doi.org/10.36721/PJPS.2026.39.11.305.1

Duo Nang Decoction enhances endometrial receptivity in PCOS rats by upregulating caveolin-1 expression

Guozeng Wang[1,2], Wenrong Zhao[3], Longfei Ma[4], Zhongping Cheng[1]* and Huayun Xu[5]*

[1]Department of Obstetrics and Gynecology, Shanghai Tenth People's Hospital, School of Clinical Medicine of Nanjing Medical University, Shanghai, China

[2]Department of Obstetrics and Gynecology, Shanghai East Hospital, School of Medicine, Tongji University, Shanghai, China

[3]Department of Comprehensive Cancer Therapy, Shanghai East Hospital, School of Medicine, Tongji University, Shanghai, China

[4]Community Health Service Center of Ruijin No.2 Road Sub-district, Huangpu District, Shanghai, China

[5]Department of Traditional Chinese Medicine, Shanghai General Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China

Abstract: **Background**: Duo Nang Decoction (DND) is widely used for treating polycystic ovary syndrome (PCOS)-related infertility. However, the molecular mechanisms underlying its action remain unclear. In a previous study, downregulation of caveolin-1 (Cav-1) was shown to impair endometrial angiogenesis, a key determinant of endometrial receptivity. **Objectives**: This research study aimed to elucidate the influence and potential molecular mechanisms of DND on endometrial receptivity, specifically focusing on Cav-1 in PCOS rats. **Methods**: Sprague Dawley (SD) rats (females, 3-week-old) were randomly categorized into the DND and aspirin cohorts. After successful PCOS modeling, the rats were orally administered DND or aspirin, respectively. Then, ovulation was induced and mating was performed. The rats were euthanized on the 2nd and 5th day of conception and the endometrium was extracted for histological evaluation *via* hematoxylin and eosin (HE) staining. Furthermore, immunohistochemistry (IHC) staining was carried out to assess Cav-1, vascular endothelial growth factor (VEGF) and β-catenin levels, as well as endometrial microvascular density (MVD). Moreover, reverse transcription polymerase chain reaction (RT-PCR) was used to measure the mRNA levels of VEGF and Cav-1 in the endometrium of both groups. **Results**: The HE and IHC staining, as well as RT-PCR analysis of endometrial tissue slices, revealed that on the 2nd and 5th day of conception, both groups indicated significantly increased endometrial thickness, MVD and elevated levels of VEGF, Cav-1 and β-Catenin. However, the MVD in the DND group was substantially higher relative to the aspirin group. **Conclusion**: This study revealed that DND significantly enhanced endometrial angiogenesis and improved endometrial receptivity in PCOS rats. Mechanistically, the effects of DND on endometrial receptivity may be associated with the upregulation of Cav-1 and β-catenin. However, the specific mechanism of action warrants further research.

Keywords: Cav-1; Duo Nang Decoction; Endometrial angiogenesis; Endometrial receptivity; Polycystic ovarian syndrome

Submitted on 09-10-2025 – Revised on 10-05-2026 – Accepted on 25-05-2026

INTRODUCTION

Polycystic ovarian syndrome (PCOS) is a multifaceted reproductive endocrine and metabolic condition frequently observed in females of reproductive age, having a rate of prevalence ranging from 11% to 13% (Lizneva *et al.*, 2016; Stener-Victorin *et al.*, 2024). It is a major cause of female infertility, accounting for about 75% of ovulation disorders (Ramezani Tehrani *et al.*, 2014). The ovulation rate of PCOS females can be improved clinically; however, their pregnancy rate remains very low, which requires an urgent solution. Successful conception entails the development of a responsive endometrium during the implantation window (Schulte *et al.*, 2015). It has been observed that in PCOS patients, insulin resistance, high luteinizing hormone levels and hyperandrogenism lead to insufficient uterine blood flow perfusion, which contributes significantly to infertility after induced ovulation due to decreased endometrial receptivity (Lam *et al.*, 2009; Li *et al.*, 2017).

DND is a traditional Chinese medicine developed by Professor Xiaosun Cai and used to treat PCOS-related infertility. The literature has indicated that DND can tonify the kidneys, nourish blood, dissolve phlegm, clear the meridians and effectively support pregnancy. Cav-1 is the primary structural protein of caveolae, predominantly expressed in vascular endothelial cells and associated with angiogenesis (Ito *et al.*, 2019). Moreover, it has been found to mediate tumor angiogenesis (Zhang *et al.*, 2009). In some tumors, Cav-1 can activate the signaling pathway of β-catenin (Yu *et al.*, 2014) and modulate its downstream target gene, VEGF, to promote angiogenesis and tumor invasion (Thirunavukkarasu *et al.*, 2008). In a previous study, a close association was observed between reduced endometrial angiogenesis during the implantation

**Corresponding author:* e-mail: mdcheng18@tongji.edu.cn; bullforg_xu@126.com

window and decreased Cav-1 expression in PCOS rats (Wang and Xu 2024). As an extension of the previous study, this research investigated the effects of DND and aspirin on PCOS rats to evaluate the related molecular mechanisms of DND on endometrial receptivity, specifically focusing on Cav-1. The findings of this study will provide novel experimental evidence supporting the application of DND against PCOS-related infertility.

MATERIALS AND METHODS

Experimental animals

Sprague Dawley rats (n = 12, age = 3 weeks, female, virgin, weight = 50 ± 10 g) with 4–5 days of estrus cycle were procured from the Beijing Vital River Laboratory Animal Technology Co., Ltd (SYXK-2021-0007) and kept in standard animal care facilities. All *in vivo* analyses were carried out per the Animal Research: Reporting of *In Vivo* Experiments (ARRIVE) guidelines (Percie du Sert, *et al.*, 2020) and approved by the Ethical Committee of the Shanghai Jiao Tong University, School of Medicine (project approval number: 2021AWS0171).

Construction of the PCOS model

All rats were adaptively fed a high-fat pellet diet for 3 days, then randomly assigned to the DND and aspirin groups (n = 6 per group). Based on a previously reported (Lee*, et al.*, 1991) method, 60 mg/kg of dehydroepiandrosterone (DHEA) was dissolved in oil injection (0.2 mL). Both groups were given DHEA + oil (0.2 mL) subcutaneously on the back of the neck for 20 days. Vaginal smears were collected starting on day 10 to assess two consecutive estrous cycles. The successful establishment of the PCOS model was confirmed by the presence of keratinocytes.

DND preparation

The DND was prepared per the original decoction composition and contained 12 g *Rehmanniae Radix* Preparata (Shudi), 27 g *Gleditsiae Spina* (Zaojiaoci), 12 g *Angelicae Sinensis* Radix (Danggui), 15 g *Astragali Radix* (Huangqi), 9 g Chuanxiong *Rhizoma* (Chuanxiong), 6 g *Citri Reticulatae* Pericarpium Viride (Qingpi), 9 g *Rehmanniae Radix* (Shengdi), 6 g *Citri Reticulatae* Pericarpium (Chenpi), 9 g Cistanches Herba (Roucongrong) and 12 g *Epimedii Folium* (Yinyanghuo). These compounds were then boiled at 100℃ for 20 minutes, filtered and concentrated to form a water decoction with a concentration of 0.50 g/mL. The aspirin tablet was dissolved in distilled water at a rate of 4.81 mg/kg to form a suspension.

Animal grouping and treatments

In the previous study (Wang and Xu, 2024), a control group and a PCOS model group were established. In the present study, 12 PCOS model rats were randomly allocated to two groups: the DNDtreated group (n = 6) and the aspirin treated group (n = 6). The DND and aspirin groups received 12.28 g of DND/kg and aspirin suspension, respectively, *via* daily gavage. Both groups received a 20 mL/kg gastric lavage once daily for 10 consecutive days. The medication doses were recalculated every 5 days after weighing. Twenty-four hours after receiving the drugs, both rat groups were given 0.52 mg/kg letrozole by gavage. On day 2 after gavage, the rats were mated with male SD rats at 16:00. The presence of pessaries was assessed the following morning and rats with pessaries were considered pregnant.

Tissue processing

Rats were euthanized on day 2 or day 5 after conception. Under sterilized conditions, the bilateral uteruses were excised and the uterine horns were cut from the uterus to separate the endometrium.

Estrous cycle and weight change

Starting on the 10th day of oil injection, vaginal smears from rats were collected every morning and fixed for microscopic examination of estrous cycle changes. The rats' body weights were measured every week.

HE staining

On the 2nd to 5th day of conception, the uterine tissue of rats was collected, submerged in paraffin, sliced (5 µm thick) and stained with HE. The samples were analyzed using a light microscope to observe endometrial thickness.

Immunohistochemistry for endometrial MVD, Cav-1, VEGF and β-catenin

On the 2nd and 5th day of pregnancy, the endometrial tissue of rats was collected and submerged in paraffin as described above. The IHC staining was performed as mentioned previously (Wang and Xu, 2024). The following primary antibodies were employed: MVD (Abcam, ab198823), Cav-1 (Abcam, ab32577), VEGFA (Abcam, ab1316) and β-catenin (Abcam, ab32572). The secondary antibodies included Biotinylated goat-anti-rabbit IgG (Beyotime, A0208) and Biotinylated goat-anti-mouse IgG (Beyotime, A0216). The IHC staining of endometrial tissues was performed per the protocol of Weidner *et al*, (Weidner*, et al.*, 1991) to evaluate MVD.

RT-PCR analysis

The endometrial tissue from both groups was collected on the 5th day of pregnancy for total RNA extraction. Then, the purity and concentration of acquired RNA were evaluated. The RNA was then used to prepare cDNA according to the instructions provided in the reverse transcription kit (Ambion). Subsequently, PCR amplification was carried out. The relative mRNA expression of Cav-1 and VEGF was assessed via the$2^{-\Delta\Delta ct}$ method. Table 1 enlists the primer sequences.

Table 1: The primer sequences of genes utilized for the analysis of RT-PCR.

Gene	Reverse (5'-3')	Forward (5'-3')
β-actin	AGGGAGCGCGTAACCC	TCGTACCACTGGCATTGTGAT
Cav-1	CATAGGGATGCCGAAGATGGT	CAACGACGACGTGGTCAAGA
VEGF	AATTGGACGGCAATAGCTGC	CGACAGAAGGGGAGCAGAAAG

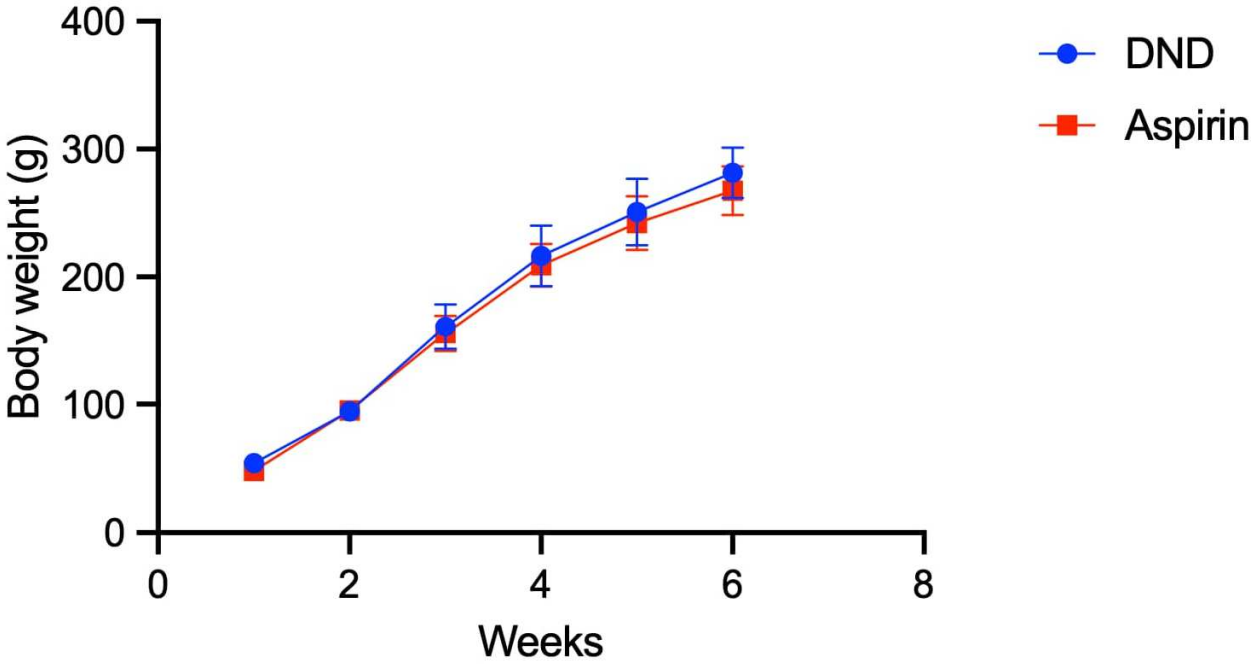

Fig. 1: Graph indicating the increase in body weight of the two groups of rats. Due to high-fat feeding, the body weight of the DND and aspirin groups increased significantly from the 4th week, but no significant difference was observed at the 6th week.

Statistical analysis

Data were analyzed using SPSS 21.0 (IBM Corp., Armonk, NY, USA. Data with normal distributions are depicted as mean ± standard deviation. The inter-group differences were analyzed by an independent *t*-test. Furthermore, the associations between Cav-1 and β-catenin, as well as between β-catenin and VEGF, were assessed using Pearson correlation analysis. A probability (p) value of ≤ 0.05 was deemed statistically significant.

RESULTS

PCOS rats had increased body weight and an arrested estrous cycle

The results showed that high-fat feeding increased body weight in both groups of rats. The body weight of rats increased from the 4th week onward; however, by week 6, there was no significant difference between the groups (Fig. 1). The vaginal smear analysis revealed that the regular estrous cycle was arrested in both groups, indicating the successful establishment of the PCOS model.

DND increased endometrial thickness

HE staining of the endometrium was performed to assess endometrial thickness in the Control, PCOS, DND and aspirin groups (Fig. 2). The results showed that compared with control rats, on days 2 and 5 of pregnancy (implantation window), the endometrium thickness of PCOS rats was substantially reduced ($p < 0.01$). Furthermore, relative to the PCOS rats, the endometrium thickness of the DND rats was markedly increased ($p < 0.01$). However, no significant differences were observed relative to the rats ($p > 0.05$).

DND upregulated endometrial Cav-1 and VEGF, as well as increased MVD in PCOS rats during the implantation window

To investigate the alterations in Cav-1, VEGF and MVD expression in four groups, IHC staining was carried out. The results revealed that the endometrial expression of Cav-1, VEGF and MVD of the PCOS cohort at the implantation window stage was significantly reduced relative to the control group (Fig. 3). Furthermore, DND substantially elevated these levels in PCOS rat groups ($p < 0.01$), similar to the effect of aspirin ($p > 0.05$).

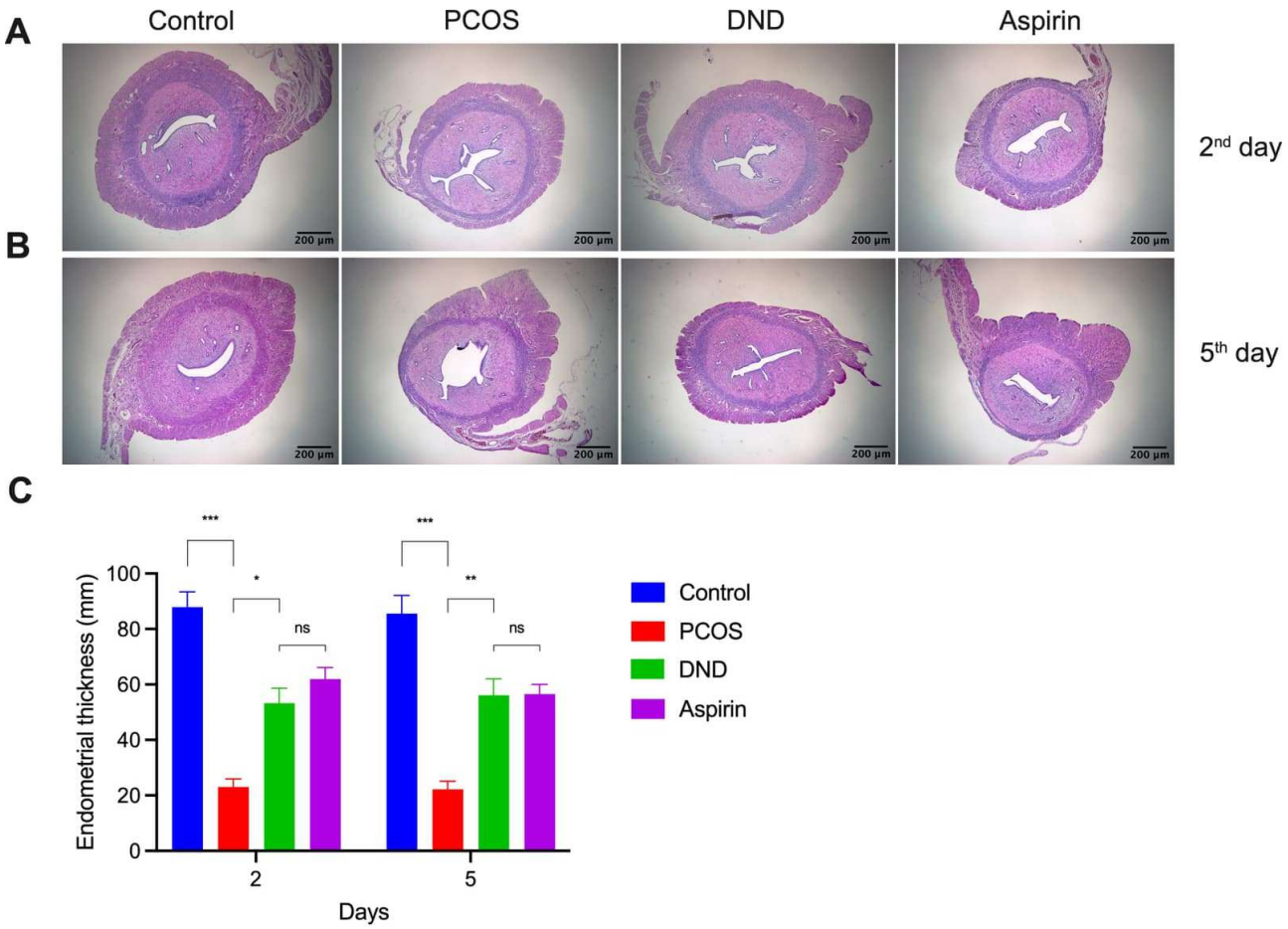

Fig. 2: The endometrial thickness was evaluated by HE. (A and C) The study was carried out on days 2 and 5 of pregnancy; **(**B and C) to analyze endometrial thickness. Magnification: 100×. HE: hematoxylin-eosin staining. Data are expressed as means ± SD. ns, non-significant, $^{*}p < 0.05$, $^{**}p < 0.01$ and $^{***}p < 0.001$.

However, as the gestation progresses, the effect of DND on increasing MVD becomes more pronounced relative to that of aspirin ($p < 0.05$). Moreover, on day 5 of conception, the VEGF and Cav-1 mRNA levels in the endometria of PCOS animals were reduced relative to the control rats; these levels were evidently increased after DND intervention ($p < 0.01$) and were not significantly different from the aspirin group ($p > 0.05$).

During the implantation window, DND upregulated β-catenin in PCOS rats

IHC staining of endometrial tissues from the four groups was performed on days 2 and 5 of pregnancy to assess β-catenin levels (Fig. 4). The results demonstrated that endometrial β-catenin levels in PCOS rats were substantially reduced during the implantation window relative to the control cohort ($p < 0.01$). Furthermore, compared with the PCOS group, β-catenin levels in the DND group were significantly increased ($p < 0.05$), but did not differ significantly from those in the aspirin group ($p > 0.05$).

Endometrial Cav-1 expression is associated with β-catenin, which in turn is related to VEGF

The correlation analysis revealed a positive correlation between Cav-1 levels and endometrial β-catenin ($r = 0.821$, $p < 0.05$) in the PCOS group, during the implantation window (Fig. 5A). Moreover, β-catenin was positively correlated with VEGF ($r = 0.856$, $p < 0.05$) (Fig. 5B). These data revealed that Cav-1 essentially modulates endometrial angiogenesis, which may be related to the β-catenin signaling pathway.

DISCUSSION

PCOS is a common endocrine and metabolic disorder affecting ovulation in females of reproductive age. The literature suggests that in PCOS patients, endometrial development and embryonic receptivity disorders are important causes of infertility after ovulation induction (Schulte*, et al.*, 2015). Effective angiogenesis is essential for establishing endometrial receptivity and is a prerequisite for successful embryo implantation and pregnancy. Therefore, angiogenesis has become a significant focus in the investigation of endometrial receptivity.

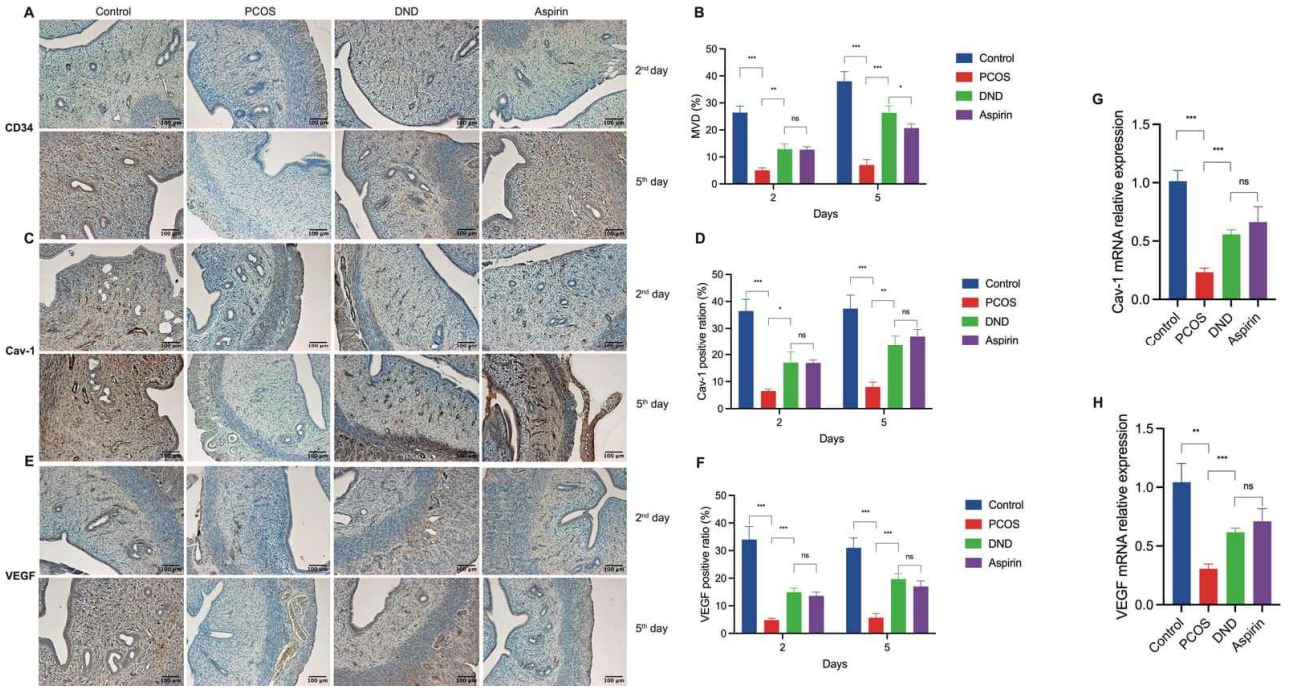

Fig. 3: The endometrial tissue protein expression levels of CD34, Cav-1, and VEGF were assessed by IHC, while the endometrial tissue mRNA levels of VEGF and Cav-1 were evaluated by RT-PCR. (A and B) IHC assessment of CD34 on days 2 and 5 of pregnancy; (C and D) Cav-1; and (E and F) VEGF; (G and H) RT-PCR assessment of VEGF and Cav-1 on day 5 of pregnancy. Magnification: 200×. IHC: Immunohistochemistry. MVD: Micro-vascular density. RT-PCR: Real-time reverse transcription polymerase chain reaction. Data are expressed as means ± SD. ns, non-significant, $^{*}p < 0.05$, $^{**}p < 0.01$ and $^{***}p < 0.001$.

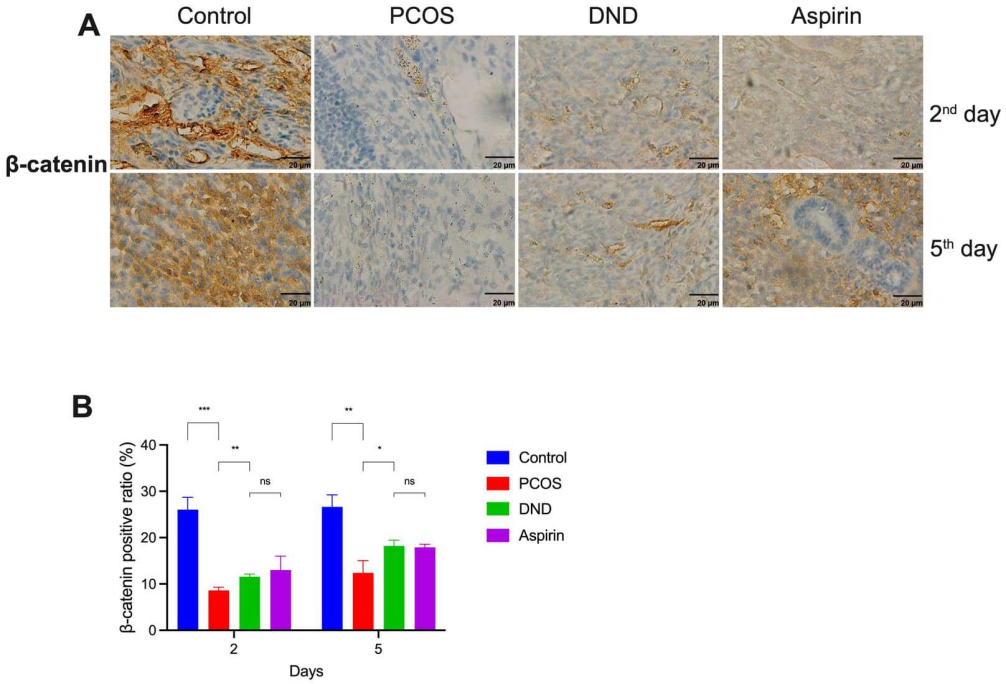

Fig. 4: Representative IHC images indicated β-catenin expression in endometrial tissues. (A and B) On days 2 and 5 of pregnancy, β-catenin expression in the endometria of PCOS rats was substantially reduced relative to the control group, but was higher in the DND group than in the PCOS group, with significant differences. Original magnification: 400×. IHC: immunohistochemistry. Data are expressed as means ± SD. ns, non-significant, $^{*}p < 0.05$, $^{**}p < 0.01$, and $^{***}p < 0.001$.

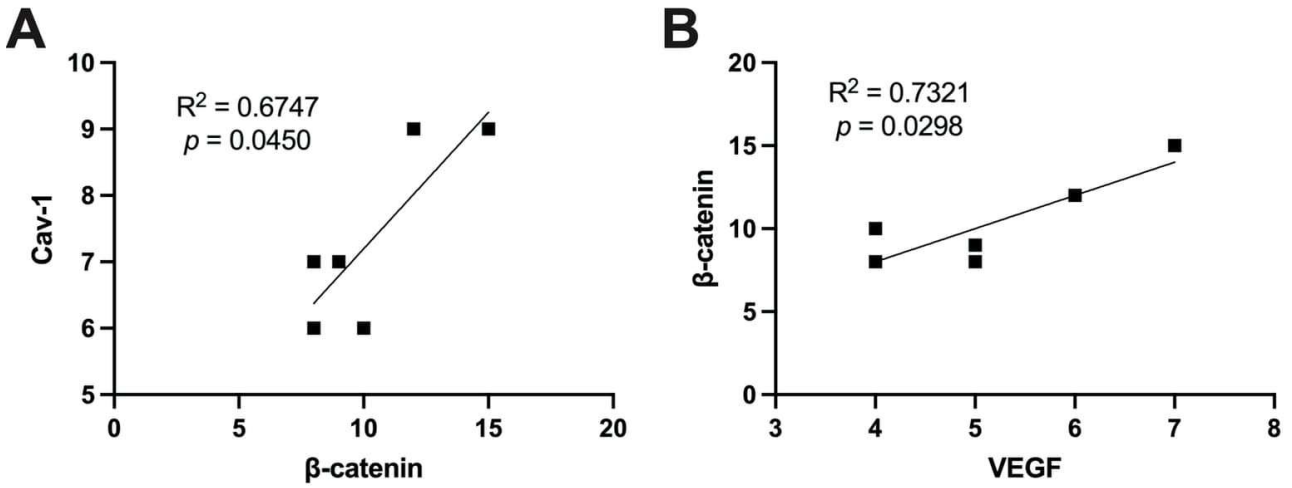

Fig. 5: Association of β-catenin with Cav-1 and VEGF. (A and B) The correlational analysis indicated that in the PCOS group, β-catenin expression was positively correlated with Cav-1 and VEGF. The correlation coefficient for β-catenin and Cav-1 was r = 0.821 (p = 0.045), while that for β-catenin and VEGF was r = 0.856 (p = 0.030).

Caveolae are structures resembling cytoplasmic membrane sacs, created by the inward invagination of the cytoplasmic membrane, with caveolin as the primary component of their outer layer. The Caveolin family comprises Cav-1, Cav-2 and Cav-3. Cav-1 serves as the principal structural protein, resembling a hairpin within Caveolae and functions as a distinguishing protein. It is prominently expressed in vascular endothelial cells. The research indicated that Cav-1 is linked with angiogenesis (Zhang *et al.*, 2020) and acts as a scaffold protein, playing an important role in regulating the proliferation, migration and other signal transduction processes of endothelial cells (Caliceti *et al.*, 2014). Our previous study revealed that Cav-1 could modulate endometrial angiogenesis in PCOS rats during the implantation period and was positively associated with VEGF (Wang and Xu, 2024). Consistently, some studies showed that Cav-1 gene silencing markedly reduced the number of VEGF-mediated blood vessels (Chidlow and Sessa, 2010). Therefore, it is inferred that Cav-1 may be a key and upstream molecule of VEGF, as they both modulate angiogenesis. β-catenin is considered a key factor in the classical Wnt signaling pathway and has been associated with Cav-1 in hepatocellular carcinoma (Gao *et al.*, 2022) and esophageal squamous cell carcinoma (Zhang *et al.*, 2020). In the classical Wnt/β-catenin signaling pathway, high Cav-1 levels increase intracellular free β-catenin levels, which then translocate to the nucleus and stimulate VEGF (a downstream target gene) (Gao *et al.*, 2022; Yu *et al.*, 2014). VEGF is a key marker of endometrial receptivity (Guo *et al.*, 2021) and is related to endometrial neovascularization and embryo implantation (Zhao *et al.*, 2019). In PCOS rats, the endometrial Cav-1, β-catenin and VEGF levels were decreased during the implantation window. Furthermore, β-catenin was found to be positively linked with the Cav-1 and VEGF expression. Therefore, reduced Cav-1 levels may impair endometrial receptivity in PCOS patients by impairing angiogenesis in the endometrium, a process linked to the Cav-1/β-catenin signaling pathway.

Professor Xiaosun Cai is a seventh-generation heir of the Cai family's gynecology department in Shanghai and is a national expert in traditional Chinese medicine. He discovered DND for treating PCOS-related infertility. The DND comprises Cistanches Herba (Roucongrong) combined with *Epimedii Folium* (Yinyanghuo), which can tonify the kidneys and fill essence, *Angelicae Sinensis* Radix (Danggui) and Chuanxiong *Rhizoma* (Chuanxiong), which promote blood circulation and regulate menstruation, *Astragali Radix* (Huangqi), which tonifies qi and promotes blood production, *Gleditsiae Spina* (Zaojiaoci), which promotes blood circulation and unblocks collaterals, *Citri Reticulatae* Pericarpium Viride (Qingpi) combined with *Citri Reticulatae* Pericarpium (Chenpi) , which dries dampness and reduces phlegm and *Rehmanniae Radix* (Shengdi) and *Rehmanniae Radix* Preparata (Shudi), which nourish blood and regulate menstruation. MVD is an important parameter reflecting angiogenesis. The endometrial blood flow was assessed by IHC staining of endometrial microvascular endothelial cells with a CD34 antibody to elucidate endometrial MVD (Yu *et al.*, 2019). In a previous study, Cav-1 was shown to modulate endometrial angiogenesis in PCOS rats during the implantation period and to be positively associated with VEGF (Wang and Xu 2024). However, this research found that DND can markedly increase MVD and this effect is more significant than that of aspirin ($p < 0.05$). In addition, DND can substantially elevate levels of Cav-1, β-catenin and VEGF, as well as endometrial thickness, which is similar to aspirin ($p > 0.05$). These results are consistent with previous studies, suggesting that kidney-tonifying and blood-circulating medications may elevate estradiol levels (Li *et al.*, 2020),

induce angiogenesis, promote endometrial blood supply, substantially enhance endometrial receptivity (Huang *et al.*, 2010; Hyun *et al.*, 2024) and improve the clinical pregnancy rate (Lian *et al.*, 2013).

The study has several limitations. First, the study involved only animal experiments and the sample size was relatively small. Second, toxicological verification of the administered dose was not performed and should be addressed in future investigations. Third, due to funding constraints, further optimization of the Western blot analysis of β-catenin pathway-related protein expression could not be performed. In future studies, the safety and efficacy of DND in patients with PCOS-related infertility will be further evaluated, and the optimal therapeutic dosage will be determined through clinical trials.

CONCLUSION

In summary, this study revealed that during the implantation window, PCOS rats exhibit reduced endometrial angiogenesis, attributable to reduced Cav-1 expression. Furthermore, DND significantly improved endometrial angiogenesis, Cav-1 and β-catenin expression and endometrial thickness and the specific mechanism warrants further research.

Acknowledgements
None.

Authors' contributions
Guozeng Wang: Contributed to the conception and design of the work, acquisition of data, analysis and interpretation of data and drafting of the manuscript; Wenrong Zhao and Longfei Ma: Contributed to animal experiment and collected the data; Zhongping Cheng and Huayun Xu: Organized the whole study and rewrote the manuscript. All authors read and approved the final manuscript.

Funding
This research was supported by the Special Project of Traditional Chinese Medicine Scientific Research of Shanghai Health and Family Planning Commission (2016LP024) and "Xinglin Xinxing" Talent Project of Shanghai [ZY(2018-2020)-RCPY-3006].

Ethical approval
This experimental protocol was approved by the Clinical Center Laboratory Animal Welfare and Ethics Committee of Shanghai General Hospital (Ethics approval number: 2021AWS0171). This study was performed in adherence with the ARRIVE guidelines. See supplementary file for the ARRIVE checklist.

Data availability statement
The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Conflict of interest
The authors declare no conflict of interest.

Supplementary data
https://www.pjps.pk/uploads/2026/07/SUP1784976670.pdf

REFERENCES

Caliceti C, Zambonin L, Rizzo B, Fiorentini D, Vieceli Dalla Sega F, Hrelia S and Prata C (2014). Role of plasma membrane caveolae/lipid rafts in VEGF-induced redox signaling in human leukemia cells. *Biomed Res. Int.,* **2014**(1): 857504.

Chidlow JHJ and Sessa WC (2010). Caveolae, caveolins and cavins: complex control of cellular signalling and inflammation. *Cardiovasc. Res.,* **86**(2): 219–225.

Gao J, Zhang J, Xia L, Liang X, Ding W, Song M, Li L and Jia Z (2022). Up-regulation of caveolin 1 mediated by chitosan activates Wnt/ beta-catenin pathway in chronic refractory wound diabetic rat model. *Bioengineered,* **13**(1): 1388–1398.

Guo X, Yi H, Li TC, Wang Y, Wang H and Chen X (2021). Role of Vascular Endothelial Growth Factor (VEGF) in Human Embryo Implantation: Clinical Implications. *Biomolecules,* **11**(2): 253.

Huang DM, Huang GY and Lu FE (2010). Effects of Bushenyiqihexue formula on the endometrial gland apoptosis in mice with blastocyst implantation dysfunction. *J. Tradit. Chin. Med.,* **30**(3): 196–200.

Hyun JY, Jung HS and Park JY (2024). Herbal therapeutics for female infertility: A systematic review and meta-analysis. *J. Ethnopharmacol.,* **319**(Pt 2): 117258.

Ito A, Shiroto T, Godo S, Saito H, Tanaka S, Ikumi Y, Kajitani S, Satoh K and Shimokawa H (2019). Important roles of endothelial caveolin-1 in endothelium-dependent hyperpolarization and ischemic angiogenesis in mice. *Am. J. Physiol.-Heart Circul. Physiol.,* **316**(4): H900–H910.

Lam P, Johnson I and Raine-Fenning N (2009). Endometrial blood flow is impaired in women with polycystic ovarian syndrome who are clinically hyperandrogenic. *Ultrasound Obstet. Gynecol.,* **34**(3): 326–334.

Lee MT anderson E and Lee GY (1991). Changes in ovarian morphology and serum hormones in the rat after treatment with dehydroepiandrosterone. *Anat. Rec.,* **231**(2): 185–192.

Li HF, Shen QH, Chen WJ, Chen WM, Feng ZF and Yu LY (2020). Efficacy of traditional Chinese medicine tonifying kidney (Bushen) and activating blood (Huoxue) prescription for premature ovarian insufficiency: A systematic review and meta-analysis. *Evid.-based Complement Altern. Med.,* **2020**: 1789304.

Li R, Wu J, He J, Wang Y, Liu X, Chen X, Tong C, Ding Y, Su Y, Chen W, Zhang C and Gao R (2017). Mice endometrium receptivity in early pregnancy is impaired

by maternal hyperinsulinemia. *Mol. Med. Rep.,* **15**(5): 2503–2510.

Lian F, Wang RX, Ma FM, Sun ZG, Wang LH and Shi L (2013). Effects of Chinese medicines for tonifying the kidney on DNMT1 protein expression in endometrium of infertile women during implantation period. *J. Altern. Complement Med.,* **19**(4): 353–359.

Lizneva D, Suturina L, Walker W, Brakta S, Gavrilova-Jordan L and Azziz R (2016). Criteria, prevalence and phenotypes of polycystic ovary syndrome. *Fertil. Steril.,* **106**(1): 6–15.

Percie du Sert N, Hurst V, Ahluwalia A, Alam S, Avey MT, Baker M, Browne WJ, Clark A, Cuthill IC, Dirnagl U, Emerson M, Garner P, Holgate ST, Howells DW, Karp NA, Lazic SE, Lidster K, MacCallum CJ, Macleod M, Pearl EJ, Petersen OH, Rawle F, Reynolds P, Rooney K, Sena ES, Silberberg SD, Steckler T and Würbel H (2020). The ARRIVE guidelines 2.0: Updated guidelines for reporting animal research. *PLoS. Biol.*, **18**(7): e3000410.

Ramezani Tehrani F, Minooee S and Azizi F (2014). Comparison of various adiposity indexes in women with polycystic ovary syndrome and normo-ovulatory non-hirsute women: A population-based study. *Eur. J. Endocrinol.,* **171**(2): 199–207.

Schulte MMB, Tsai J-h and Moley KH (2015). Obesity and PCOS: The effect of metabolic derangements on endometrial receptivity at the time of implantation. *Reprod. Sci.,* **22**(1): 6–14.

Stener-Victorin E, Teede H, Norman RJ, Legro R, Goodarzi MO, Dokras A, Laven J, Hoeger K and Piltonen TT (2024). Polycystic ovary syndrome. *Nat. Rev. Dis. Primers,* **10**(1): 27.

Thirunavukkarasu M, Han Z, Zhan L, Penumathsa SV, Menon VP and Maulik N (2008). Adeno-sh-beta-catenin abolishes ischemic preconditioning-mediated cardioprotection by downregulation of its target genes VEGF, Bcl-2 and survivin in ischemic rat myocardium. *Antioxid. Redox Signal.,* **10**(8): 1475–1484.

Wang G and Xu H (2024). Decreased Expression of Cav-1 Is Associated with Compromised Endometrial Angiogenesis during the Implantation Window in PCOS Rats: A Prospective Randomized Laboratory-Based Study. *Clin. Exp. Obstet. Gynecol.,* **51**(1): 4–8.

Weidner N, Semple JP, Welch WR and Folkman J (1991). Tumor angiogenesis and metastasis--correlation in invasive breast carcinoma. *N. Engl. J. Med.,* **324**(1): 1–8.

Yu H, Shen H, Zhang Y, Zhong F, Liu Y, Qin L and Yang P (2014). CAV1 promotes HCC cell progression and metastasis through Wnt/beta-catenin pathway. *PloS one,* **9**(9): e106451.

Yu X, Gao C, Dai C, Yang F and Deng X (2019). Endometrial injury increases expression of hypoxia-inducible factor and angiogenesis in the endometrium of women with recurrent implantation failure. *Reprod. Biomed. Online,* **38**(5): 761–767.

Zhang C, Wu Q, Huang H, Chen X, Huang T, Li W, Zhang J and Liu Y (2020). Caveolin-1 upregulates Fut8 expression by activating the Wnt/beta-catenin pathway to enhance HCC cell proliferative and invasive ability. *Cell Biol. Int.,* **44**(11): 2202–2212.

Zhang ZB, Cai L, Zheng SG, Xiong Y and Dong JH (2009). Overexpression of caveolin-1 in hepatocellular carcinoma with metastasis and worse prognosis: Correlation with vascular endothelial growth factor, microvessel density and unpaired artery. *Pathol. Oncol. Res.,* **15**(3): 495–502.

Zhao DM, Shan YH, Li F, Jiang L and Qu QL (2019). Correlation between endometrial receptivity with expressions of IL-1 and VEGF in rats with polycystic ovary syndrome. *Eur. Rev. Med. Pharmacol. Sci.,* **23**(13): 5575–5580.