

Research Article



Resveratrol Attenuates the Endometriosis-Mediated Inflammatory and Oxidative Stress Responses

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Abstract | Endometriosis (END) is a long-term gynecological illness that is marked by the implantation of endometrial tissue in extra-pelvic sites. It is commonly accompanied by pelvic inflammation, oxidative stress, immunological dysregulation, and infertility. Emerging evidence implicates the aryl hydrocarbon receptor (AhR), a ligand-activated transcription factor, in the regulation of immune and inflammatory pathways in various diseases, including END. Resveratrol (RES), a natural AhR modulator, has demonstrated anti-inflammatory and antioxidant properties that may be therapeutically relevant in this context. This study aimed to evaluate the impact of AhR modulation by RES and the AhR antagonist CH223191 on inflammatory status, redox system balance, and selected hematological parameters in a rat model of induced endometriosis. To this point, adult female rats were allocated into five groups as follows; Naïve (control) received no treatment. END, endometriotic rats without treatment. END+RES, endometriotic rats received RES. END+AhR⁻, endometriotic rats received CH223191. END+DMSO, endometriotic rats received vehicle. Serum and peritoneal exudate (PE) samples were collected for downstream analysis. Splenic *Ahr* gene expression was assessed by qPCR. Data were analyzed using One-way ANOVA followed by Tukey's multiple comparisons test to compare group means. The results showed that resveratrol treatment significantly ($P < 0.01$) upregulated *Ahr* gene expression in splenocytes, whereas CH223191 significantly ($P < 0.05$) downregulated it. Rats in the END, END+AhR⁻, and END+DMSO groups revealed significantly ($P < 0.01$) elevated levels of interleukin-1 β (IL-1 β) and Malondialdehyde (MDA) in serum and PE along with significant ($P < 0.01$) increase in circulating WBC and lymphocyte counts compared with the Naïve and END+RES groups. Altogether, this study concludes that AhR modulates the inflammatory response in endometriosis and that RES might have a potential novel therapeutic effect in endometriosis through AhR pathway.

Keywords | Endometriosis, Resveratrol, Aryl hydrocarbon receptor, CH223191, Inflammation, Oxidative stress, Rat model

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INTRODUCTION

Aryl Hydrocarbon receptor (AhR) is a ligand-dependent transcription factor that belongs to the basic helix-loop-helix/Per-ARNT-Sim protein family

(Kwong *et al.*, 2024). It is widely expressed in multiple tissues throughout the body (Hu *et al.*, 2025). In its dormant state, AhR localizes in the cytoplasm in association with chaperone proteins, including heat shock protein 90, P23, and AhR interacting protein. After interacting with

exogenous or endogenous ligands, AhR migrates into the nucleus and forms a heterodimer with AhR nuclear translocator. This heterodimer then binds to xenobiotic response elements in the promoter regions of target genes, leading to the transcriptional activation of genes that participate in xenobiotic metabolism (Kwong *et al.*, 2024). In addition to its traditional contribution to xenobiotic metabolism, AhR is now recognized as a key mediator of various physiological processes, such as cell differentiation, immune response, and reproduction (Abdulla *et al.*, 2021; Bustani *et al.*, 2025). Dysregulation of AhR signaling may contribute to hormonal imbalance and immunological and inflammatory disorders linked with the pathogenesis of several conditions, including autoimmune disorders, cancers, and reproductive illnesses, including endometriosis (Sulentic *et al.*, 2025; Bianchi-Smiraglia and Chaudhry, 2024; Huang *et al.*, 2022; Gawron *et al.*, 2024). Also, it can contribute to the development of gut dysbiosis and disruption of the estrobolome, which can disrupt estrogen metabolism and trigger inflammation and immune modulation, leading to increased endometriosis severity (Alghetaa *et al.*, 2018, 2023b).

Endometriosis (END) is a chronic gynecological disease marked by abnormal localization of endometrial-like tissue, typically on pelvic structures, leading to chronic pelvic pain, infertility, and impairment in quality of life (Allaire *et al.*, 2023). The pathogenesis is complex, encompassing genetic, epigenetic, immunological, and molecular factors (Mariadas *et al.*, 2025; Blanco *et al.*, 2025). Several theories have been proposed to explain the development of endometriotic lesions. Retrograde menstruation suggests that menstrual blood flows backward into the pelvic cavity, allowing endometrial cells to implant. coelomic metaplasia proposes that peritoneal cells can transform into endometrial-like cells. Meanwhile, the stem cell recruitment hypothesis suggests that stem cells from the bone marrow or endometrium migrate to ectopic sites and contribute to lesion formation (Lamceva *et al.*, 2023). The molecular pathways involve PI3K/AKT, NF- κ B, Wnt/ β -catenin, and TGF- β that induce endometrial lesion proliferation, angiogenesis, and apoptosis resistance (Terzic *et al.*, 2021; Driva *et al.*, 2023). It remains a disease without definitive cure, and the current therapeutic strategies are directed exclusively on symptomatology (Parmar *et al.*, 2025). Conventional approaches include hormonal treatments, analgesics, and surgical interventions are the main steps to relieve pain, reduce lesion progression, and improve fertility (Brown *et al.*, 2017; Kalaitzopoulos *et al.*, 2021). However, these options are often associated with significant limitations, including adverse side effects, therapeutic resistance, and high recurrence rate (Allaire *et al.*, 2023). In an attempt to achieve these challenges, increasing attention has been directed toward the use of natural compounds as complementary or alternative therapeutic options. These

compounds, such as curcumin, naringenin, apigenin, genistein, butyrate, quercetin, and resveratrol, show diverse biological effects that are related to the pathophysiology of endometriosis. They exhibit anti-inflammatory, antioxidant, anti-angiogenic, anti-proliferative, pro-apoptotic activities, and phytoestrogenic effects (Mujezin *et al.*, 2024; Paul *et al.*, 2025; Mohammed and Al-Okaily, 2024), together resulting in lesion suppression, regulation of immune responses, and alleviation of pelvic pain.

Resveratrol (RES), a polyphenolic molecule with the ability to modulate AhR, is naturally found in multiple dietary sources, including grapes, peanuts, berries, and red wine (Ispiryan *et al.*, 2024). Comprehensive studies have shown that RES exhibits a variety of biological activities, such as anti-cancer effects, cardio-protection, neuroprotection, vasorelaxation, phytoestrogenic properties, alleviation of pulmonary inflammation, bone health and improvement of reproductive health (Khayoon and Al-Rekabi, 2020; Alghetaa *et al.*, 2021; Dawood and Alghetaa, 2023; Al-Tamemi and Al-Okaily, 2024; Wasan and Maha, 2024). RES is evolving as a prospective therapeutic agent for END due to its ability to regulate essential pathogenic mechanisms including, anti-inflammatory and antioxidant properties, reducing cellular proliferation and angiogenesis, inducing apoptosis of ectopic endometrial cells, and regulating estrogen receptor signaling (Al-Khaqani and Mohammed, 2024; Sienko *et al.*, 2024). Through these multi-pathways, RES offers a promising approach for managing the intricate pathophysiology of endometriosis, suggesting it's a complementary or alternative therapeutic approach (Zou *et al.*, 2024; Huang *et al.*, 2025).

MATERIALS AND METHODS

EXPERIMENTAL ANIMALS

This research was conducted in the laboratory and animal facility of the College of Veterinary Medicine at the University of Baghdad. Eighty-four adult female rats (*Rattus norvegicus*), aged 8 to 10 weeks and weighing roughly 180 to 220 grams, were employed. All animals were housed in a specialized pathogen-free environment with regulated conditions (22 $\pm$ 2°C, 12-hour light/dark cycle), with unrestricted access to standard food and water. Before research, all rats experienced a two-week acclimation phase. The animal protocols received approval from the Institutional Animal Care and Use Committee at the College of Veterinary Medicine, University of Baghdad, obtaining ethical clearance (AUP# P.G.407) in compliance with international standards for the care and use of laboratory animals.

INDUCTION OF ENDOMETRIOSIS LESION

Figure 1 illustrates the induction of experimental

endometriosis. Briefly, experimental rats were randomly assigned to the subsequent groups; Naïve group (n=12): served as a non-endometriotic, untreated control group. Donor group (n=24); euthanized to provide endometrial tissue for transplantation. Recipient group (n=48): underwent to experimental induction of endometriosis. Endometriosis (END) was induced in recipient rats according to the methodology established by (Persoons *et al.*, 2020; Alghetaa *et al.*, 2023b; Al-Salamy and Alghetaa, 2025), with certain alterations. Donor rats received two subcutaneous injections of 0.6 mg/kg estradiol benzoate (E2) at three-day intervals to stimulate endometrial growth (Persoons *et al.*, 2020). One day after the final injection, donor rats were deeply anesthetized with a ketamine and xylazine combination (75mg/kg and 10mg/kg, respectively, administered intraperitoneally) and euthanized with cervical dislocation upon complete loss of reflexes (Irwin *et al.*, 2023). A midline laparotomy was conducted to excise the uterine horns, which were subsequently immersed in sterile, pre-warmed phosphate-buffered saline (PBS). The horns were longitudinally incised with precision scissors, and the endometrial layer was meticulously dissected with tiny forceps. The endometrium was minced into ~1mm² fragments using a fine scalpel and suspended in sterile PBS. Approximately 50 µg of endometrial tissue was injected into the peritoneal cavity of each recipient rat using a sterile syringe (Alghetaa *et al.*, 2023b).

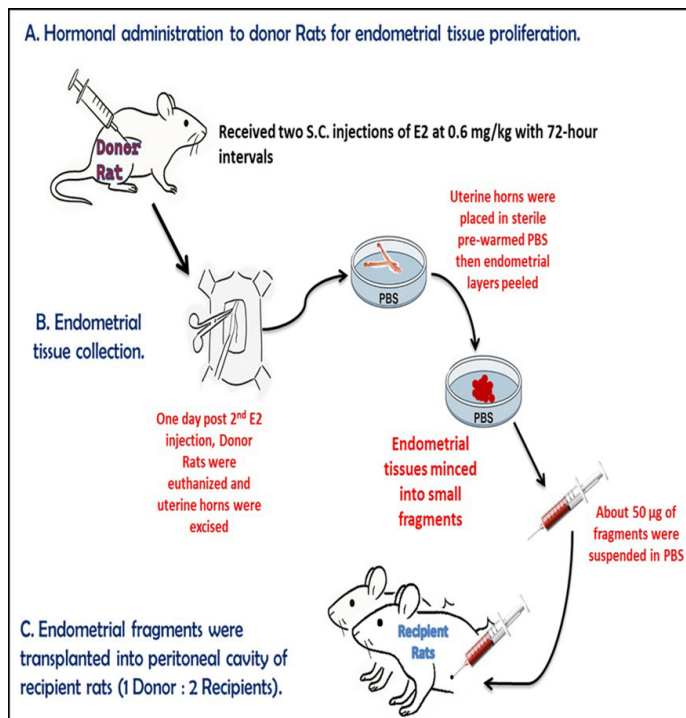


Figure 1: Experimental endometriosis induction in rats.

One donor rat was employed to prepare transplants for two recipient rats. All rats with endometrial transplants were administered AhR modulation substances the next day

after transplantation, in accordance with the experimental design, which will be explained next. Naïve rats received a 500 µL intraperitoneal injection of PBS.

TREATMENTS PREPARATION

Resveratrol (purity ≥ 98%) and CH223191 (purity ≥ 95%) powders were purchased from Hebei Guanlang Biotechnology, China. Both compounds were initially dissolved in DMSO and subsequently diluted with distilled water to create the working solutions at the appropriate concentration, as described in previous studies (Bustani and Alghetaa, 2025b).

The Endometriotic Rats (n=48) were randomly divided into four subgroups (n=12), as follows: END; endometriotic rats that received no treatment, serving as control group. END+RES; endometriotic rats were given resveratrol (RES) orally at a dose of 100mg/kg/day for four weeks (Alghetaa *et al.*, 2023a). END+AhR⁻, endometriotic rats received intraperitoneal injections of CH223191, an Aryl hydrocarbon receptor antagonist (AhR⁻), at a dose of 10mg/kg (0.1ml/100g) every three days for four weeks (Neamah *et al.*, 2019). END+DMSO; endometriotic rats administered dimethyl sulfoxide (DMSO), the vehicle for AhR⁻, via intraperitoneal injection at a volume of 0.1ml/100g body weight every three days for four weeks (Bustani *et al.*, 2024; Bustani and Alghetaa, 2025a) to match the volume used in the END+AhR⁻ group to normalize any biological effects of the vehicle.

SAMPLE COLLECTION AND ANALYSIS

At the end of the experiments, five rats from each group were euthanized under deep anesthesia (xylazine-ketamine overdose) and the following samples were collected; blood samples were obtained via cardiac puncture and processed for complete blood count (CBC) using an automated blood analyzer (Genix, USA) as well as for evaluating the serum concentrations of IL-1β, Malondialdehyde (MDA), and total antioxidant (TAO) levels using ELISA kits (BT LAB, China). Peritoneal exudates have been collected aseptically and analyzed for IL-1β, MDA, and TAO concentrations using ELISA kits (BT LAB, China). Approximately 10mg of spleen tissue was collected, mechanically homogenized, and preserved in 3ml of RNeasy lysis solution (Qiagen, Crawley, UK) and stored at -20°C until RNA extraction (Ferreira *et al.*, 2022). Total RNA was reverse transcribed into cDNA using a One-Step RT-PCR Premix Kit (Bio-Rad, Hercules, CA, USA). The resulting cDNA was used for quantitative PCR (qPCR) to assess gene expression. Gapdh was employed as the housekeeping gene, and relative expression levels were calculated using the 2^{-ΔΔCt} method. Primer sequences are listed in Table 1.

Table 1: Aryl hydrocarbon receptor (*Ahr*), and glyceraldehyde-3-phosphate dehydrogenase (*Gapdh*) primers with their reference IDs from NCBI database.

Gene	Primer 5`-3`	Reverse 5`-3`	NCBI accession No.
<i>Ahr</i>	GTC AGC CAT GGT CAG TCC TCA G	GCT CGG ACT CTG AAA CTT GCT T	NM_013149.3
<i>Gapdh</i>	AGA GAC AGC CGC ATC TTC TT	ATG AAG GGG TCG TTG ATG GC	NM_021578.2

STATISTICAL ANALYSIS

All data were analyzed using GraphPad Prism software (Version 10, 2024; San Diego, CA, USA; <https://www.graphpad.com>). One-way analysis of variance (ANOVA) was employed to evaluate statistical differences among multiple groups under various experimental conditions and treatments. Tukey’s multiple comparisons test was used to compare group means. The probability level less than 0.05 was considered statistically significant. Statistical differences among groups were marked as follows: *P<0.05, **P<0.01, ***P<0.001 and ****P<0.0001.

RESULTS

EXPRESSION OF *AHR* GENE IN SPLENOCYTES

Analysis of *Ahr* gene expression in endometriotic rats revealed significant differences among the experimental groups (Figure 2). Statistical significance (P<0.05) upregulation of *Ahr* expression was observed in the END+RES group in comparison among the experimental groups, while treatment with the AhR antagonist CH223191 significantly (P<0.05) downregulated *Ahr* expression in the END+AhR⁻ group compared with other experimental groups.

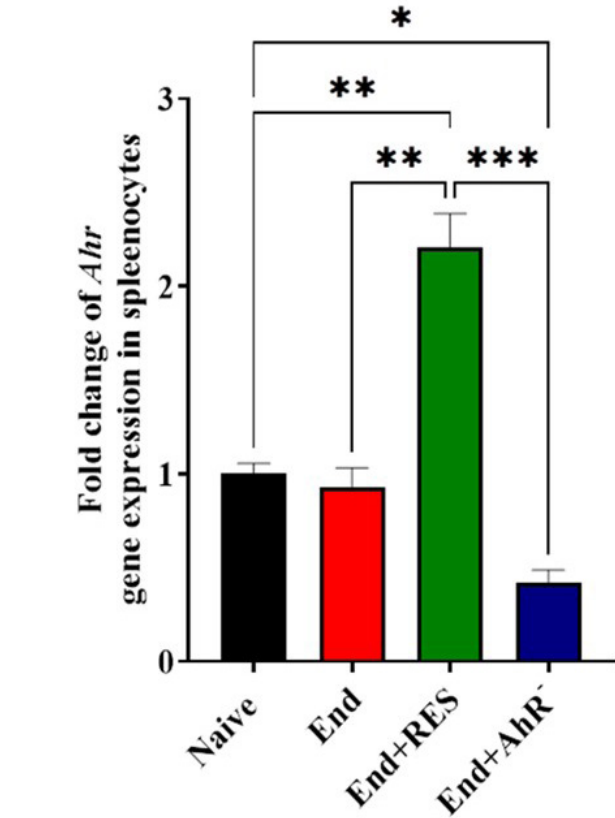


Figure 2: Fold changes in *Ahr* gene expression in endometrial tissue-transplanted rats in response to resveratrol and CH223191 treatments for 30 days. Naïve group: non-endometriotic rats (negative control). END group: untreated endometriotic rats (positive control). END+RES group: Endometriotic rats were treated with resveratrol (100mg/kg/day, orally). END+AhR⁻ group: Endometriotic rats were treated with the AhR antagonist CH223191 (10mg/kg, intraperitoneally, every three days). Statistical analysis was conducted using One-way ANOVA followed by Tukey’s multiple comparisons test. n=3. *P<0.05, **P<0.01, and ***P<0.001.

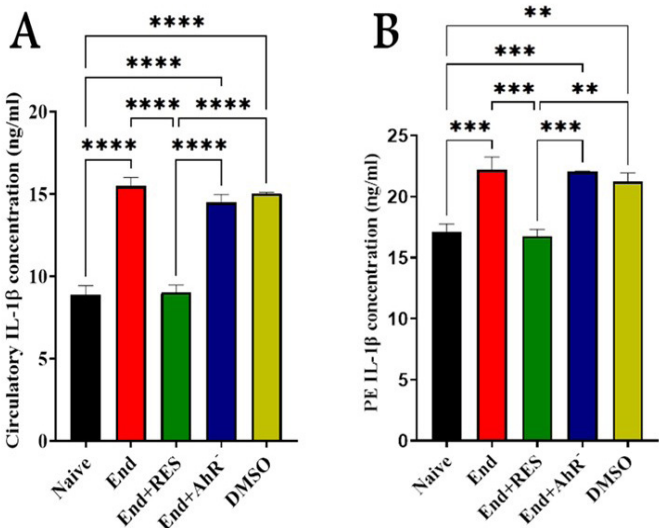


Figure 3: Circulatory and peritoneal exudate (PE) concentrations of interleukin-1beta (IL-1β) following AhR signaling manipulation by using AhR ligands for 30 days in endometrial tissue transplanted rats (n=5). Naïve group: non-endometriotic rats (negative control). END group: untreated endometriotic rats (positive control). END+RES group: Endometriotic rats were treated with resveratrol (100mg/kg/day, orally). END+AhR⁻ group: Endometriotic rats were treated with the AhR antagonist CH223191 (10mg/kg, intraperitoneally, every three days). END+DMSO group: Endometriotic rats administered vehicle control (DMSO, 0.1ml/100g body weight, intraperitoneally, every three days). (A) Circulatory IL-1β concentration (ng/ml) and (B) IL-1β concentrations in peritoneal exudate (ng/ml). Statistical analysis was conducted using One-way ANOVA followed by Tukey’s multiple comparisons test. Significant levels are: **P<0.01, ***P<0.001, and ****P<0.0001.

INTERLEUKIN-1BETA (IL-1 β) LEVELS IN CIRCULATION AND PERITONEAL EXUDATE (PE)

The concentrations of IL-1 β (ng/ml) in the circulation and PE among the experimental groups are illustrated in Figure 3A, B, respectively. Statistical analysis indicated a significant ($P<0.05$) increase of IL-1 β in the END, END+AhR⁻, and END+DMSO groups compared to the Naïve and END+RES groups. No significant distinction was observed between the Naïve and END+RES groups or among the END, END+AhR⁻, and END+DMSO groups.

MALONDIALDEHYDE (MDA) LEVELS IN CIRCULATION AND PE

The concentrations of MDA (nmol/ml) in the circulation and PE of the experimental groups are illustrated in Figure 4A, B, respectively. MDA levels were significantly ($P<0.05$) increased in the END, END+AhR⁻, and END+DMSO groups in comparison with the Naïve and END+RES groups. However, no significant differences were detected between the Naïve and END+RES groups or among the END, END+AhR⁻, and END+DMSO groups in either compartment.

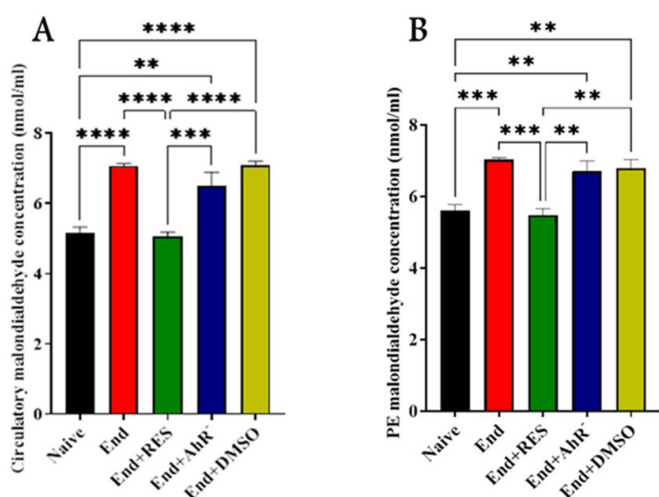


Figure 4: Circulatory and peritoneal exudate (PE) concentrations of Malondialdehyde (MDA) following AhR signaling manipulation by using AhR ligands for 30 days in endometrial tissue transplanted rats (n=5). Naïve group: non-endometriotic rats (negative control). END group: Untreated endometriotic rats (positive control). END+RES group: Endometriotic rats were treated with resveratrol (100mg/kg/day, orally). END+AhR⁻ group: Endometriotic rats were treated with the AhR antagonist CH223191 (10mg/kg, intraperitoneally, every three days). END+DMSO group: Endometriotic rats administered vehicle control (DMSO, 0.1ml/100g body weight, intraperitoneally, every three days). A) Circulatory MDA concentration (nmol) and B) MDA concentrations in PE (nmol). Statistical analysis was conducted using One-way ANOVA followed by Tukey's multiple comparisons test. Significant levels are: ** $P<0.01$, *** $P<0.001$, and **** $P<0.0001$.

TOTAL ANTIOXIDANT (TAO) LEVELS IN CIRCULATION AND PE

The concentrations of TAO (U/ml) in the circulation and PE across the experimental groups are presented in Figure 5A, B, respectively. A significant ($P<0.05$) elevation in TAO levels was observed in both the circulation and PE of the END+RES group compared to all other experimental groups. In the circulation, TAO levels were significantly ($P<0.05$) elevated in the END, END+AhR⁻, and END+DMSO compared to the Naïve group; however, no significant variations were detected among END, END+AhR⁻, and END+DMSO groups. In the PE, TAO levels exhibited no significant variations among the Naïve, END, END+AhR⁻, and END+DMSO groups.

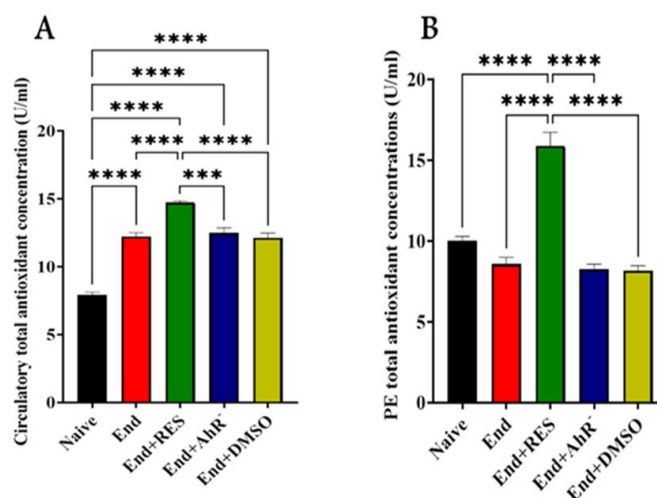


Figure 5: Circulatory and peritoneal exudate (PE) concentrations of total antioxidant (TAO) following AhR signaling manipulation by using AhR ligands for 30 days in endometrial tissue transplanted rats (n=5). Naïve group: non-endometriotic rats (negative control). END group: untreated endometriotic rats (positive control). END+RES group: Endometriotic rats were treated with resveratrol (100mg/kg/day, orally). END+AhR⁻ group: Endometriotic rats were treated with the AhR antagonist CH223191 (10mg/kg, intraperitoneally, every three days). END+DMSO group: Endometriotic rats administered vehicle control (DMSO, 0.1ml/100g body weight, intraperitoneally, every three days). A) Circulatory MDA concentration (U/ml) and B) MDA concentrations in PE (U/ml). Statistical analysis was conducted using One-way ANOVA followed by Tukey's multiple comparisons test. Significant levels are: *** $P<0.001$, and **** $P<0.0001$.

CIRCULATORY SYSTEM COUNTS OF WHITE BLOOD CELL (WBC) AND LYMPHOCYTE

Figure 6A, B illustrates the counts of WBC ($\times 10^3$ cells/ μ l) and lymphocyte ($\times 10^3$ cells/ μ l), respectively. Significant increases ($P<0.05$) in WBC and lymphocyte counts were observed in the END and END+DMSO groups compared to the Naïve and END+RES groups.

No significant variations were detected in WBC counts between the Naïve and END+RES groups. However, the lymphocyte counts were significantly higher ($P < 0.05$) in the END+RES group compared to the Naïve group. No significant differences were found among the END, END+AhR⁻, and END+DMSO groups for any measured parameters.

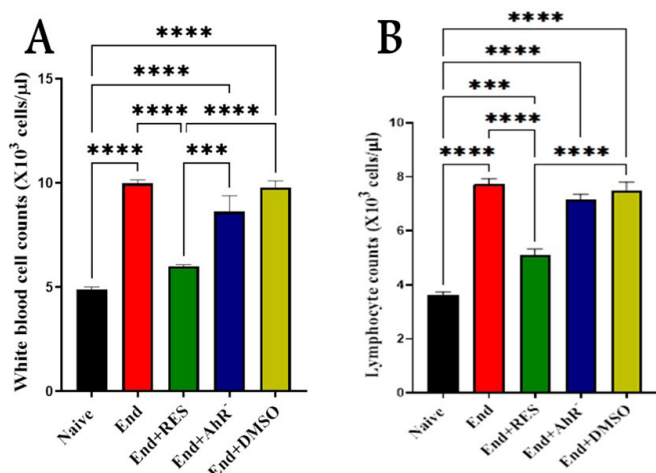


Figure 6: Counts of WBC and Lymphocyte following AhR signaling manipulation by using AhR ligands for 30 days in endometrial tissue transplanted rats (n=5). Naïve group: non-endometriotic rats (negative control). END group: untreated endometriotic rats (positive control). END+RES group: Endometriotic rats were treated with resveratrol (100mg/kg/day, orally). END+AhR⁻ group: Endometriotic rats were treated with the AhR antagonist CH223191 (10mg/kg, intraperitoneally, every three days). END+DMSO group: Endometriotic rats administered vehicle control (DMSO, 0.1ml/100g body weight, intraperitoneally, every three days). (A) WBC counts (X 10³ cells/μl) and (B) lymphocyte counts (X 10³ cells/μl). Statistical analysis was conducted using One-way ANOVA followed by Tukey's multiple comparisons test. Significant levels are: *** $P < 0.001$, and **** $P < 0.0001$.

DISCUSSION

Endometriosis is recognized as a hormone-dependent, immuno-inflammatory, and oxidative condition with systemic implications. Recent interest has been given to the aryl hydrocarbon receptor (AhR), a ligand-activated transcription factor that normalizes xenobiotic metabolism, immunological responses, and oxidative stress pathways (Bahman *et al.*, 2024). The present study demonstrated that resveratrol (RES), a natural AhR agonist, it was upregulated *Ahr* expression in splenocytes, reduced systemic and peritoneal interleukin-1 beta (IL-1β) levels, decreased oxidative stress marker (MDA), enhanced total antioxidant capacity, and normalized WBC and lymphocyte counts. To further investigate the molecular

basis underlying these systemic effects, quantitative PCR analysis was conducted, revealing that *Ahr* expression was significantly amplified in the splenocytes of resveratrol-treated rats and downregulated in CH223191-treated rats. This differential AhR regulation was correlated with differences in biochemical and hematological parameters, suggesting that a causal relationship between AhR activity and disease modulation (Polonio *et al.*, 2025; Haupt *et al.*, 2025). A basic feature of endometriosis is chronic inflammation, evidenced by elevated of IL-1β, a pro-inflammatory cytokine that promotes angiogenesis and lesion growth (Yin *et al.*, 2024). In our study, IL-1β was significantly increased in both serum and peritoneal exudate of END, END+AhR⁻, and END+DMSO rats, indicating a sustained pro-inflammatory state. On the other hand, resveratrol treatment significantly lowered IL-1β concentrations almost to those of naïve. IL-1β stimulates macrophages activation and lymphocyte proliferation (Aggeletopoulou *et al.*, 2024). Therefore, the observed reduction in lymphocyte counts in RES-treated rats likely reflects suppression of IL-1β. This is consistent with RES known ability to inhibit NF-κB signaling, thereby reducing pro-inflammatory cytokines production, including IL-1β and TGF-β (Wang *et al.*, 2022; Liu *et al.*, 2025; Alharris *et al.*, 2022; Ashrafizadeh *et al.*, 2020). Oxidative stress is another key pathogenic factor in endometriosis. Elevated reactive oxygen species and lipid peroxidation products such as MDA are well demonstrated in human and animal experimental studies (Naji *et al.*, 2016; D'Amico *et al.*, 2022; Huang *et al.*, 2025). The present study indicated significantly increased of MDA levels in the END, END+AhR⁻, and END+DMSO groups, while RES restored MDA to near-normal levels and enhanced total antioxidant capacity in both serum and peritoneal compartments. RES effects have been linked to modulation Nrf2 and other redox-regulating pathways (Farkhondeh *et al.*, 2020; Al-Tamemi and Al-Okaily, 2023). Numerous studies confirm that RES improves the activity of important endogenous antioxidant enzymes, such as CAT, GSH-Px, and SOD, and reducing MDA in a dose-dependent manner to protect tissues against oxidative stress and inflammation (Ahmed *et al.*, 2022; Subhi and Al-Okaily, 2023; Aghetaa *et al.*, 2023; Ahmed and Mohammed, 2022). Furthermore, endometriotic rats exhibited increased WBC and lymphocyte counts in the END, END+AhR⁻, and END+DMSO groups, consistent with systemic inflammation (Moini *et al.*, 2021; Nouri *et al.*, 2025). RES normalized WBC counts to Naïve levels and reduced lymphocyte counts compared to untreated END groups. Interestingly, lymphocyte counts in the END+RES group remained slightly higher than naïve controls. This may reflect a partial immune rebalancing rather than full suppression, as RES immunomodulatory effects can downregulate excessive inflammatory lymphocyte activity

while preserving baseline adaptive immune function (Bissacotti *et al.*, 2025; Malaguarnera, 2019). Therefore, the effectiveness of RES as an anti-inflammatory, antioxidant, anti-angiogenic, anti-invasive, anti-adhesive, and pro-apoptotic agent can impede disease progression and avert the spread of endometrial lesions (Khudair and Al-Okaily, 2022; Wang *et al.*, 2021; Abdulla and Al-Okaily, 2022; Al-Khaqani and Mohammad, 2024). The strength of this study represented by inducing experimental endometriosis-like status in lab animal model to enable future studies to focus on the pathogenic mechanisms. However, some shortness had limited the potency of the results particularly the pathological investigation due to the difficulty of spotting the exact endometriotic-related lesions in peritoneal cavity as well as in the reproductive system.

CONCLUSION

This study highlights the crucial role of AhR signaling in the development and regulation of endometriosis. Our findings indicates that resveratrol may serve as a promising therapeutic agent for mitigating inflammation and oxidative stress associated with induced endometriosis in a rat model by upregulating AhR expression. In contrast, the inhibition of AhR via CH223191 did not provide protective effects, indicating the importance of receptor context and ligand-specific dependence in endometriosis. These data collectively offer foundational evidence about the therapeutic potential of AhR-targeted therapies in endometriosis. They also support the further exploration of RES and other natural AhR modulators as promising candidates for non-hormonal treatment approaches. Further investigation is warranted to elucidate the precise molecular pathways implicated in AhR-mediated endometriosis progression.

ACKNOWLEDGMENT

Not applicable.

NOVELTY STATEMENT

This research article provides deep insight into the mechanistic roles of resveratrol in modulation inflammatory and oxidative stress markers associated with endometriosis.

AUTHOR'S CONTRIBUTION

HA design, conceptualization, review the draft and last version of this manuscript. AA wrote the draft, revised and wrote the last version of this manuscript. Both HA and AA have reviewed and approved the submitted version of the manuscript.

DATA AVAILABILITY

The data is available from the corresponding author in reasonable request.

GENERATIVE AI AND AI-ASSISTED TECHNOLOGY STATEMENT

Authors disclose that they have not used any generative artificial intelligence or AI-assisted technology in forming this manuscript nor in generating its data.

CONFLICT OF INTEREST

The authors have declared that they have no conflict of interest regarding the publication of this article.

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