the C, 1.280 ± 0.060 in the V, 2.153 ± 0.065 in the PCOS, 1.260 ± 0.048 in the CAR, and 1.729 ± 0.056 ng/ml in the PCOS + CAR. AMH levels between the groups showed statistically significant differences ($p < 0.001$). AMH levels were statistically higher in PCOS + CAR, and PCOS groups than in C, CAR, and V groups. AMH levels in the PCOS + CAR group significantly differed from those in the PCOS group. AMH levels are shown in Fig. 2B.

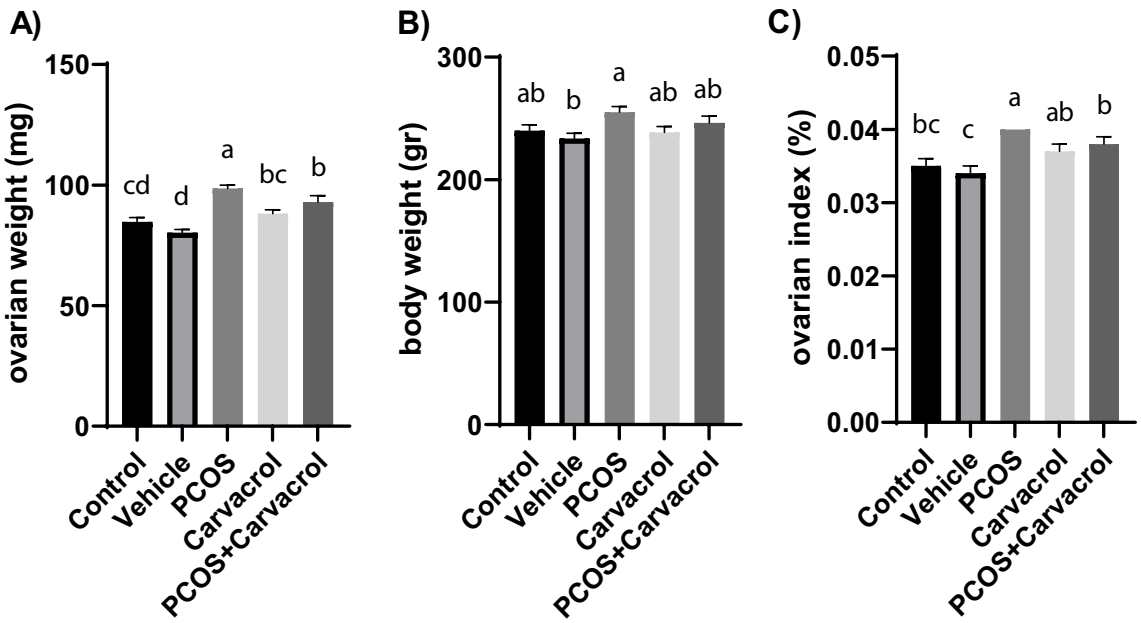

Fig. 1 **A** Ovary weight (mg). **B** Live body weight (g). **C** Ovary index (%). Values are Mean ± SEM, and the letters on the columns indicate statistical differences. Groups similar to each other have the same letter, while groups different from each other have different letters

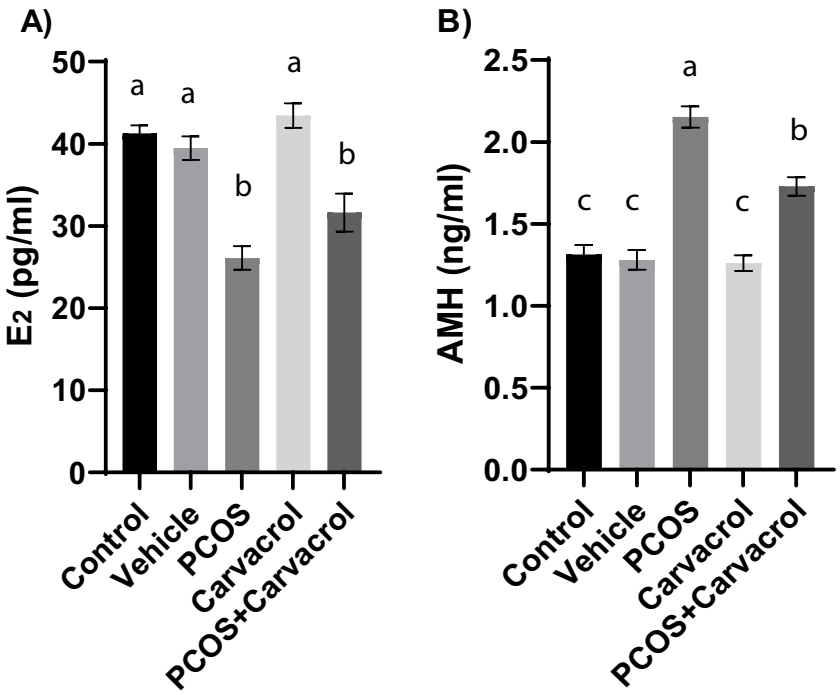

Fig. 2 **A** E_2. **B** AMH. Values are Mean ± SEM, and the letters on the columns indicate statistical differences. Groups similar to each other have the same letter, while groups different from each other have different letters

Oxidative stress parameters

The MDA level was 3.500 ± 0.136 in the C, 3.530 ± 0.110 in the V, 4.864 ± 0.205 in the PCOS, 3.609 ± 0.143 in the CAR, and 4.132 ± 0.303 in the PCOS + CAR. A statistically significant difference was observed in the MDA levels between the groups ($p < 0.001$). The MDA levels are shown in Fig. 3A.

Glutathione was 6.867 ± 0.083 in the C, 6.870 ± 0.093 in the V, 5.594 ± 0.183 in the PCOS, 6.886 ± 0.079 in the CAR, and 6.613 ± 0.133 in the PCOS + CAR. The groups had a statistically significant difference in GSH levels ($p < 0.001$). When the PCOS + CAR group GSH levels were compared with the PCOS group, it was seen that they were statistically different from each other. GSH levels are shown in Fig. 3B.

The GSH-Px was 33.864 ± 1.144 in the C, 34.293 ± 1.118 in the V, 27.216 ± 0.837 in the PCOS, 34.746 ± 2.143 in the CAR, and 33.538 ± 0.978 in the PCOS + CAR. There was a statistical difference between the GSH-Px levels between the groups ($p = 0.002$). When the GSH-Px levels of the PCOS + CAR group were compared with the PCOS group, it was seen that they were statistically different from each other. GSH-Px levels are shown in Fig. 3C.

Catalase was 33.584 ± 1.224 in the C, 34.407 ± 1.592 in the V, 25.588 ± 1.119 in the PCOS, 36.213 ± 0.744 in the CAR, and 31.694 ± 1.450 in the PCOS + CAR. The groups displayed a statistically significant difference in catalase levels ($p < 0.001$). A comparison of the catalase levels between the PCOS + CAR group, and the PCOS group revealed a statistically significant difference. Catalase levels are shown in Fig. 3D.

Inflammatory cytokines (TNF-α, and IL-6)

The TNF-α levels of the groups (C, V, PCOS, CAR, and PCOS + CAR) were 12.158 ± 0.548, 12.026 ± 0.606, 20.024 ± 0.645, 12.477 ± 0.384, 16.238 ± 0.861, respectively. There was a statistically significant difference in TNF-α levels between the groups ($p < 0.001$). Comparing the TNF-α levels of the PCOS + CAR group to the PCOS group revealed a statistically significant difference. TNF-α levels of the groups are shown in Fig. 4A.

The IL-6 levels of the groups (C, V, PCOS, CAR, and PCOS + CAR) were 7.474 ± 0.681, 7.728 ± 0.344, 12.875 ± 0.391, 6.801 ± 0.522, 9.455 ± 0.691, respectively. There was a statistically significant difference in IL-6 levels between the groups ($p < 0.001$). A comparison of the IL-6 levels in the PCOS + CAR group with those in the PCOS group showed a statistically significant difference between the two groups. IL-6 levels of the groups are shown in Fig. 4B.

Histological findings

In the histological section of the ovary obtained from the control group (C), follicles at various stages of development, corpus luteum, and germinative epithelium surrounding the organ from the outside, and tunica albuginea underneath were observed in the cortex region. Also, prominent vascular structuring in the medulla region was observed in standard histological structure (Fig. 5A). The vehicle group (V) was compared with the control, and similar histological

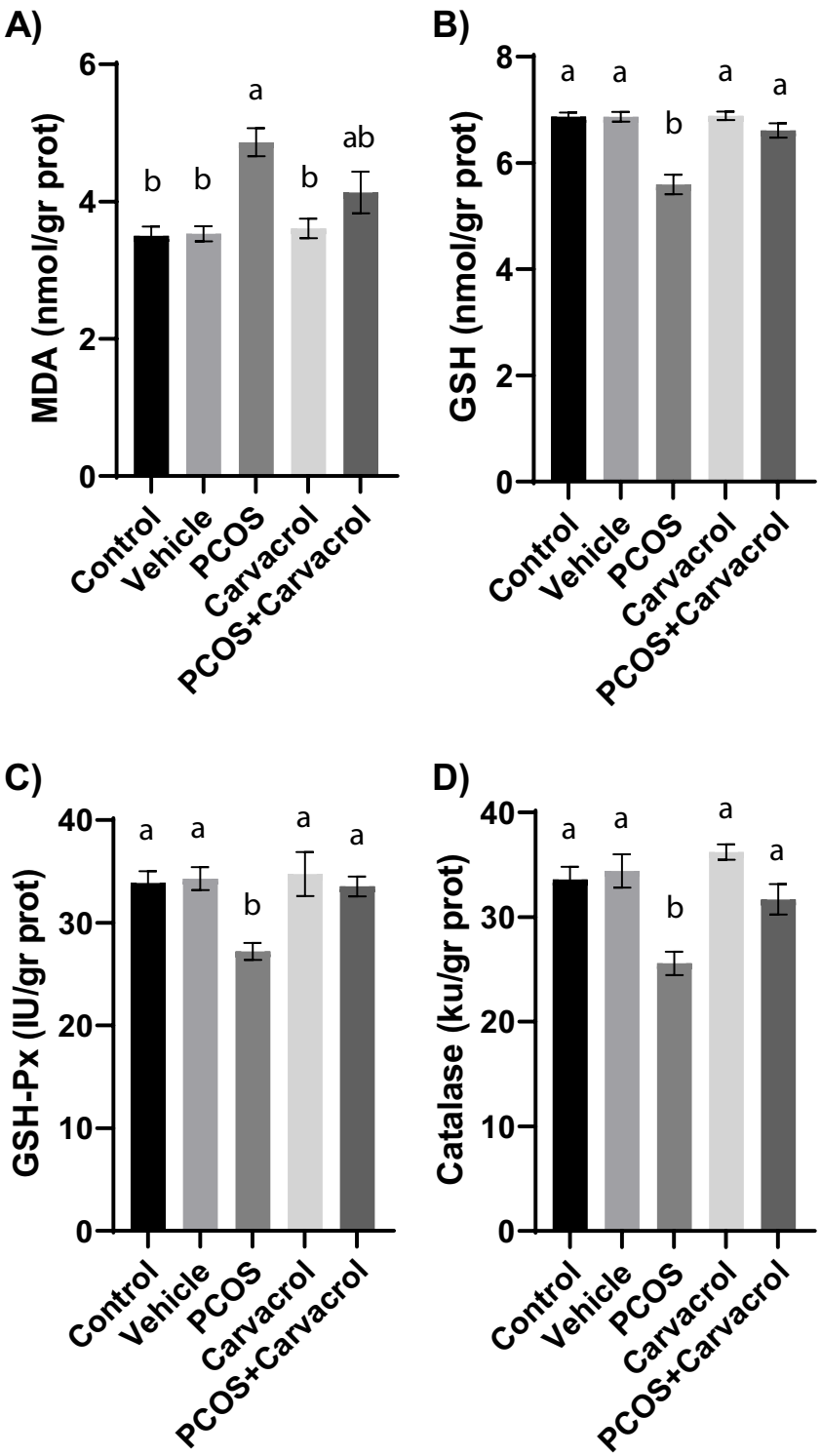

Fig. 3 **A** MDA. **B** GSH. **C** GSH-Px **D** Catalase. Values are Mean ± SEM, and the letters on the columns indicate statistical differences. Groups similar to each other have the same letter, while groups different from each other have different letters

structures were observed in the cortex, and medulla (Fig. 5B). The PCOS group was compared with the other groups; edema, and haemorrhage in the interstitial area, a decrease in the number of corpus luteum, cystic follicle formation, and thinning of the granulosa cell layer surrounding some cystic follicles were observed. Also, intense vascular dilatation was observed in both cortex, and medulla in this group, which differed from the control, vehicle, and carvacrol groups (Fig. 5C and Fig. 5D). The carvacrol-treated group (CAR) showed histological structures similar to the control group. In this group, dilatation of the vessels in the cortex region was observed, while the vessels in the

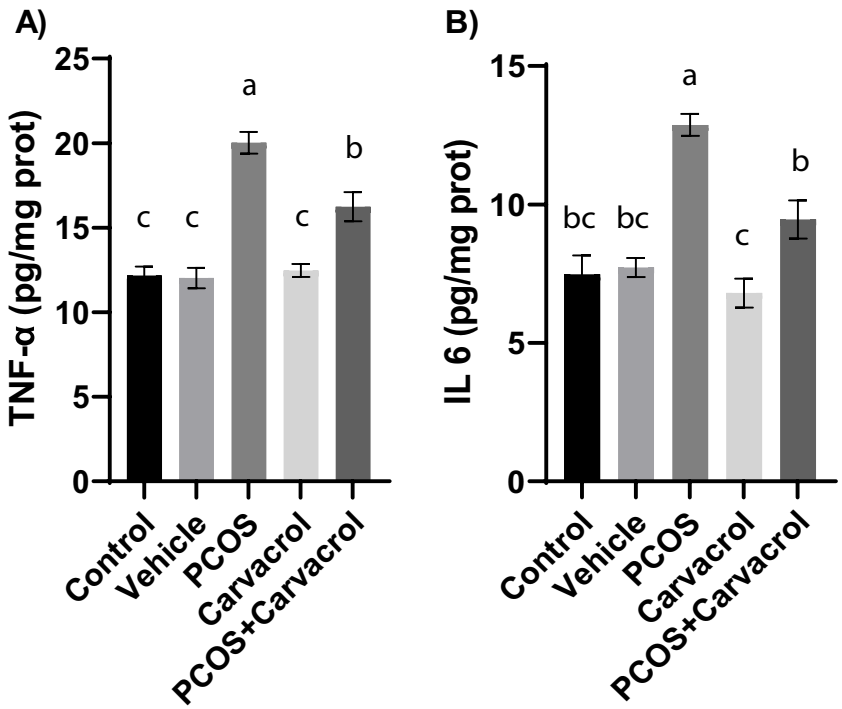

Fig. 4 **A** TNF-α. **B** IL 6. Values are Mean ± SEM, and the letters on the columns indicate statistical differences. Similar groups have the same letter, while groups that are different from each other have different letters

medulla were similar to those in the control, and vehicle group. However, no edema was observed (Fig. 5E). In the PCOS + CAR group a decrease in the dilatation intensity of the vessels in the cortex, and medulla was observed. Edema, and haemorrhage in the interstitial area were significantly reduced compared to the PCOS group. Also, the number of cystic follicles decreased, whereas the corpus luteum increased compared to the PCOS group. In addition, in the PCOS + CAR group the granulosa cell layer surrounding some cystic follicles was thinner than in the control, vehicle, and carvacrol groups, and thicker than in the PCOS group (Fig. 5F and Fig. 5G).

Ovarian tissue was evaluated histologically in terms of tissue damage, cystic follicle, hyperaemia, haemorrhage, and edema as '-: undamaged', '+: slightly damaged', '++: moderately damaged', '+++: significantly damaged' (Table 1).

Discussion

Polycystic ovary syndrome is a disease that significantly impacts female reproductive health with a range of clinical symptoms (Rudnicka et al. 2021; Xing et al. 2024). Letrozole usage causes COS-like symptoms in experimental studies (Yang et al. 2020; Prajapati et al. 2022; Namlı Kalem et al. 2023). In the present study, the PCOS model induced by letrozole was confirmed by the findings obtained. Also, letrozole administration led to statistically significant increases in ovarian weights, and index, but no statistical difference was observed between the groups in body weight. Importantly, it was observed that carvacrol caused a statistically significant decrease in letrozole-induced increased ovarian weights.

Letrozole is an aromatase enzyme inhibitor, and causes decreases in estrogen by preventing the conversion of androgens to estrogen (Guo et al. 2023). In experimental studies, decreases in estrogen are observed in PCOS induced by letrozole (Yang et al. 2020; Namlı Kalem et al. 2023; Cellat et al. 2024). Likewise, a study observed that estradiol decreased in blood samples taken on the 21st day in rats administered letrozole (Prajapati et al. 2022). In this study, similar to previous studies, letrozole administration caused a decrease in estrogen in rats. However, estrogen levels that decreased with letrozole did not return to the control group levels with carvacrol treatment.

Anti-mullerian hormone is secreted by granulosa cells, and is critical in follicle selection (Johnson 2015). Experimental studies have shown that high AMH concentrations were observed due to the formation of multiple follicles in PCOS (Patel 2018; Furat Rencber et al. 2018; Namlı Kalem et al. 2023). This study observed high AMH in the PCOS group treated with letrozole, consistent with the literature. It was also observed that carvacrol caused statistically significant decreases in AMH that increased due to letrozole.

Oxidative stress is considered an inducing factor in the pathogenesis of PCOS, and significant changes occur in the oxidant-antioxidant balance in PCOS patients (Murri et al. 2013; Zuo et al. 2016). Malondialdehyde is high in women with PCOS as an indicator of lipid peroxidation (Murri et al.

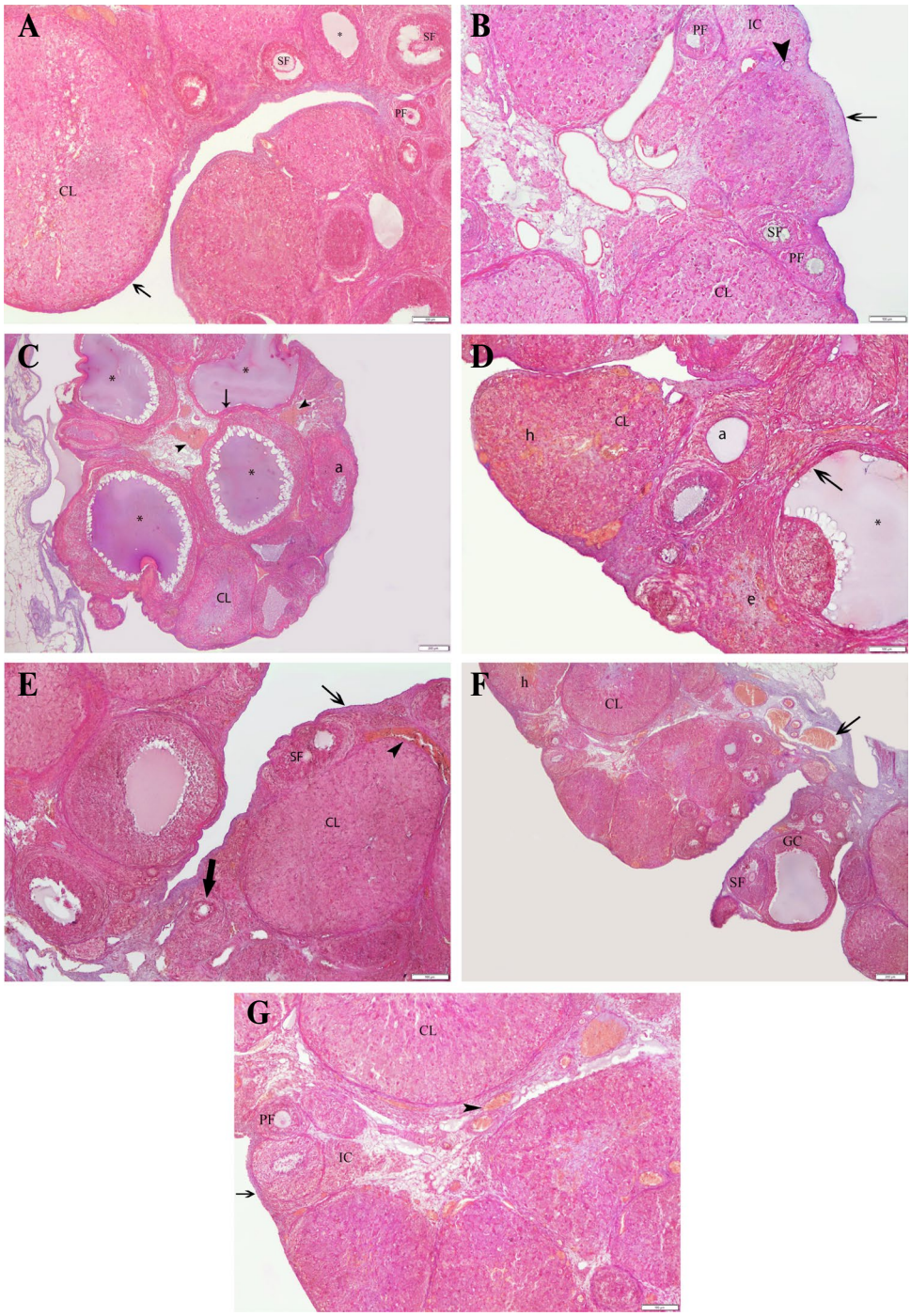

Fig. 5 **A** Control group; histological section of rat ovary. CL: Corpus Luteum, SF: Secondary Follicle, PF: Primary Follicle, Arrowhead: Germinative Epithelium, *: Atretic Follicle. Crosman's modified triple staining technique, Bar: 100 µm. **B** Vehicle group; Histological section of rat ovary. CL: Corpus Luteum, SF: Secondary Follicle, PF: Primary Follicle, IC: Interstitial cells Arrow: Germinative Epithelium, Arrowhead: Primordial Follicle. Crosman's modified triple staining technique, Bar: 100 µm. **C** PCOS group; histological section of rat ovary. CL: Corpus Luteum, Arrowhead: Vascular dilatation, Arrow: Thinned granulosa cell layer, *: Cystic follicle, a: Atretic follicle. Crosman's modified triple staining technique, Bar: 200 µm. **D** PCOS group; histological section of rat ovary. CL: Corpus Luteum, h: haemorrhage, a: Atretic follicle, e: edema, Arrow: Thinned granulosa cell layer, *: Cystic follicle. Crosman's modified triple staining technique, Bar: 100 µm. **E** Carvacrol group; histological section of rat ovary. CL: Corpus Luteum, SF: Secondary Follicle, Thick arrow: Primary Follicle, Arrow: Germinative Epithelium, Arrowhead: Vascular dilatation in the cortex. Crosman's modified triple staining technique, Bar: 100 µm. **F** PCOS + CAR group; histological section of rat ovary. CL: Corpus Luteum, SF: Secondary follicle, h: haemorrhage, GC: Granulosa cell layer in the cystic follicle, Arrow: Vascular dilatation. Crosman's modified triple staining technique, Bar: 200 µm. **G** PCOS + CAR group; histological section of rat ovary. CL: Corpus Luteum, PF: Primary follicle, Arrow: Germinative epithelium, Arrowhead: Vascular dilatation. Crosman's modified triple staining technique, Bar: 100 µm

Table 1 Histological evaluation of ovarian in the groups

	Control	Vehicle	PCOS	Carvacrol	PCOS + CAR
Tissue damage	-	-	+ +	-	+
Cystic Follicle	-	-	+ + +	-	+
Vascular Dilatation	-	-	+ + +	+	+ +
Haemorrhage	-	-	+ +	-	+
Edema	-	-	+	-	-

'-: undamaged', '+: slightly damaged', '+ +: moderately damaged', '+ + +: significantly damaged'

2013). Moreover, decreases in GSH are observed in women with PCOS (Sabuncu et al. 2001; Dincer et al. 2005). In addition, a study showing the relationship between PCOS, and oxidative stress showed increased MDA, and decreased catalase in PCOS patients (Ozer et al. 2016). In the study, similar to previous studies, it was observed that ovarian MDA was high, and GSH were low in the PCOS group. This situation can be explained as the increased oxidant status due to hormonal or biochemical changes stimulating lipid peroxidation, and reducing glutathione stores. In addition, in this study, it was observed that there were statistically significant decreases in the antioxidant enzymes GSH-Px, and catalase in the PCOS. Carvacrol has antioxidant effects due to the hydroxyl group covalently bonded to the aromatic ring in its structure both in vivo, and in vitro (Shoorei et al. 2019). Carvacrol has been reported to positively affect oocyte quality by increasing antioxidant capacity under in vitro conditions (Morais et al. 2023). Studies have reported that carvacrol in ovarian damage affects oxidative stress by increasing antioxidant enzymes, and reducing oxidant status (Sahin et al. 2022; Dinc et al. 2023). In a study, it has been reported that carvacrol in ovarian ischemia–reperfusion caused beneficial effects on histopathological changes in the ovary by reducing MDA, total oxidant capacity, and increasing GSH, and total antioxidant capacity in ovary (Sahin et al. 2022). In addition, a study has reported that antioxidant therapies significantly affect pregnancy rates in PCOS patients (Panti et al. 2018). This study observed that carvacrol administration reduced ovarian oxidative stress by increasing GSH, GSH-Px and catalase.

Inflammation is significant in the pathogenesis of PCOS, and it is stated that nuisances in ovarian activities are closely related to inflammatory processes (Gonzalez et al. 2006). Studies have shown severe increases in components of the inflammatory system in PCOS (Furat Rencber et al. 2018; Rudnicka et al. 2021). A study on rats showed that inflammatory cytokines were high in the PCOS model induced with letrozole (Areloegbe et al. 2022). In this study, similarly, increases in inflammatory cytokines were observed in the ovarian tissue in the PCOS group administered letrozole. It is stated that controlling the inflammatory status is an essential approach to the sustainable treatment of PCOS (Patel 2018). Studies have reported that carvacrol exhibits anti-inflammatory properties by reducing pro-inflammatory cytokines (Somensi et al. 2019; Dinc et al. 2023). It has been stated that carvacrol suppresses the pro-inflammatory response through different molecular pathways such as ERK1/2 and NF-kB (Somensi et al. 2019). Carvacrol used in ovarian ischemia and reperfusion was observed to cause decreases in inflammatory cytokines (Sahin et al. 2022). In another study, carvacrol used in ovarian damage was observed to cause decreases in inflammatory cytokines (Dinc et al. 2023). In this study, similar to previous studies, decreased TNF-α and IL-6, which increased with letrozole, were observed in treatment with carvacrol.

The findings obtained from the control, and vehicle groups showed similar histopathological findings to the studies conducted (Gozukara et al. 2016; Celikci et al. 2021). However, no histological study was found in the literature review examining the effect of carvacrol on the ovary in healthy individuals. In this study, unlike the control, and vehicle groups, vascular dilatation in the cortex was observed in the carvacrol group. In studies examining the histological effect of letrozole on the ovary, it was reported that, despite different dose applications, cystic follicle formation, thinning or loss of the granulosa cell layer surrounding the cystic follicle, and a significant decrease in the number of corpus luteum were detected, similar to our findings (Kafali et al. 2004; Mihanfar et al. 2021). To the best of our knowledge, the effect of carvacrol on the letrozole-induced PCOS model in rats has not been addressed yet. In addition, Dinc et al. (2023) reported in their study that carvacrol reduced the degeneration caused by cisplatin on the ovary, haemorrhage in the corpus luteum, edema in the interstitial area and dilatation in the vessels. Sahin et al. (2022) reported in their study that ischemia–reperfusion-induced ovarian damage was significantly prevented by carvacrol. In this study, it was similarly determined that carvacrol had positive effects on letrozole-induced PCOS. These positive effects were decreased vascular dilatation, haemorrhage, edema and cystic follicle formation. In addition to these findings, thickening of the granulosa cell layer in cystic follicles and an increase in the number of corpus luteum were detected.

Conclusion

As a result, carvacrol used in PCOS in this study caused antioxidant, and anti-inflammatory effects on the ovary, and recovered ovarian morphology, and hormonal changes especially AMH. This study sparks curiosity about the potential benefits of investigating the effectiveness of carvacrol in combination with other pharmacological and lifestyle

interventions used to treat PCOS, which could lead to significant advancements in the field.

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Authors' contribution İ.G. and A.G. conceived and designed the research. İ.G., A.G. and G.U. conducted experiments. İ.G. and T.T. conducted laboratory analyses. İ.G. analyzed data and wrote the manuscript. All authors read and approved the manuscript. The authors declare that all data were generated in-house and that no paper mill was used.

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Data availability All source data for this work (or generated in this study) are available upon reasonable request.

Declarations

Ethics approval Ethical approval for this study was obtained from Hatay Mustafa Kemal University Animal Experiments Local Ethics Committee (Decision No: 2023/09–2).

Conflict of interest The authors declare no competing interests.

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