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Curcumin mitigates polycystic ovary syndrome in mice by suppressing TLR4/MyD88/NF-κB signaling pathway activation and reducing intestinal mucosal permeability

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Polycystic ovary syndrome (PCOS) is an endocrine-metabolic disorder closely associated with chronic inflammation. Curcumin, a polyphenolic lipophilic compound, has been shown to improve the intestinal mucosal barrier and reduce low-grade systemic inflammation. This study aimed to assess the effects of curcumin on attenuation of PCOS in a mouse model and to explore the underlying mechanisms involved. C57BL/6J mice were divided into 4 groups ($n = 15$ per group): CON: control group, CON/CUR: CON with curcumin group, MOD: model group, MOD/CUR: MOD with curcumin group. The MOD and MOD/CUR groups were injected with dehydroepiandrosterone (DHEA) (6 mg/100 g BW) dissolved in soybean oil to induce a PCOS-like state. After curcumin intervention (200 mg/kg) for 45 days, the mice were euthanized for analysis of various physiological and biochemical parameters. In MOD/CUR group, significant decreases in body weight (BW) ($p = 0.0254$), testosterone (T) levels ($p = 0.0052$), luteinizing hormone (LH) levels ($p = 0.0438$), and the LH/follicle-stimulating hormone (FSH) ($p = 0.0271$) levels were observed, while estradiol (E2) ($p = 0.0415$) level and insulin sensitivity ($p = 0.0441$) were increased. Histological examination (HE) staining of ovarian and colon tissues showed that curcumin ameliorated both PCOS-associated morphological changes and colon tissue pathology. Western blot and immunohistochemistry analyses of colon tissues revealed increased levels of tight junction proteins, ZO-1 (Western blot, $p = 0.0360$; immunohistochemistry, $p = 0.0273$) and occluding (Western blot, $p = 0.0189$; immunohistochemistry, $p = 0.0224$) in the MOD/CUR group. Additionally, inflammatory indicators from plasma and ovary, including IL-17 A (plasma, $p = 0.0120$; ovary, $p = 0.0414$), IL-6 (plasma, $p = 0.0344$; ovary, $p = 0.0379$), TNF-α (plasma, $p = 0.0078$; ovary, $p = 0.0488$), and lipopolysaccharides (LPS) (plasma, $p = 0.0144$), were decreased, while IL-10 (plasma, $p = 0.0270$; ovary, $p = 0.0267$) was increased in MOD/CUR group. The levels of NF-κB p65 ($p = 0.0229$), TLR-4 ($p = 0.0462$) and MyD88 ($p = 0.0152$) in ovarian tissues were significantly increased in MOD/CUR group. Our results revealed that curcumin alleviates PCOS by inhibiting TLR4/MyD88/NF-κB signaling pathway activation and reducing intestinal mucosal permeability. These findings suggest that curcumin may provide a potential clinical approach for managing PCOS.

Keywords Curcumin, PCOS, TLR4/MyD88/NF-κB, Intestinal mucosal permeability

Polycystic ovary syndrome (PCOS) stands out as one of the prevalent endocrine-metabolic disorders, significantly impacting female fertility, with a reported global prevalence ranging from 4–21%[1]. PCOS is Characterized by ovulatory dysfunction and hyperandrogenism, and patients often experience various metabolic disturbances,

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including insulin resistance and hyperinsulinemia[2,3]. Furthermore, PCOS is associated with several potential complications, such as type 2 diabetes (T2DM), metabolic syndrome, cardiovascular diseases, endometrial cancer, and chronic inflammatory conditions, all of which severely compromise reproductive health and quality of life[4,5]. Despite extensive research, the precise etiology of PCOS remains unclear, and there is a lack of effective pharmaceutical interventions, highlighting the need for the exploration of novel therapeutic strategies.

Emerging evidence highlights the pivotal role of gut microbiota in the progression and pathogenesis of PCOS[6]. Dysbiosis of the intestinal microbiota can compromise the integrity of the intestinal mucosal, resulting in increased intestinal mucosal permeability[7–9]. lipopolysaccharides (LPS) from Gram-negative gut bacteria activate Toll-like receptor 4 (TLR4), which in turn triggers downstream MyD88-dependent NF-κB signaling, promoting a pro-inflammatory milieu[10–13]. The activated NF-κB induces the release of pro-inflammatory cytokines, leading to low-grade systemic and ovarian inflammation, disrupted follicular development, and the subsequent onset of PCOS[11,14,15].

Curcumin, a polyphenolic lipophilic compound derived from turmeric, is reputed for its diverse biological activities, including anti-inflammatory, anti-tumor, and antioxidant properties[16–18]. Research suggests that curcumin may help delay the onset and progression of T2DM by improving intestinal permeability, strengthening the intestinal barrier function, reducing circulating LPS levels, and mitigating systemic low-grade inflammation. PCOS is also characterized as an endocrine disorder with a state of chronic inflammation[18,19]. However, whether curcumin can prevent the progression of PCOS by improving intestinal barrier function and inhibiting the activation of the TLR4/MyD88/NF-κB signaling pathway has not yet been reported.

In this study, leveraging a murine PCOS model, we aimed to elucidate the effects of curcumin on PCOS pathogenesis and uncover the underlying mechanisms involved. Our findings provide insights into the complex interplay between PCOS, intestinal mucosal barrier integrity, and inflammation, potentially paving the way for novel clinical interventions.

Methods

Animal experiments
The experiments were approved by the Ethics Committee of Southwest Medical University (NO. KY2020031), and were reported in accordance with the ARRIVE guidelines[20]. All methods followed relevant guidelines and regulations. In this study, 21-day-old female C57BL/6J mice were purchased from Chengdu Dossy Experimental Animals Co., Ltd., Chengdu, China, and housed in specialized cages with a controlled temperature (25 ± 1 °C) under a 12-hour light/dark cycle. All mice were randomly divided into 4 groups (15 mice/group): control group (CON), CON with curcumin group (CON/CUR), model group (MOD), and MOD with curcumin group (MOD/CUR). According to the previous method[21–23], The mice in the MOD and MOD/CUR groups were subcutaneously injected with dehydroepiandrosterone (DHEA) (6 mg/100 g BW) dissolved in soybean oil for 20 days to induce the PCOS model. PCOS mice with successful induction exhibited acyclic/irregular ovarian cyclicity. The CON and CON/CUR groups received daily injections of an equivalent amount of soybean oil.

After 20 days, the mice in the CON/CUR and MOD/CUR groups received Curcumin (200 mg/kg) dissolved in 1% carboxymethyl cellulose (CMC) for 45 days. Meanwhile, the CON and MOD groups were administered an equivalent dosage of 1% CMC as a control. After the 45-dayintervention, the mice were anesthetized by intraperitoneal injection with ketamine (20 mg/kg) and xylazine (3 mg/kg). The state of anesthesia was confirmed by observing slow breathing, muscle relaxation, and no response to experimental manipulation. Blood was then collected using the eyeball extraction method, centrifuged at 4000 rpm at 4 °C for 10 min, and stored at -80 °C for further serum analysis. The mice were euthanized by cervical dislocation. Ovarian and colon samples were collected immediately after euthanasia and stored at -80 °C for subsequent analysis.

Vaginal smear
From the first day of modeling to the last day of treatment, vaginal smears were collected at 9:00 AM to evaluate the estrous cycle of all mice using Wright-Giemsa staining microscopy. In normal mice, the estrous cycle progresses in the order of proestrus, estrus, metestrus, and diestrus, typically lasting 4–5 days[24]. A prolonged estrous cycle or a disordered pattern is considered indicative of an estrous cycle disorder[25].

Hematoxylin-eosin (HE) staining
After the mice were sacrificed, the isolated ovary and colon tissues were immediately fixed in 4% paraformaldehyde. The tissues were then dehydrated, embedded in paraffin, and sectioned for histological analysis. To evaluate ovarian and colon damage, the sections were with hematoxylin and eosin (HE) and observed for morphological changes using an Olympus light microscope (Melville, NY). For the stained ovarian sections, the number of cystic follicle and corpora luteum was counted by two individuals who were blinded to the source of the sections. As described in previous literature, cystic follicles are defined as follicles without oocytes, characterized by large fluid-filled cysts with a thin granulosa cell layer and a thick theca cell layer[19].

Insulin tolerance tests (ITT)
ITT were performed immediately after 45 days of curcumin treatment. After fasting the mice for 6 h, basal blood glucose levels of mice in each group were measured. Subsequently, intraperitoneal insulin (1 IU/kg body weight) was injected immediately, and blood glucose levels were measured at 30, 60, and 90 min post-injection. The total area under the glucose response curve (AUC) was calculated using GraphPad Prism software.

Enzyme linked immunosorbent assay (ELISA)
To measure the levels of testosterone (T), estradiol (E2), luteinizing hormone (LH), follicle-stimulating hormone (FSH) in plasma, as well as the levels of various inflammatory factors, including TNF-α (tumor necrosis factor-

alpha, TNF-α), IL-6 (interleukin-6, IL-6), IL-10 and IL-17 A in ovaries and plasma, ELISA was conducted following the manufacturers' instructions (Jiangsu Enzyme Immune Industrial Co., Ltd, Yancheng, China).

Western blot analysis

The total protein concentration of frozen ovarian tissue and colon tissue was determined using BCA protein assay kit. Proteins were separated by SDS-PAGE and transferred to PVDF membrane. The membrane was then blocked with 5% nonfat milk powder for 2 h. Following this, the membrane was incubated overnight at 4 °C with primary antibodies, which included TLR-4, MyD88, NF-κB p65, occludin, and ZO-1. The PVDF membrane was washed three times with TBST. Primary antibodies for TLR-4, MyD88, and NF-κB p65 were purchased from Wuhan Sanying Biotechnology Co., LTD., and those for occludin and ZO-1 were purchased from Beijing Bioss Biotechnology Co., LTD. The dilution ratio of all primary antibodies was 1:2000.

Subsequently, the PVDF membrane was incubated with an appropriate HRP-conjugated secondary antibody for 2 h at room temperature and washed three times with TBST. Chemiluminescence was used for color development, with GAPDH as the internal reference. The band intensity was analyzed using ImageJ software, and the blot of each protein was captured using a gel imaging system.

Immunohistochemistry

Paraffin slices underwent an antigen unmasking process and were treated with 3% H_2O_2 to eliminate endogenous peroxidase activity. Following this, the tissues were incubated with 10% bovine serum albumin for 60 min to block nonspecific binding. The slices were then incubated overnight at 4 °C with primary antibodies: anti-occludin (13409-1-AP, Proteintech) and anti-ZO-1 (21773-1-AP, Proteintech).

On the following day, the slices were incubated with the corresponding HRP labeled secondary antibody at room temperature for 60 min. Finally, the slices were stained with DAB and examined under a light microscope at 200× magnification.

Plasma LPS analysis

Limulus amebocyte lysate kit was used to detect the plasma LPS levels of mice in each group (Xiamen Bioendo Technology Co., Ltd, Xiamen, China). According to the manufacturer's instructions, 50 μL of diluted plasma (diluted 1:4 with endotoxin-free water) was added to each well of a 96-well plate. Subsequently, 50 μL/ well of limulus amebocyte lysate reagent was added to each well. The plates were then incubated at 37 °C for 30 min. After incubation, 100 μL of chromogenic, pre-warmed to 37 ° C, was added to each well. the plates were incubated again at 37 °C for 6 min. The reaction was terminated by adding 100μL of 25% glacial acetic acid solution. Finally, the optical density of the microplate at 545 nm was measured using a reader (Thermo Scientific, USA).

Statistical analysis

All experimental data were analyzed using GraphPad Prism software 6.01 (GraphPad Software Inc., CA, USA). The results were expressed as mean ± SEM. Differences among multiple comparisons were performed using one-way analysis of variance (ANOVA). Tukey's post hoc test was used to identify the significance of pairwise comparison of mean values among the groups. Results with $p < 0.05$ were considered statistically significant.

Results

Routine parameters of mice in diverse groups

At the beginning of the study, there were no significant differences in body weights among 4 groups. After 45 days of treatment, the body weight of mice in MOD/CUR group decreased significantly compared with that in MOD group($p = 0.0254$), and there was no significant change in body weight of mice in CON/CUR group compared with that in CON group, indicating that curcumin effectively reduced weight in PCOS mice.

T and LH levels were significantly higher in MOD group compared to the CON group (T, $p < 0.0001$; LH, $p = 0.0030$). Compared with the MOD group, T and LH levels were significantly lower in the MOD/CUR group (T, $p = 0.0052$; LH, $p = 0.0438$). Additionally, the LH/FSH ratio in the MOD group was significantly higher than that in the CON group ($p = 0.0025$), while the LH/FSH ratio in the MOD/CUR group was notably lower than in the MOD group ($p = 0.0415$). FSH levels were significantly lower in the MOD group compared to the CON group ($p = 0.0481$), with no differences observed between the MOD and MOD/CUR groups. Furthermore, estradiol (E2) levels in the MOD group were significantly lower than in the CON group ($p = 0.0053$), but curcumin intervention significantly increased E2 levels compared to the MOD group ($p = 0.0498$) (Table 1).

Curcumin intervention improved the estrous cycles of PCOS in mice

Wright-Giemsa staining was performed on vaginal smears to evaluate differences in estrous cycles of mice in each group (Fig. 1). The CON (Fig. 1E) and CON/CUR (Fig. 1F) groups showed a regular estrous cycle, lasting 4–5 days. In contrast, as the modeling progressed, the estrous cycle in the MOD group became disordered, with a prolonged estrus phase (Fig. 1G). Remarkably, after curcumin intervention, the estrous cycle of mice in the MOD/CUR group gradually returned to normal (Fig. 1H), indicating that curcumin can improve the estrous cycle disorder associated with PCOS.

Curcumin ameliorated ovarian histopathological injury in PCOS

HE staining was used to assess the alteration of ovarian pathology in mice from each group (Fig. 2A-D). Compared to the CON group, the MOD group exhibited a significant increase in the number of cystic follicles ($p = 0.0022$) and a reduction or absence of corpus luteum ($p = 0.0388$), indicating impaired ovarian function Intriguingly, curcumin intervention resulted in a significant reduction in the number of cystic follicles ($p = 0.0488$) and an

Measurements	CON	CON/CUR	MOD	MOD/CUR	Unpaired t tests		
					a	b	c
Body Weight, g	20.78 ± 0.34	20.95 ± 0.41	22.76 ± 0.29	21.38 ± 0.29	0.9841	0.0006	0.0254
T, ng/ml	0.48 ± 0.06	0.50 ± 0.06	1.30 ± 0.12	0.85 ± 0.06	0.9981	< 0.0001	0.0052
FSH, mIU/ml	11.41 ± 1.97	11.24 ± 2.13	5.08 ± 0.60	8.02 ± 0.94	0.9998	0.0481	0.5540
LH, mIU/ml	5.95 ± 0.33	5.90 ± 0.43	8.39 ± 0.42	6.72 ± 0.42	0.9997	0.0030	0.0438
LH/FSH,	0.59 ± 0.11	0.60 ± 0.12	1.75 ± 0.31	0.91 ± 0.15	> 0.9999	0.0025	0.0415
E2, μmol/l	51.99 ± 1.25	52.29 ± 1.32	41.64 ± 3.06	49.31 ± 0.91	0.9994	0.0053	0.0498

Table 1. Routine parameters of mice with diverse groups in PCOS. CON: control group, CON/CUR: CON with curcumin group, MOD: model group, MOD/CUR: MOD with curcumin group, a: CON vs. CON/CUR, b: CON vs. MOD, c: MOD vs. MOD/CUR, the values of a, b, and c are *P*-values.
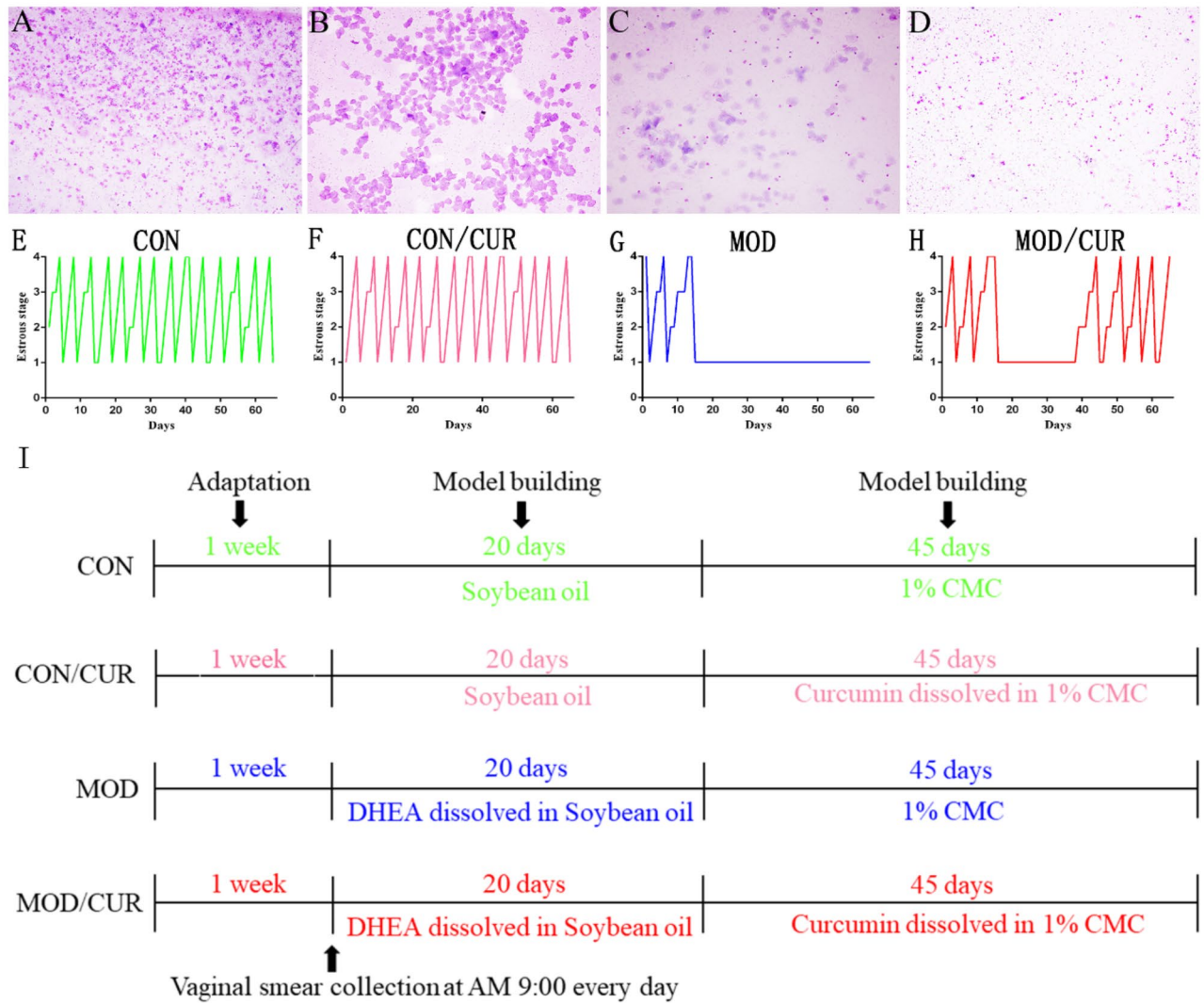
Fig. 1. Estrous cycle changes in each group of mice. (**A**) Vaginal smears of proestrus stage. (**B**) Vaginal smears of estrous stage. (**C**) Vaginal smears of metestrus stage. (**D**) Vaginal smears of diestrus stage. (**E–H**) Representative estrous cycles of diverse groups, 1: diestrus stage, 2: proestrus stage, 3: estrus stage, 4: metestrus stage. Original magnification (×100). (**I**) Schematic time diagram of experimental design.
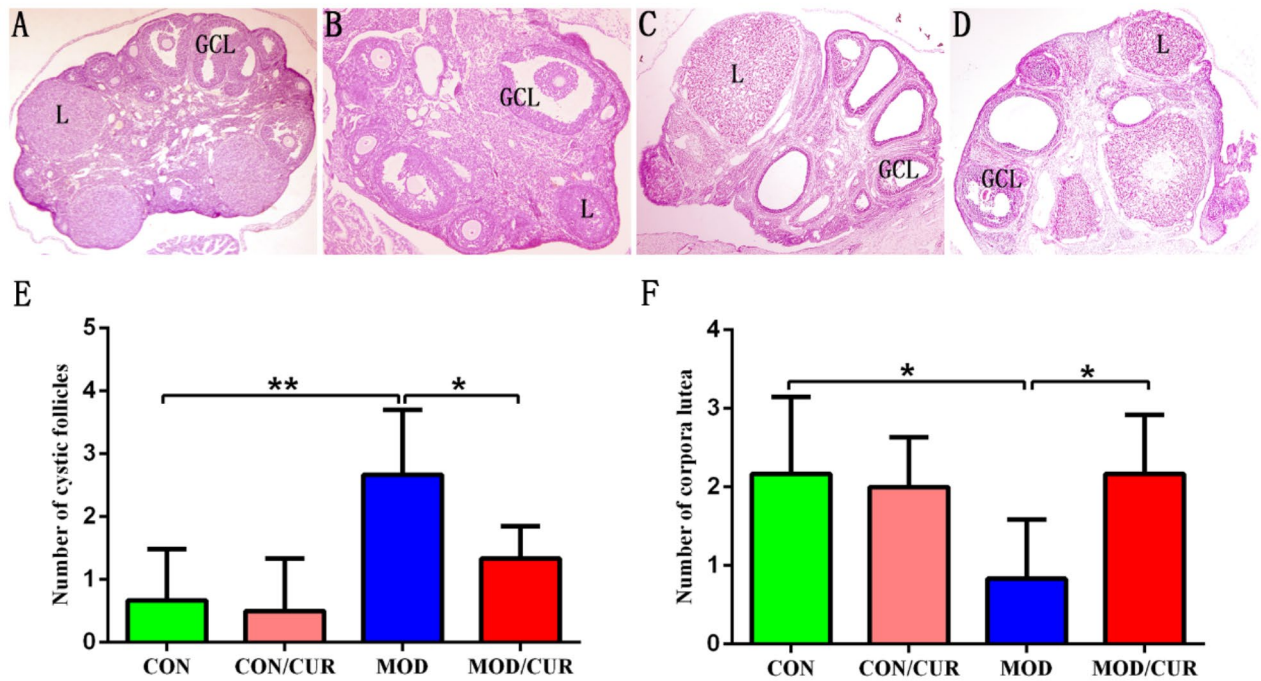
Fig. 2. Effects of curcumin on ovarian tissue morphology in PCOS with Hematoxylin-eosin (H&E) staining. (**A**) CON, (**B**) CON/CUR, (**C**) MOD, (**D**) MOD/CUR, (**E**) Changes in the number of cystic follicles, (**F**) Changes in the number of corpus luteum. GCL: granular cell layer, L: luteum, CON: control group, CON/CUR: CON with curcumin group, MOD: model group, MOD/CUR: MOD with curcumin group. *$P < 0.05$, **$P < 0.01$. Original magnification (40×).
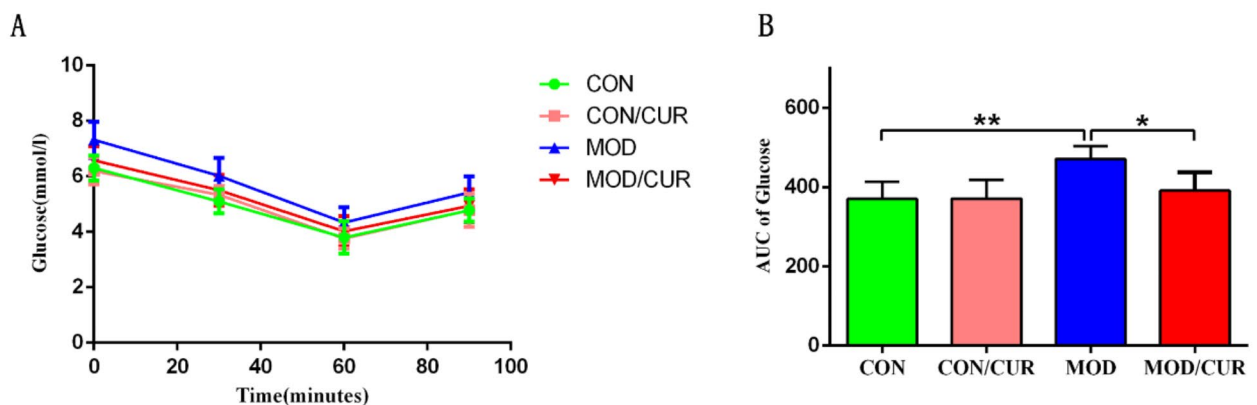

Fig. 3. Insulin tolerance test. (**A**) blood glucose levels, (**B**) AUC of glucose. *$P < 0.05$, **$P < 0.01$.

increase in corpus luteum formation ($p = 0.0388$), indicating that curcumin helps improve pathological changes in ovarian tissue (Fig. 2E–F).

Curcumin improved insulin resistance in PCOS
According to area under the curve AUC from insulin tolerance tests, Insulin sensitivity in the MOD group was significantly lower than in the CON group ($p = 0.0092$). However, insulin sensitivity was increased in the MOD/CUR group ($p = 0.0441$) compared to the MOD group (Fig. 3).

Curcumin improved the mucosal barrier of colon
colonic tissue revealed significant pathological injury in the MOD group, characterized by colon mucosal erosion, disordered and sparse villus structure, and discontinuous brush border. In contrast, curcumin intervention alleviated these issues, showing reduced mucosal erosion, improved villus structure, and continuity

of the brush border. These findings indicate that curcumin helps improve the pathological changes in colon tissue (Fig. 4A–D).

Western blot showed that, compared to the CON group, the levels of colon tissue ZO-1 ($p = 0.0043$) and occludin ($p = 0.0010$) were significantly decreased in the MOD group. In the MOD/CUR group, curcumin treatment resulted in a significant increase in the levels of ZO-1 ($p = 0.0360$) and occludin ($p = 0.0189$) compared to the MOD group. These results indicate that curcumin can enhance the levels of ZO-1 and Occludin in colonic tissue, thereby ameliorating the intestinal mucosal barrier (Fig. 4E–G).

To assess the effects of curcumin on intestinal barrier integrity, immunohistochemistry was used to analyze the expression of tight junction proteins, including occluding (Fig. 5A–D) and ZO-1(Fig. 5E–H). Compared to the CON group, the levels of occludin ($p = 0.0002$) and ZO-1 ($p = 0.0001$) were significantly decreased in the MOD group. However, compared with the MOD group, the expression of both occludin ($p = 0.0224$) and ZO-1 ($p = 0.0273$) was significantly increased in the MOD/CUR group. These results suggest that curcumin may improve intestinal barrier function by enhancing the expression of occludin (Fig. 5I) and ZO-1 proteins (Fig. 5J).
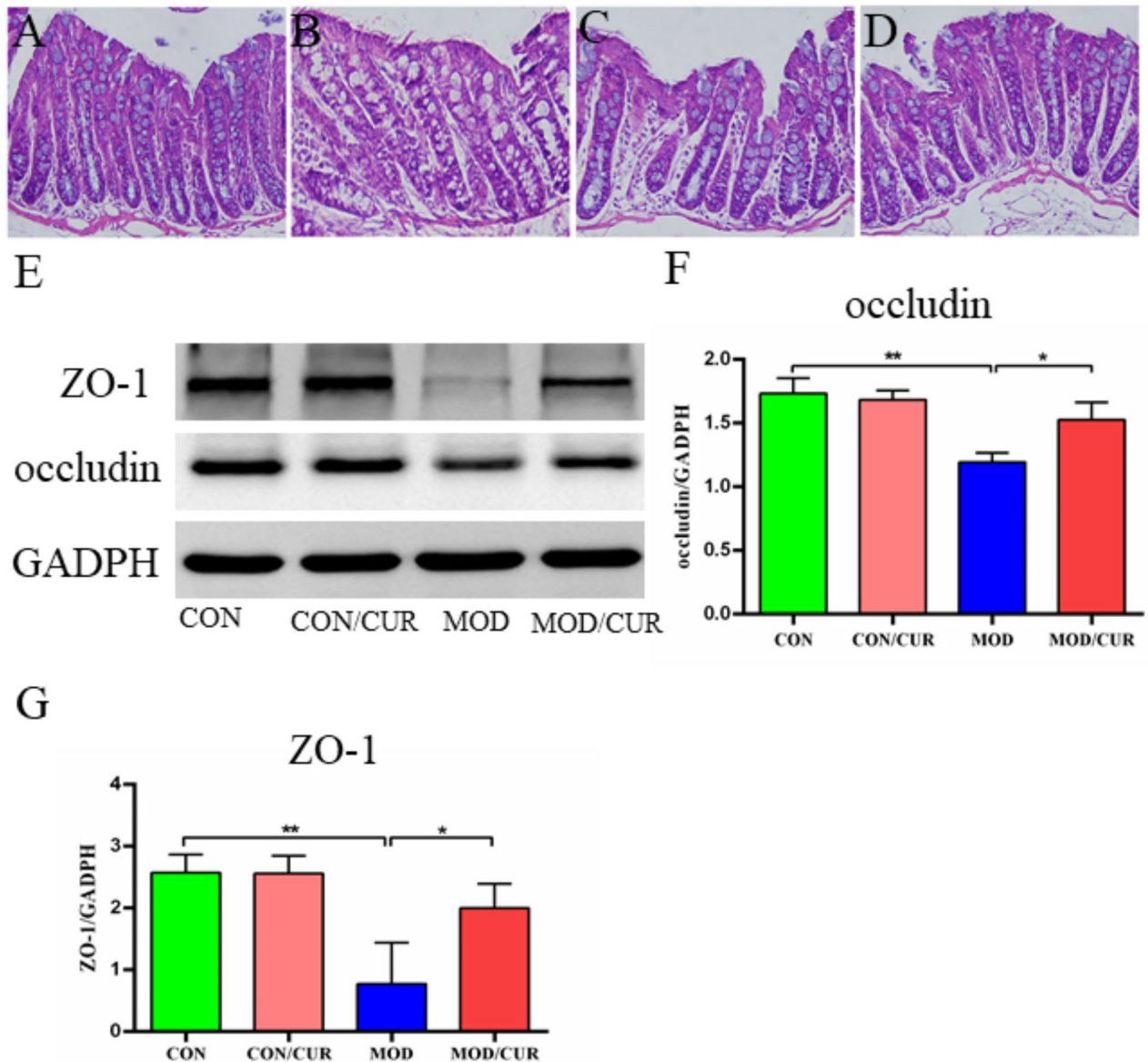

Fig. 4. changes of Pathology for colon tissue and intestinal mucosal barrier in each group. (A–D) Colon tissue in each group with Hematoxylin-eosin (H&E) staining, (E) Western blot bands of ZO-1 and occludin in colonic tissues, (F) occludin expression levels, G: ZO-1 expression levels. Original magnification (200×). *$P <$ 0.05, **$P <$ 0.01.
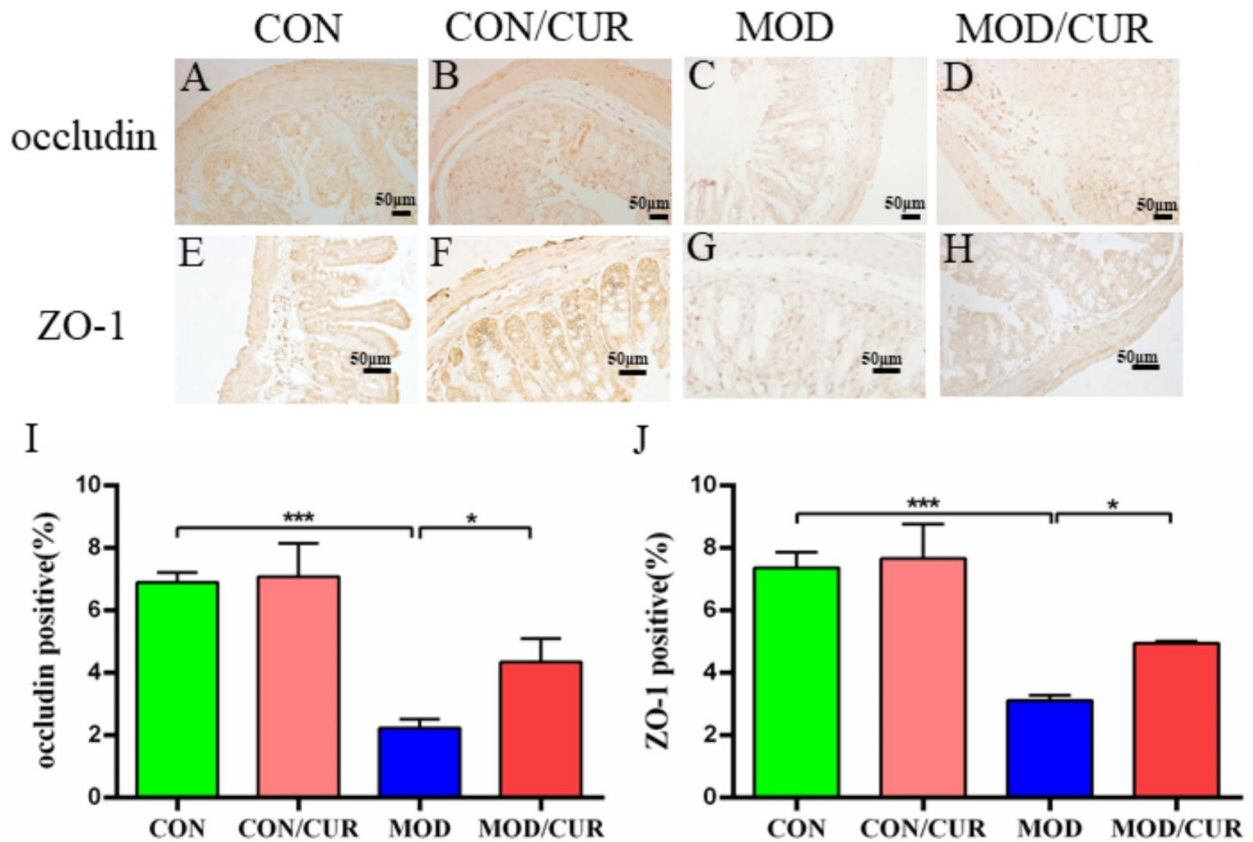
Fig. 5. Curcumin enhanced the expression of occludin and ZO-1 proteins in each group. (**A–D**) occludin was assessed by immunohistochemistry in each group, (**E–H**) ZO-1 was assessed by immunohistochemistry in each group, (**I**) occludin expression levels, (**J**) ZO-1 expression levels. CON: control group, CON/CUR: CON with curcumin group, MOD: model group, MOD/CUR: MOD with curcumin group. Original magnification (200×). *$P<0.05$, **$P<0.01$, ***$P<0.001$.

Curcumin reduced inflammation of plasma and ovary in PCOS

Experimental analysis revealed that the levels of IL-17 A (plasma, $p=0.0031$; ovary, $p=0.0090$) (Fig. 6A and E), IL-6 (plasma, $p=0.0139$; ovary, $p=0.0233$) (Fig. 6B and F), and TNF-α (plasma, $p=0.0033$; ovary, $p=0.0280$) (Fig. 6D and H)were significantly elevated in the MOD group compared to the CON group, while the level of IL-10 (plasma, $p=0.0041$; ovary, $p=0.0086$) (Fig. 6C and G) was significantly lower. Following curcumin intervention, levels of IL-17 A (plasma, $p=0.0120$; ovary, $p=0.0414$), IL-6 (plasma, $p=0.0344$; ovary, $p=0.0379$), and TNF-α (plasma, $p=0.0078$; ovary, $p=0.0488$) were significantly decreased, and the level of IL-10 (plasma, $p=0.0270$; ovary, $p=0.0267$) was significantly increased(Fig. 6A and H). These results indicate that curcumin reduced inflammation in the plasma and ovaries of PCOS by suppressing pro-inflammatory cytokines and enhancing anti-inflammatory IL-10.

Curcumin attenuated metabolic endotoxemia by decreasing LPS and TLR4/MyD88/NF-κB signaling pathway

Plasma-translocated LPS derived from Gram-negative bacteria was detected with Limulus reagent. Compared to the CON group, plasma LPS was significantly increased in the MOD group ($p=0.0012$). However, plasma LPS was significantly lower in the MOD/CUR group compared to the MOD group ($p=0.0144$), indicating that curcumin can reduce endotoxemia in PCOS (Fig. 6I). In addition, the relative expression of TLR4, MyD88 and NF-κB p65 was significantly elevated in the MOD group ($p=0.0100$, $p=0.0004$, $p=0.0020$) but these levels were reduced following curcumin administration ($p=0.0462$, $p=0.0152$, $p=0.0229$) (Fig. 6L, K, J, M, J and K).

Discussion

In this study, we explored the therapeutic potential of curcumin for treating PCOS. Through various conventional indicators such as pathological examination, weight loss, improvement in insulin resistance, and normalization of abnormal hormone levels, we established that curcumin effectively alleviates PCOS symptoms, aligning with previous research findings[26–32]. Our results demonstrated that curcumin offers promising preventive and therapeutic benefits for PCOS management. Furthermore, our study suggest that the amelioration of PCOS
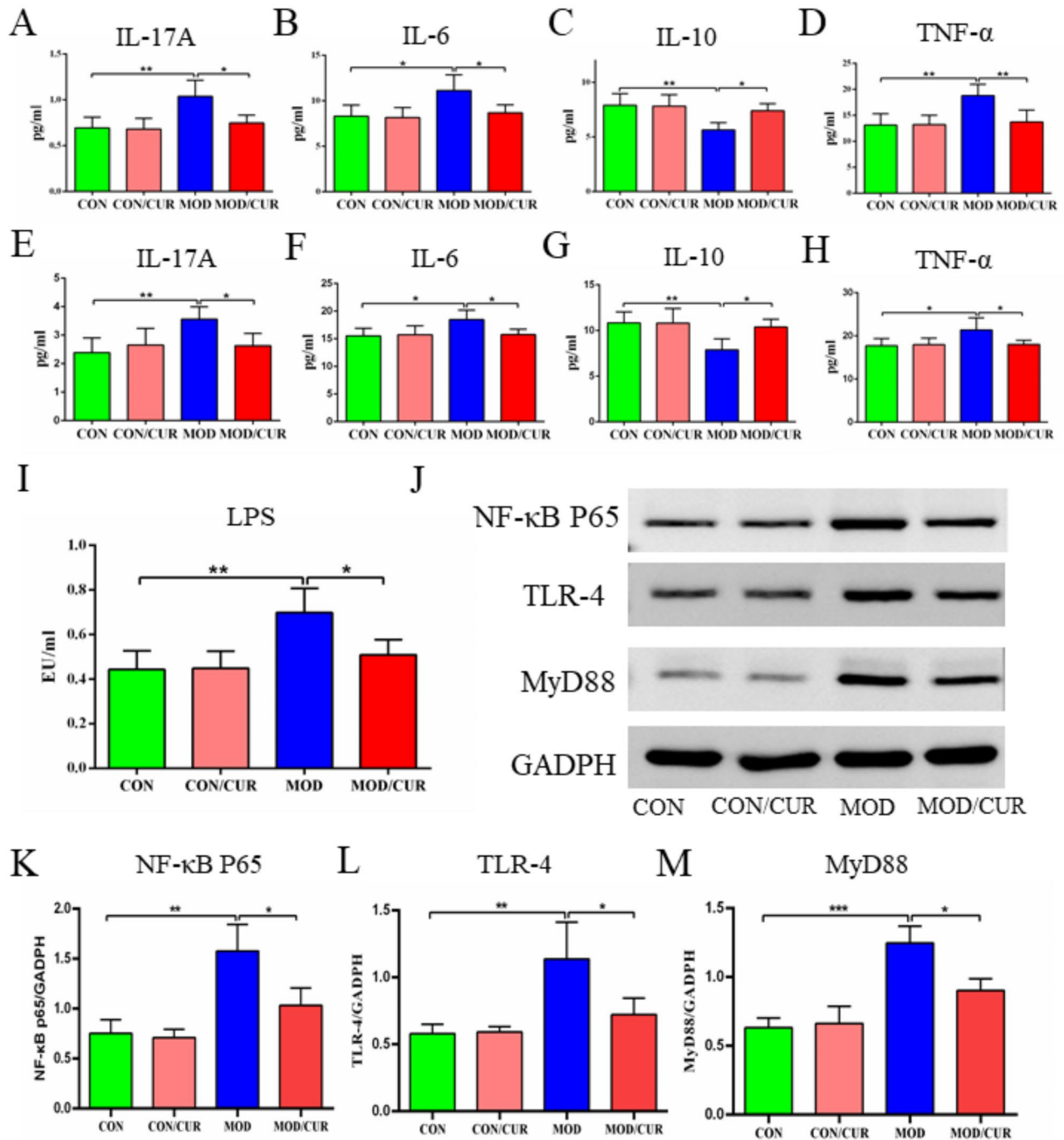
Fig. 6. Detection of plasma or ovarian inflammatory in diverse groups of mice. (**A–D**) Plasma in each group was collected respectively for detection of IL-17 A (**A**), IL-6 (**B**), IL-10 (**C**), TNF-α (**D**). (**E–H**) Ovary in each group was collected respectively for detection of IL-17 A (**E**), IL-6 (**F**), IL-10 (**G**), TNF-α (**H**). (**I**) Plasma LPS levels. (**J**) Western blot bands of NF-κB p65, TLR4 and MyD88 in ovary tissues. (**K–M**) The expression levels of NF-κB p65, TLR4 and MyD88. Data are expressed as mean ± SEM. *$P<0.05$, **$P<0.01$, ***$P<0.001$.

phenotype may be closely associated with the reduction in intestinal mucosal permeability and the inhibition of TLR4/MyD88/NF-κB signaling pathway.

Numerous studies have shown that dysregulation of gut microbiota in PCOS leads to increased intestinal mucosal permeability[33–35]. This disruption allows LPS translocation from gram-negative bacteria to enter the bloodstream, triggering systemic low-grade inflammation and subsequent ovarian inflammation[10,11,36]. Our findings demonstrated marked colonic tissue pathology in the MOD group, with decreased expression of tight junction proteins (ZO-1, Occludin) and elevated plasma LPS levels. Remarkably, curcumin intervention

ameliorated colonic pathological damage, increased tight junction protein expression, and decreased plasma LPS levels. These results suggest that curcumin may reduce intestinal mucosal permeability, reduce intestinal LPS transport to the liver and blood circulation, and eventually contributing to the reduction of ovarian inflammation.

Proinflammatory cytokines were increased and anti-inflammatory cytokines decreased in PCOS[37,38]. Notably, aberrant levels of pro-inflammatory cytokines such as TNF-α, IL-6, and IL-17 A in plasma and follicular fluid have been associated with poor oocyte quality and compromised reproductive outcomes[37,39,40]. These cytokines, including TNF-α, IL-6 and IL-10, play crucial roles in the occurrence and development of inflammation and oxidative stress[19]. Our study showed that curcumin intervention significantly reduced the levels of these pro-inflammatory cytokines and increased the levels of the anti-inflammatory cytokine IL-10. This suggests that curcumin may help alleviate PCOS by reducing pro-inflammatory cytokines and increasing anti-inflammatory cytokines, which is consistent with findings from previous studies[18,41,42].

The TLR4/MyD88/NF-κB is crucial for the LPS-induced intestinal innate immune response, particularly in PCOS[12,43,44], and is known to exacerbate insulin resistance[15,16]. Activation of TLR4 by LPS from Gram-negative gut bacteria triggers downstream MyD88-dependent NF-κB signaling. creating a pro-inflammatory environment that contributes to low-grade systemic and ovarian inflammation[10–13]. Our study demonstrated that curcumin intervention effectively down-regulated the expression levels of TLR4, MyD88 and NF-κB p65 in ovarian tissue, suggesting that curcumin may reduce the inflammatory cascade and, consequently, alleviate PCOS.

In this study, several limitations should be considered. the role of curcumin in improving gut microbiota and its impact on intestinal mucosal permeability and ovarian inflammation in PCOS remains unclear. Future research will be needed to address these questions and further clarify the mechanisms by which curcumin exerts its effects.

Conclusion

This study highlights the significant role of intestinal mucosal barrier damage and systemic inflammatory response in PCOS pathophysiology, particularly implicating the activation of the TLR4/MyD88/NF-κB signaling pathway. Curcumin emerges as a promising therapeutic intervention, demonstrating the ability to mitigate ovarian tissue damage, restore intestinal mucosal integrity, reduce mucosal permeability, and alleviate systemic and ovarian inflammation by inhibiting the TLR4/MyD88/NF-κB signaling pathway. These findings support curcumin's potential as a promising intervention for the prevention and treatment of PCOS.

Data availability

Data is provided within the manuscript or supplementary information files.

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Declarations

Competing interests

The authors declare no competing interests.

Additional information