Journal of Experimental and Clinical Application of Chinese Medicine

REVIEW

Open Access

Research Progress on Cangfu Daotan Pills in the Treatment of Polycystic Ovary Syndrome

Sisi Liu [1,#], Yiyang Lu [2,#], Jiayi Lin [3], Qihui Shao [1], Hailing Pan [4], Xiaohong Fang [2,*], Meiya Li [5,*]

1. The fourth school of clinical meducine, Zhejiang Chinese Medicial University, 310053 Hangzhou , China
2. Hangzhou TCM Hospital Affiliated to Zhejiang Chinese Medicial University, 310007 Hangzhou, China
3. The Second school of clinical meducine, Zhejiang Chinese Medicial University, 310053 Hangzhou, China
4. Department of Oncology, Traditional Chinese Medical Hospital of Wenling affiliated to Zhejiang Chinese Medical University, 317500 Taizhou, Zhejiang, China
5. Academy of Chinese Medical Sciences, Zhejiang Chinese Medical University, 310053 Hangzhou, China

# The authors contributed equally to this work.

DOI: https://doi.org/10.62767/jecacm601.5826

Keywords

Polycystic ovary syndrome
Cangfu Daotan Pills
Sex hormones
Metabolic disorders
Endometrial blood flow
Varian granulosa cell autophagy

* **Correspondence**

Meiya Li,
Academy of Chinese Medical Sciences, Zhejiang Chinese Medical University, Hangzhou 310053, China
E-mail: lmeiya@126.com
Xiaohong Fang,
Hangzhou TCM Hospital Affiliated to Zhejiang Chinese Medicial University, Hangzhou 310007, China
E-mail: fxh13527806@163.com

Received: 15 December 2024
Revised: 15 January 2025
Accepted: 19 February 2025
Published: 28 March 2025

Journal of Experimental and Clinical Application of Chinese Medicine **2025; 6(1): 45-57**

Abstract

Polycystic ovary syndrome (PCOS) is a heterogeneous disease characterized clinically by high androgen levels, persistent anovulation, and polycystic ovarian changes, whose incidence has been on the rise, becoming a major factor in anovulatory infertility among women of childbearing age. Cangfu Daotan Pills, as a traditional Chinese medicine compound formula, has the effects of dispelling dampness and phlegm, tonifying the kidney, promoting blood circulation, and removing blood stasis, and can regulate physiological functions of the body through multiple targets and pathways. This study reviews the research progress on the treatment of PCOS with Cangfu Daotan Pills, exploring its mechanisms of action, which significantly improve ovarian function and promote ovulation in PCOS patients by regulating sex hormone levels, improving the inflammatory microenvironment, correcting metabolic disorders, regulating uterine blood flow, and reducing autophagy of ovarian granulosa cells, thus increasing pregnancy rates. Additionally, the main active ingredients of Cangfu Daotan Pills are summarized, highlighting their therapeutic effects through the regulation of multiple key targets and signaling pathways. In terms of clinical application, Cangfu Daotan Pills used alone, in combination with Western medicine, or in conjunction with external treatments has shown good efficacy and low side effects. Future research is expected to further explore the efficacy principles of Cangfu Daotan Pills through multidisciplinary approaches, providing a scientific basis for the refinement of clinical treatment plans and the development of new drugs.

1 Introduction

Polycystic ovary syndrome (PCOS) is a heterogeneous disorder that is clinically characterized by hyperandrogenism, persistent anovulation, and polycystic changes in the ovaries. The clinical manifestations mainly encompass metabolic abnormalities such as insulin resistance (IR) and obesity, menstrual disorders, and infertility, often accompanied by symptoms like acne, hirsutism, and acanthosis nigricans [1]. According to statistical data, the prevalence of PCOS was 5.6% in 2010, which increased to 8.6% by 2020, affecting 24 million women and emerging as a major factor contributing to anovulatory infertility among women of childbearing age [2]. The pathogenic mechanism of PCOS remains unclear, however, current research indicates that it is related to genetic, environmental, chronic inflammation, and autoimmune factors [1].

Currently, the treatment for PCOS predominantly relies on Western medicine, which demonstrates significant efficacy but is also associated with numerous side effects. Research indicates that traditional Chinese medicine (TCM) offers an effective alternative for treating PCOS with fewer toxic side effects [3]. The Chinese herbal medicine formula Cangfu Daotan Pills possesses functions such as dispelling dampness and phlegm, tonifying the kidneys, promoting blood circulation, and alleviating blood stasis, it components can regulate physiological functions of the body through multiple targets, pathways, and mechanisms [4].

This study aims to review the latest insights into the use of Cangfu Daotan Pills in the management of PCOS. It summarizes its clinical efficacy and explores its mechanisms of action from various prespectives, including hormone level regulation, correction of metabolic disorders, adjustment of endoimetrial blood flow, and reduction of autophagy in ovarian granulosa cells. These findings provide a valuable reference for further clinical application of Cangfu Daotan Pills.

2 The mechanism of action of Cangfu Daotan Pills in the treatment of PCOS

The mechanism of action of Cangfu Daotan Pills in the treatment of PCOS is relatively intricate. It engages in various biological processes by regulating hormone secretion levels, modulating inflammatory responses, enhancing insulin sensitivity, correcting lipid metabolism disorders, regulating blood flow to the uterine endometrium, and reducing autophagy in ovarian granulosa cells. These processes are interrelated an collectively contribute to and the therapeutic effects observed in PCOS management.

2.1 Regulation of hormone levels

The hypothalamic-pituitary-ovarian (HPO) axis constitutes a comprehensive and coordinated neuroendocrine system. The hypothalamus regulates the synthesis and secretion of luteinizing hormone (LH) and follicle-stimulating hormone (FSH) by the pituitary gland through the release of gonadotropin-releasing hormone (GnRH). This regulatory mechanism ultimately influences ovarian membrane cells and granulosa cells, thereby governing normal follicular development as well as synthesis and release of sex hormones [5].

Patients with PCOS exhibit defects in both the synthesis and secretion of gonadotropins, frequently characterized by elevated LH levels alongside an altered LH/FSH ratio [5]. Increased LH levels can adversely affect follicular maturation, diminish granulosa cells populations, and reduce aromatase expression. These changes lead to decresased estrogen levels, inhibition of FSH secretion, and consequently result in impaired normal ovulation [6]. Furthermore, due to the inherently unstable feedback effect of estrogen on pituitary LH secretion, negative feedback regulation may causes an upregulation of the LH/FSH ratio. This alteration further disrupts normal follicular development and contributes to ovulatory dysfunction [7].

Elevated LH concentrations promote excessive androgen production from ovarian membrane cells [8], while a high androgen environment can inhibit both follicular development and maturation. This results in follicular atresia while maintaining estradiol levels in a persistently low state within the ovaries. Numerous studies have domonstrated that Cangfu Daotan Pills can effectively regulate hormone levels via the HPO axis, significantly enhancing ovarian function in patients with PCOS, promoting ovulation, and increasing pregnancy rates [9].

Luo S [10] conducted a study using modified Cangfu Daotan Pills on PCOS rat models. Revealing that this

treatment could significantly reduce serum levels of testosterone (T) and LH, while increasing estrodial (E2) and FSH levels. Furthermore, the treatment was associated with an increase in the number of ovarian luteal tissues, thickening of the ovarian granulosa cell layer, thinning of the ovarian membrane cells, and a reduction in cystic follicles. These findings suggest that modified Cangfu Daotan Pills may ameliorate ovarian morphological abnormalities and enhance function by modulating hormonal levels. Clinical trials have corroborated these results, demonstrating that Cangfu Daotan Pills can effectively regulate hormone levels. Huang W [11] further supported these findings through clinical trials indicating that the modified Cangfu Daotan Pills granules can assist in the treating phlegm-damp type PCOS-related infertility by improving ovulation rates, reducing LH and T levels, enhancing ovarian function, and decreasing the risk of early miscarriage. Additionally, some studies have suggested that this drug may exert its therapeutic effects by regulating the peripheral blood PI3K/AKT signaling pathway [12].

2.2 Alleviating inflammatory conditions

The pathogenesis of PCOS is associated with chronic low-grade inflammation. Patients typically present with bilateral ovarian enlargement, thickening and sclerosis of tunica albuginea, significant cortical fibrosis, and pronounced proliferation of ovarian stroma, accompanied by extensive infiltration of inflammatory cells within the ovarian tissue [5]. Furthermore, levels of inflammatory mediators such as white blood cell count, C-reactive protein (CRP), tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), interleukin-18 (IL-18), and interleukin-1 beta (IL-1β) are markedly elevated in affected individuals [13]. Systemic chronic low-grade inflammation is often associated with obesity, IR, and hyperandrogenemia, additionally, localized ovarian inflammation can adversely impact follicular development and ovulation [14].

Clinical trials and animal studies suggest that Cangfu Daotan Pills may reduce the levels of inflammatory factors in patients with PCOS and model animals, likely through the MEK-ERK/NF-κB pathway. Clinical trials conducted by Li X [15] demonstrate that a modified version of Cangfu Daotan Pills can lower the levels of inflammatory factors in PCOS patients, including TNF-α, IL-17, and CRP, thereby inhibiting inflammatory responses. Research by Ling J [16] confirmed throughanimal experiments that Cangfu Daotan Pills inhibits the activation of the MEK-ERK signaling pathway and the transcription activity of NF-κB by reducing the expression of TNF-α as well as its receptors TNFR1 and TNFR2, thus improving the ovarian morphology and function in PCOS rat models. Additionally, research conducted by Luo S [17] indicated that Cangfu Daotan Pills might alleviate body weight issues in PCOS rats while enhancing ovarian morphology and hormone levelsthis is achieved through downregulation of the serum TNF-α levels alongside an increase in TNF-α receptor expression, which reverses the upregulation of p65, p-p65, and JNK expression. These findings collectively reveal that Cangfu Daotan Pills has potential therapeutic effects on PCOS symptoms via modulation inflammatory signaling pathways and mitigation of inflammatory responses.

2.3 Addressing metabolic disorders

2.3.1 Enhance Insulin Sensitivity

IR plays an important role in the pathogenesis of PCOS. IR is defined as the diminished effectiveness of insulin in facilitating glucose uptake and utilization by various organs, tissues, and cells when the physiological levels of insulin are present in the body. To maintain relatively normal blood glucose levels, the body compensatorily elevates insulin production, resulting in compensatory hyperinsulinemia [18]. Excessive LH can directly stimulate both theca and granulosa cells within ovarian follicles or induce the synthesis of insulin-like growth factor 1 (IGF-1) receptors. This stimulation leads to an overproducion of androgens [19], which contributes to follicular atresia, inhibits ovulation, and maintains persistently low estradiol levels [5]. Concurrently, hyperinsulinemia may prompt a reduction in sex hormone-binding globulin synthesis by the liver, thereby increasing free androgens concentrations. Moreover hyperinsulinemia can inhibit ovulation through enhanced production of anti-Müllerian hormone [20], while simultaneously insulin-like growth factor binding protein 1 (IGFBP-1) production. This suppression results in elevated free IGF-1 levels that further stimulate androgen biosynthesis, consequently raising circulating free androgen levels [21]. The application of Cangfu Daotan Pills has been shown to improve IR via the NF-κB/LCN-2 signaling pathway.

Research conducted by Lan L [22] demonstrated that the

combination of Cangfu Daotan Pills with Western medicine treatments significantly reduces insulin resistance index (HOMA-IR) and resistin levels, exhibiting a more pronounced effect in the treatment group. This suggests that Cangfu Daotan Pills may enhance insulin sensitivity, thereby promoting glucose utilization and uptake by the ovaries. Furthermore, Yang S [23] indicated that Cangfu Daotan Pills can further decrease levels of C-peptide, FINS, and HOMA-IR while simultaneously increasing HOMA-β, thus effectively improving IR. Additionally, several studies have suggested that Cangfu Daotan Pills may modulate insulin-related signaling pathways by downregulating NF-κB/LCN-2 protein expression and upregulating INSR/IRS-1/Glut4 gene expression, which contributes to improved ovarian function in cases of PCOS-related IR [24].

2.3.2 Correcting lipid metabolism disorders

Patients with PCOS exhibit a complex array of metabolic abnormalities, among which lipid metabolism disorders are particularly prominent. The pathogenesis may be related to the abnormal expression of ApoA1, regulatory factors related to lipid metabolism, as well as adiponectin, leptin, and resistin, along with their corresponding genes [25,26]. Lipid metabolism disorders are primarily manifested as decreased HDL-C and increased concentrations of triglycerides (TG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), apolipoprotein B (apo B), and the apoB/apoA1 ratio [18]. Dysregulation of lipid metabolism is closely linked to obesity, IR, hyperandrogenism, and hyperlipidemia-all of which adversely affect ovulatory function. During oocyte meiosis maturation, lipids not only serve as an energy source but also regulate oocyte meiosis through various signaling pathways. Abnormal metabolism of glycerol and glycerophospholipids may lead to endoplasmic reticulum stress, impacting oocyte maturation. High concentrations of fatty acids caused by lipid metabolism disorders have "lipotoxicity" on oocyte growth and development, inhibiting oocyte development. Therefore, improving lipid metabolism is one of the important therapeutic strategies for treating PCOS. Studies have found that Cangfu Daotan Pills can improve serum lipid metabolism indicators in PCOS, thereby enhancing ovulation and the conditions for endometrial implantation.

Zhang Y [27, 28] found that Cangfu Daotan Pills significantly reduces levels of TG, TC, LDL-C, ApoB/ApoA1, and serum leptin, while increasing HDL-C and adiponectin levels. This formulation improves lipid metabolism, enhances conditions for endometrial implantation, and promotes the expression of estrogen receptors, thereby restoring ovulatory function and achieving therapeutic effects in patients with PCOS. Liu Y [29] further reported that this formula can improve lipid metabolism in obese PCOS model rats, potentially through the regulation of key factors within the Leptin/AMPK signaling pathway.

2.4 Regulating the blood flow of the endometrium

Modern medicine believes that hemodynamics is intricately linked to the functional status of the reproductive organs. Factors such as blood perfusion and blood supply within ovarian tissue have a significant impact on the growth and development of the endometrium and follicles. Consequently, abnormal hemodynamics in the ovarian artery is recognized as one of the main causes of infertility [30]. The active components in the formula of Cangfu Daotan Pills have been shown to markedly enhance blood circulation in the ovarian region, increase blood supply to the ovaries, facilitate follicle maturation, promote ovulation, and aid in corpus luteum formation [31]. Among them, *Chuanxiong Rhizoma* and *Angelicae Sinensis Radix* can improve pelvic microcirculation and augment blood flow to both the uterus and ovaries [30].

Research conducted by Ding C [32] indicates that the modifications to Cangfu Daotan Pills can elevate levels of integrin β 3, ER and PR within the endometrium. This enhance leads to improved uterine receptivity, increased blood flow in the endometrium among patients with PCOS patients, ultimately resulting in a higher pregnancy rate.

Clinical trial studies have confirmed that Cangfu Daotan Pills can reduce blood viscosity through its phlegm-resolving and dampness-drying properties [33]; this improvement positively affects hemodynamic indicators of the ovarian interstitial artery by increasing end-diastolic volume (EDV) and peak systolic velocity (PSV) on the ovulating side while simultaneously decreasing pulsatility index (PI) and resistance index (RI). Such changes enhance arterial blood flow velocity in both ovaries and uterine arteries, thereby improving overall perfusion.

The promotion blood circulation in the uterine artery

increases blood perfusion, facilitates the transition of the endometrium to type A, thickens the endometrium, improves menstrual disorders, promotes ovulation function, and enhances hormone levels. Additionally, adjunctive treatment with Cangfu Daotan Pills can further improve clinical efficacy and alleviate clinical symptoms [9,30,31].

2.5 Decreasing autophagy in ovarian granulosa cells

Autophagy is a cellular process that degrades and recycle proteins and organelles to maintain intracellular homeostasis. While it generally serves a protective function for cells, excessive autophagy can lead to cell death [34]. Additionally, autophagy plays an important role in the growth and development of ovarian follicles. Ovarian granulosa cells (GCs) are essential for follicular development, primarily by providing nutrients to oocytes, regulating their growth and maturation, and synthesizing ovarian hormones that stimulate follicle growth [35].

Under normal conditions, GCs stabilize through autophagy, thereby regulating follicular growth and steroid hormone synthesis. However, abnormal activation of GCs autophagy may contribute to the onset of PCOS [36]. Research has domonstrated that ovarian granulosa cells from patients with PCOS exhibit excessive autophagic activity. This dysregulation results in impaored sex hormone synthesis and secretion as well as reduced follicular growth and development, ultimately leading to follicular atresia and disruption of normal ovarian function [37].

The PI3K/Akt signaling pathway plays a crucial role in regulating various physiological processes, including cell proliferation, differentiation, autophagy, apoptosis, angiogenesis, and metabolism. This pathway is particularly significant in the function of granulosa cells, oocyte maturation, and IR observed in patients with PCOS [38,39]. Xie P [40] conducted animal experiments that demonstrated Cangfu Daotan Pills may inhibit GCs autophagy by activating the PI3K/Akt/mTOR signaling pathway. This activation leads to a reduction in the expression levels of Beclin 1, LC3I, LC3II, and p62 mRNA within cells while simultaneously increasing the expression of PI3K, Akt, mTOR mRNA and protein. Consequently, this modulation improves sex hormone levels and addresses follicular development disorders. Related clinical studies have further corroborated the therapeutic effect of Cangfu Daotan Pills on PCOS, these findings suggest that its mechanism may be linked to the regulation of the PI3K/AKT signaling pathway. Additional, Liu W [12] found that treatment with Cangfu Daotan Pills effectively regulates sex hormones as well as glucose-lipid metabolism. This effect is likely associated with the inhibition of peripheral blood PI3K/AKT signaling pathway.

In addition, studies have demonstrated that Cangfu Daotan Pills can regulate the TGF-β1/Smad3 signaling pathway, thereby influencing granulosa cell function. This modulation occurs through a reduction in TGF-β1 protein levels in both serum and follicular fluid, as well as decreased Smad3 and SKP1 protein levels within granulosa cells. Consequently, this leads to diminished autophagy and apoptosis of GCs， promotes stability within the ovarian microenvironment, and enhances oocyte growth and maturation [41].

Furthermore, it may also interact with the miR-17-5p/ATG7 pathway to mediate autophagy by upregulating miR-17-5p expression while inhibiting ATG7 expression. This action serves to mitigate excessive autophagy in granulosa cells [42]. Alternatively, Cangfu Daotan Pills may regulate the PKP3/MAPK/ERCC1 axis by enhancing PKP3 promoter methylation which results in reduced PKP3 expression. This process subsequently inactivates the MAPK pathway and decreases ERCC1 expression, ultimately promoting proliferation of granulosa cells while inhibiting apoptosis [43]. Additionally, it has been suggested that this formulation regulates m6A methylation within ovarian tissue; this regulation inhibits the Wnt/β-catenin signaling pathway which improves sex hormone levels while reducing ovarian autophagy and apoptosis-thereby promoting cellular proliferation [44]. Moreover, Cangfu Daotan Pills appears to inhibit overexpression of FOXK1 in ovarian granulosa cells potentially via suppression of the AMPK/mTOR pathway, such inhibition contributes to decrease in GCs apoptosis and autophagy [45]. Therefore, Cangfu Daotan Pills may effectively regulate abnormal autophagy and apoptosis of GCs through multiple pathways. This multifaceted approach not only improves overall ovarian function but also increases both quantity and quality of oocytes among patients with PCOS, consequently enhancing rates of high-quality embryos and pregnancy outcomes.

3 The primary active components of Cangfu Daotan Pills

and their mechanisms of action in the treatment of PCOS

Cangfu Daotan Pills comprises nine medicinal ingredients, each containing various effective active components. A study conducted by Hu P [46] utlized the TCM Systems Pharmacology Database and Analysis Platform (TCMSP) alongside relevant literature to search for and screen the active components and targets of Cangfu Daotan Pills. This investigation identified 140 primary components associated with the treatment of PCOS, which exert their effects through 105 potential targets. The ten key active components identified are: quercetin, kaempherol, luteolin, β -sitosterol, rotonin, cavinton, 7-hydroxy-2-methyl-3-phenylbenzopyran-4-one, mediacarpin, isorhamnetin, and plant sterols (Table 1). These active components play a crucial role in mediating various biological processes, including gene transcription regulation lipid metabolism, inflammatory microenvironment, IR, the sex hormone axis, atherosclerosis, interleukin immune regulation, and other signaling pathways. They achieve this by modulating key targets such as JUN, MAPK3, HSP90AA1, MAPK1, ESR1, NR3C1, APP, MAPK14, MAPK8, VEGFA, EGFR, RB1, AR, and IL6. Consequently, these interactions significantly influence drug response as well as nutrition and lipid metabolism; they also affect reactive oxygen species production, glucose metabolism, and steroid hormones levels to elicit therapeutic effects.

Table 1 The main active ingredients and action mechanisms of Cangfu Daotan Pills.

Ingredient	Action mechanism	Reference
quercetin	Reduce IR levels, T and LH concentrations; upregulate the expression of adiponectin receptors and AMPK/SIRT-1 axis; induce the expression of GLUT4 and ERα genes in the uterus, improving IR status. Regulate levels of IL-1β, IL-6, and TNF-α; promote MAPK phosphorylation, suppress IL-6 and IL-8 expression to improve the inflammatory microenvironment. Regulate AKT to improve glucose metabolism. Regulate related estrogen receptor signaling pathways, affecting the proliferation, apoptosis, and hormone release of ovarian cells. Regulate pathways such as progesterone, cyclin B1, and p53 to produce concentration-dependent effects on ovarian function.	[47-50]
	Inhibit the TLR/NF-κB pathway, improve the inflammatory microenvironment, and reverse IR.	[46,51]
	Restore oocyte maturation and ovulation by regulating CNP/NPR2 gene and protein.	[52]
Shanzhiside	Activate the adenosine monophosphate-activated protein kinase (AMPK)/nuclear factor E2 related factor 2 (Nrf2)/heme oxygenase-1 (HO-1) signaling pathway, inhibit apoptosis, reduce the expression of inflammatory factors and adhesion molecules, and alleviate oxidative stress.	[53]
	Inhibit the expression of transforming growth factor-β1 (TGF-β1); inhibit the Toll-like receptor 4 (TLR4), nuclear factor-κB (NF-κB), and STAT signaling pathways; inhibit IKKβ activation, block the phosphorylation of IκBα, reduce the release of inflammatory mediators, and exert anti-inflammatory and antioxidation effects.	[54]
luteolin	Activate AMPK α 1 signaling in adipose tissue macrophages to improve insulin resistance IR.	[47,55]
	Inhibit ROS production, activate antioxidant enzymes, suppress the action of iNOS, iNOS expression, and NO generation, exert antioxidant effects. Inhibit IL-1β, IL-4, IL-5, IL-6, IL-8, IL-10, IL-13, TNF-α, IFN-β, and GM-CSF, elevate IL-10 levels, and inhibit chemokines that control immune cell migration and localization; suppress COX-2 expression, reduce PGE2 production, decrease mast cell release of PGD2, inhibit the synthesis of LTB4, and reduce leukotriene release; inhibit AKT phosphorylation, suppress IκB degradation, inhibit NF-κB subunit translocation, alter HDAC and HAT	[56,57]

	activity, and suppress NF-κB signaling pathway; inhibit HMGB1 expression and the action of c-Jun and AKT, regulate MAPK and AP-1 signaling pathways; reduce the binding activity of STAT, phosphorylation of STAT1, and expression levels of IRF-1, and regulate JAK-STAT signaling pathway; lower the gene and protein levels of TNF-α, IL-6, IL-8, GM-CSF, TNF-α, and COX-2, and reduce intracellular Ca2+ release, inhibit mast cell degranulation, exert anti-inflammatory effects.	
	Inhibit the secretion of MMP-9, downregulate the expression of ERK2, and exert anti-ovarian cancer effects; increase the weight, diameter, endometrial thickness, and epithelial cell height of the uterus, showing estrogen-like effects.	[58]
β-amyranol	Reduce the level of reactive oxygen species (ROS) in oocytes, upregulate superoxide dismutase, and inhibit oxidative stress; increase the expression of anti-apoptotic gene BCL-2, inhibit the expression of pro-apoptotic genes Caspase3 and BAX, and reduce the level of cell apoptosis; enhance mitochondrial membrane potential and upregulate TFAM gene expression.	[59]
	Inhibit neutrophil recruitment, downregulate the expression of inflammatory factors such as IL-8 and myeloid differentiation factor 88, regulate immune response, and enhance anti-inflammatory capacity.	[60]
	Lower TC, TG, LDL-C, reduce blood lipid levels in the body, and regulate lipid metabolism.	[61]
	Lowering ovarian index, LH, COX-2, and T, increasing uterine index, integrin αvβ3, LIF, FSH, and P levels, improving uterine receptivity in PCOS, and enhancing hormone levels.	[62]
naringenin	Blocking RIP1 phosphorylation inhibits the RIP1-RIP3-MLKL signaling pathway, reduces inflammation levels, and alleviates necrosis and apoptosis of ovarian granulosa cells.	[63]
	Reduce pathological damage such as follicular cystic dilation, promote the phosphorylation of the PI3K/AKT pathway and pathway-related proteins IRS-1, GSK-3β, and the expression of GLUT4 protein, improve the disorder of reproductive hormone secretion, alleviate IR, and lower blood sugar, blood lipid levels, and PTEN protein expression. Alleviate IR that occurs in PCOS by inhibits the expression of PKGIα.	[64,65]
	Reduce estradiol and T levels, and increase progesterone and dehydroepiandrosterone levels; improve ovarian damage; decrease IL-1β, IL-6, and TNF-α levels in the ovaries while increasing IL-10 levels; reduce the expression levels of Cleaved Caspase-9, p75NTR, and pNF-κB in ovarian tissues. Protect the ovaries and regulate hormones by inhibiting the NF-κB signaling pathway.	[66]
	Return to esturs cycle, reduce body weight and IR, and improve ovarian function of PCOS rats with letrozole by activating SIRT1/PGC-1α and changing the characteristic intestinal microbiota and its metabolites.	[67]
nobiletin	Reduce reactive oxygen species and malondialdehyde levels, and enhance antioxidant enzyme activity; decrease the production of IL-1β and TNF-α, regulate the NF-κB signaling pathway, and exert anti-inflammatory effects; lower serum total cholesterol, triglycerides, and low-density lipoprotein, to achieve a hypolipidemic effect.	[68]
	By reducing the expression of PPARγ and C/EBPα, it inhibits lipid accumulation in adipocytes and the differentiation of 3T3-L1 preadipocytes, lowers TG content, blood	[69]

	lipids, and body weight, and regulates lipid metabolism, glucose metabolism, inflammation, energy balance, and oxidative stress.	
Dehydrocorybulbine	Regulating extracellular matrix, anti-oxidative stress and genes, exerting hepatoprotective effects and anti-hepatic fibrosis, regulating lipid metabolism, antibacterial and antiviral, analgesia and sedation.	[70]
Emodin methyl ether	Downregulate TNF- α , IL-6, and IL-17A, upregulate IL-10, exerting an anti-inflammatory effect.	[71]
2 ''-O-rhamnosyl icariside II	Affecting MAPKs and NF-κB signaling pathways, inhibiting the expression of COX-2, regulating nitric oxide synthase activity, exerting anti-inflammatory effects; inhibiting platelet aggregation, reducing thrombosis; scavenging free radicals, exerting antioxidant functions; inhibiting adipocyte differentiation, preventing obesity; lowering blood pressure, lowering blood sugar.	[72]
	Regulation of the AKT-FOXO1 signaling pathway to improve IR.	[73]
Phytosterols	Inhibit the expression of transport proteins related to cholesterol intestinal absorption, suppress the activity of rate-limiting enzymes in the process of endogenous cholesterol synthesis, increase the expression of proteins related to cholesterol reverse transport, enhance cholesterol excretion, regulate liver lipid metabolism, reduce VLDL secretion, lower cholesterol and triglycerides, and improve blood lipid levels.	[74]
	Regulate the levels of cytokines and other inflammatory factors, modulate the NF-κB signaling pathway, and exert anti-inflammatory effects.	[75]

4 Clinical Application of Cangfu Daotan Pills for PCOS

4.1 The efficacy of Cangfu Daotan Pills in Combination with Western Medicine for the treatment of PCOS

In clinical practice, traditional Western medicine treatments for patients with PCOS, including Ethinyl Estradiol and Cyproterone Acetate tablets, Clomiphene Citrate capsules and/or Clomiphene treatment, demonstrate significant efficacy when combined with modifications of the Cangfu Daotan Pills. Jing F [31] conducted a study involving PCOS patients from the hospital, dividing them into two groups. The control group received Ethinyl Estradiol and Cyproterone Acetate tablets along with Clomiphene Citrate capsules, while the observation group was administered additional treatment with Cangfu Daotan Pills. Notably, the observation group exhibited significantly greater improvements in menstrual regularity, biphasic basal body temperature patterns, pregnancy rates, and hormone levels compared to the control group. Furthermore, both ovulation rates and pregnancy rates in the control group were markedly lower than those observed in the observation group, underscoring the remarkable effectiveness of Cangfu Daotan Pills modification treatment. An F [76] randomly assigned 96 PCOS patients into two evenly distributed groups. The control group received treatment consisting of Ethinyl Estradiol and Clomiphene, conversely, the observation group underwent additional therapy incorporating Danggui Liu Huang Decoction alongside Cangfu Daotan Pills. After one year of treatment, outcomes such as total effective rate, serum hormone levels (LH, FSH, T, PRL), endometrial thickness, and pregnancy rate were significantly superior in the observation group compared to those in the control group ($p < 0.05$). Huang W [11] conducted a study involving 200 patients with PCOS, who were divided into two groups. The treatment group received Cangfu Daotan Pills in addition to the standard treatment provided to the control group. The results showed that the experimental group exhibited significantly lower levels of FSH, T and BMI compared to the control group. Furthermore, outcomes such as ovulation rate, multiple follicle development rate, clinical pregnancy rate, early miscarriage rate, total effective rate, and improvement in symptom scores were all markedly superior in the treatment group.

4.2 Cangfu Daotan Pills Combined with External Treatment for PCOS

4.2.1 Intradermal Needling

Intradermal needling involves the superficial puncturing of specific acupoints on the skin, allowing direct access to

affected areas and internal organ meridians. This technique sends stimulation signals to the disease site, thereby regulating organ functions to achieve therapeutic effects. It offers several advantages, including reduced pain and increased convenience, while minimizing discomfort associated with tranditional acupuncture and acupoint embedding. Zhang Y [28] used intradermal needling combined with Cangfu Daotan Pills to target acupoints such as Spleen Shu, Kidney Shu, San Yin Jiao, Zu San Li, Feng Long, Ba Liao, Uterus, Xue Hai, Dai Mai, and Shui Dao for the treatment of 117 obese patients with PCOS. The results indicated that except for FSH, significant improvements were observed in BMI, WHR, LH, T, blood lipid levels, fat factors, and TCM syndrome scores within the combined treatment group. These findings suggest that the combination of Cangfu Daotan Pills and intradermal needling can effectively regulate fat factor expression in the body; reduce body weight, regulate blood lipid levels, lower androgen concentrations, alleviate hyperandrogenemia and IR, as well as adjust endocrine levels in patients with PCOS.

4.2.2 Acupuncture

Acupuncture has been demonstrated to be an effective treatment for PCOS in recent years. By stimulating specific acupoints, acupuncture influences the hypothalamic-pituitary-ovarian axis, facilitates the flow of meridians and blood qi within the human body, thereby achieving therapeutic effects for patients with PCOS. Yao Fang [77] conducted a study utilizing Cangfu Daotan Pills in conjunction with acupuncture to treat 38 PCOS patients diagnosed with PCOS over a period of three months. The experimental group exhibited a higher ovulation rate compared to the control group, while also showing lower TCM syndrome scores, hormone levels, ovarian volume, and incidence of adverse drug reactions than those observed in the control group.

4.2.3 Acupoint Embedding

Acupoint embedding is a well-stablished treatment modality in TCM, recognized for its long-acting effects and reduced pain compared to conventional acupuncture. This method has demonstrated significant clinical efficacy in the management of PCOS. Existing clinical studies have indicated that the combination of Cangfu Daotan Pills with acupoint embedding can effectively regulate both intestinal flora [78] and vaginal flora [79] in patients with PCOS, thereby improving their phenotypic characteristics. In a series of clinical investigations, Xie Ch [80] reported that the integration of Jiawei Cangfu Daotan Pills with acupoint catgut embedding therapy resulted in enhanced physical health among obese PCOS patients, leading to a reduction in obesity rate as well as improvements in sex hormone levels and glucose-lipid metabolism. Furthermore, Peng X [81] found that obese PCOS patients receiving modified Cangfu Daotan Pills combined with acupoint catenary embedding exhibited more pronounced menstrual recovery and weight loss when compared to those treated solely with oral Dain-35. These findings suggest that the oral administration of modified Cangfu Daotan Pills alongside acupoint catenary embedding offers promising clinical benefits for individuals suffering from obese PCOS.

5 Conclusion and Expectation

PCOS is a prevalent gynecological disorder among women of childbearing age. Traditional clinical management primarily relies on Western medicine, which often presents numerous side effects. Through the analysis of experimental studies and clinical applications, it has been demonstrated that Cangfu Daotan Pills exhibits significant efficacy in the treatment of PCOS. Therefore, this paper aims to summarize the mechanism by which Cangfu Daotan Pills exerts its therapeutic effects on PCOS. Cangfu Daotan Pills functions through several pathways, including the regulation of hormone levels, improvement of inflammatory responses, correction of metabolic disorders, and reduction of granulosa cell autophagy, etc. Whether used in conjunction with Western medicine or as a standalone treatment, for PCOS patients, this intervention can alleviate symptoms, enhance ovarian function, and increase pregnancy rates while presenting fewer side effects compared to traditional treatment.

Furthermore, research indicates that Cangfu Daotan Pills activates the P13K/AKT signaling pathway, demonstrating notable effectiveness in treating PCOS related to processes such as cell proliferation and differentiation, autophagy apoptosis, angiogenesis and metabolic physiological functions. However, there are still limitations regarding both the clinical application and mechanistic understanding of Cangfu Daotan Pills: ①Insufficient long-term follow-up: The absence of extended follow-up periods in some studies restricts our ability to evaluate the long-term efficacy and

safety profile of Cangfu Daotan Pills; ② Incompleteness concerning autophagy mechanisms associated with apoptosis: There is a scarcity of research focused on how Cangfu Daotan Pills reduces ovarian granulosa cell autophagy; moreover, existing investigations into these mechanisms lack depth. Although further improvements are needed in both clinical practice and fundamental research surrounding Cangfu Daotan Pills' role in treating PCOS, its therapeutic benefits have been substantiated by numerous studies.

In the future, we aim to further investigate the efficacy principles of Cangfu Daotan Pills through multidisciplinary research methodologies. This will include approaches such as evidence-based medicine, molecular-level biological studies, and bioinformatics analysis. Such comprehensive research endeavors could facilitate the precise refinement of clinical treatment protocols and provide a srobust scientific foundation for the development of novel pharmaceuticals.

Acknowledgements

Not applicable.

Conflicts of Interest

No conflict of interest with industry or government funding agency.

Author Contributions

Conceptualization: M.L. and X.F.; Data curation: S.L. and J.L.; Writing-orginal draft: Y.L. and Q.S.; Formal analysis: S.L. and H.P.; Writing-review and editing: M.L. and Y.L. All authors have read and agreed to the published version of the manuscript.

Ethics Approval and Consent to Participate

No ethical approval was required for this review article.

Funding

This research received no external funding.

Availability of Data and Materials

The analyzed data sets generated during the study are available from the corresponding author on reasonable request.

Supplementary Materials

Not applicable.

References

[1] Zhao H, Zhang J, Cheng X, et al. Insulin resistance in polycystic ovary syndrome across various tissues: an updated review of pathogenesis, evaluation, and treatment. *Journal of Ovarian Research* 2023; 16(1): 9.

[2] Yang R, Li Q, Zhou Z, et al. Changes in the prevalence of polycystic ovary syndrome in China over the past decade. *The Lancet Regional Health-Western Pacific* 2022; 25: 100494.

[3] Xu D, Lu M, Liu Y, et al. An Analysis of the Clinical Medication Rules of Traditional Chinese Medicine for Polycystic Ovary Syndrome Based on Data Mining. *Evidence-Based Complementary and Alternative Medicine* 2023; 2023: 6198001.

[4] Qin H, Ma H. Research progress on traditional Chinese medicine for the treatment of polycystic ovary syndrome based on network pharmacology. *Chinese Journal of Traditional Chinese Medicine* 2022; 40(11): 218-222.

[5] Ge Y, Xu W, Guan S, et al. Research progress on the etiology and pathogenic mechanism of polycystic ovary syndrome. *Journal of Jilin University (Medical Edition)* 2024; 50(01): 288-294.

[6] Yang M. Characteristics of LH/FSH in polycystic ovary syndrome and correlation analysis with other clinical indicators. Master ' s Degree. Qinghai University: Xining City, China, 2018.

[7] Gou Y, Zhao F, Hu Z. Research progress on the etiology, pathogenesis, and treatment of polycystic ovary syndrome. *Journal of Practical Internal Medicine of Traditional Chinese Medicine* 2022; 36(04): 11-13.

[8] Tang M, Nie A, Cen M, et al. Expression and significance of serum LH, FSH, E2, T, P, and PRL in patients with infertility. *Contemporary Medicine* 2021; 27(32): 58-61.

[9] Peng X, Li Q, Liao W. Study on the Effect of Cangfu Daotan Pill on Pregnancy Outcomes in Polycystic Ovary Syndrome and Its Mechanisms. *World Traditional Chinese Medicine* 2020; 15(18): 2767-2771.

[10] Luo S, Xu Z, Peng X. Effects of modified Cangfu Daotan Decoction on ovarian morphology and sex hormone levels in rats with polycystic ovary syndrome. *Traditional Chinese Medicine Information* 2014; 31(03): 118-120.

[11] Huang W, Zhou Y, Li F. Clinical effects of modified Cangfu Daotan Decoction granules in assisting the treatment of phlegm-damp type infertility in polycystic ovary syndrome. *Journal of Clinical Rational Drug Use* 2021; 14(31): 91-93.

[12] Liu W, Chen Y, Yang Y, et al. Efficacy of Cangfu Daotan Pill in Treating Phlegm-Damp Type Polycystic Ovary Syndrome and Its Effect on Peripheral Blood PI3K/AKT Signaling Pathway. *Advances in Modern Biomedical Research* 2023; 23(22): 4284-4288.

[13] Zhai Y, Pang Y. Systemic and ovarian inflammation in women with polycystic ovary syndrome. *Journal of Reproductive Immunology* 2022; 151: 103628.

[14] Qu H, Gui W. Chronic low-grade inflammation in women with polycystic ovary syndrome. *International Journal of Reproductive Health / Family Planning* 2024; 43(1): 48-52.

[15] Li X. Efficacy of modified Cangfu Daotan Decoction in treating polycystic ovary syndrome and its effects on serum TNF-α and IL-17 levels. *Sichuan Traditional Chinese Medicine* 2022; 40(09): 171-174.

[16] Ling J, Zhang M, Peng X. Study on the anti-inflammatory mechanism of Cangfu Daotan Decoction in rats with polycystic ovary syndrome. *World Latest Medicine Information Digest* 2021; 21(98): 321-323.

[17] Luo S, Huang C, Ling J, et al. Research on the upregulation of TNF-α and activation of P65 and JNK by Cangfu Daotan Decoction to improve polycystic ovary syndrome. *Jiangxi Traditional Chinese Medicine* 2021; 52(06): 58-61.

[18] Zhao X, Qin L, Liu W. Discussion on the mechanism of treating polycystic ovary syndrome based on abnormal lipid metabolism from the perspective of phlegm. *Shaanxi Traditional Chinese Medicine* 2022; 43(07): 921-924.

[19] Liu X. The Pathogenesis and Progress in Pharmacological Treatment of Polycystic Ovary Syndrome. *Medical Equipment* 2020; 33(06): 203-204.

[20] Xie L, Zhang Y, Gong L, et al. Study on the Pathogenesis of Polycystic Ovary Syndrome Associated with Insulin Resistance. *Chinese Journal of Maternal and Child Health Care* 2019; 34(08): 1926-1929.

[21] Zeng Y, Zhao L. Research Progress on Glucose and Lipid Metabolism Abnormalities in Polycystic Ovary Syndrome. *Journal of Dalian Medical University* 2022; 44(03): 263-268.

[22] Lan L, Bi X, Hu S, et al. Effects of Modified Cangfu Daotan Decoction Combined with Western Medicine on Insulin Resistance Index and Leptin Levels in Patients with Polycystic Ovary Syndrome of Phlegm-Dampness Obstruction Type. *Hebei Journal of Traditional Chinese Medicine* 2019; 41(03): 357-361.

[23] Yang S, Liu J, Tan Y, et al. The Effect of Cangfu Daotan Pill on Pregnancy Outcomes in Obese Patients with PCOS. *Hebei Medical Journal* 2022; 44(01): 31-35.

[24] Liu S, Zhang Y, Yang F, et al. Modified Cangfu Daotan Decoction Ameliorates Polycystic Ovary Syndrome with Insulin Resistance via NF-κB/LCN-2 Signaling Pathway in Inflammatory Microenvironment. *Frontiers in Endocrinology* 2022; 13: 975724.

[25] Wang K, Wu C, Liu M, et al. Clinical Application Value of Combined Detection of TG/HDL-C, ApoB/ApoA1, and Lipid Accumulation Index in Polycystic Ovary Syndrome with Metabolic Syndrome. *Journal of Jiangsu University (Medical Edition)* 2024; 34(05): 438-441.

[26] Hao J, Dou Z, Zhao X, et al. Research Progress on the Impact of Lipid Metabolism Abnormalities in Polycystic Ovary Syndrome on Uterine Receptivity. *Practical Journal of Gynecological Endocrinology* 2024; 11(03): 35-37.

[27] Cheng T. Clinical Observation and Mechanism Study of Cangfu Daotan Decoction in Treating PCOS with Phlegm-Dampness and Lipid Metabolism Abnormalities. Master's Degree. Liaoning University of Traditional Chinese Medicine: Shenyang, China, 2022.

[28] Zhang Y, Zhao J, and Su J. The Effects of Intradermal Needling Combined with Cangfu Daotan Pill on Adipokines, Blood Lipids, Sex Hormones, and Clinical Efficacy in Patients with Obese Polycystic Ovary Syndrome. *Hebei Journal of Traditional Chinese Medicine* 2022; 37(02): 26-30.

[29] Liu Y, Wang X, Zhang Y, et al. Exploring the Mechanism of Cangfu Daotan Decoction in Treating Obese Polycystic Ovary Syndrome Rats from the Perspective of Lipid Metabolism. *Shizhen Guoyi Guoyao* 2023; 34(01): 6-9.

[30] Chen J. The Effect of Cangfu Daotan Pills Combined with Clomiphene Citrate Capsules on Polycystic Ovary Syndrome. *Henan Medical Research* 2021; 30(09): 1674-1676.

[31] Jing F. Clinical Observation of Cangfu Daotan Pills in Treating Infertility due to Phlegm-Dampness Obstruction Type Polycystic Ovary Syndrome. *Clinical Research of Traditional Chinese Medicine* 2020; 12(04): 16-18.

[32] Ding C, Wang C, Yang X, et al. Clinical Study on the Effects of Modified Cangfu Daotan Decoction on Uterine Receptivity in PCOS Patients. *Chinese Journal of Traditional Chinese Medicine* 2013; 31(09): 1997-2000.

[33] Xu D, Xie B, Xu L, et al. Clinical Research on the Efficacy of Modified Cangfu Daotan Pill in Treating Infertility due to Phlegm-Dampness Obstruction Type Polycystic Ovary Syndrome. *Sichuan Traditional Chinese Medicine* 2015; 33(07): 92-94.

[34] Liu S, Yao S, Yang H, et al. Autophagy: Regulator of cell death. *Cell Death & Disease* 2023; 14(10): 648.

[35] Xie T, Zhou H. Research progress on signaling pathways related to proliferation and apoptosis of granulosa cells in polycystic ovary syndrome. *Guangxi Medical Journal* 2024; 46(05): 746-752.

[36] Zhen J, Zhao Z, Wang Z, et al. Autophagy of granulosa cells in the pathological mechanism of polycystic ovary syndrome. *International Journal of Reproductive Health/Family Planning* 2024; 43(02): 150-154.

[37] Kumariya S, Ubba V, Jha RK, et al. Autophagy in ovary and polycystic ovary syndrome: role, dispute and future perspective. *Autophagy* 2021; 17(10): 2706-2733.

[38] Gao Y, Ding J, Yang J. Research progress on the role of the PI3K/Akt signaling pathway in the pathogenesis of polycystic ovary syndrome. *Medical Review* 2022; 28(03): 563-568.

[39] Li X, Liu H, Wang H, et al. Follistatin could promote the proliferation of duck primary myoblasts by activating PI3K/Akt/mTOR signaling. *Bioscience Reports* 2014; 34(5): e00143.

[40] Xie P, Liu J, Zeng L. The effect of Cangfu Daotan Wan serum on autophagy of ovarian granulosa cells in rats. *Chinese Pharmacy* 2021; 32(05): 547-551.

[41] Zhao Y. Exploring the effect of Cangfu Daotan Wan formula granules on IVF-ET outcomes in patients with phlegm-dampness

type polycystic ovary syndrome based on the TGF-β1/Smad3 pathway. Master's Degree. Shandong University of Traditional Chinese Medicine: Jinan, China, 2022.

[42] Yu X. Exploring the mechanism of Cangfu Daotan Wan on phlegm-dampness type polycystic ovary syndrome based on miR-17-5p/ATG7 mediated autophagy. Master's Degree. Shandong University of Traditional Chinese Medicine: Jinan, China, 2022.

[43] Li Y, Wu H, Guo Y, et al. Cangfu Daotan Wan alleviates polycystic ovary syndrome with phlegm-dampness syndrome via disruption of the PKP3/ERCC1/MAPK axis. *Journal of Ovarian Research* 2023; 16(1): 134.

[44] Zhang Y, Zhou H, Ding C. The ameliorative effect of CangFu Daotan Decoction on polycystic ovary syndrome of rodent model is associated with m6A methylation and Wnt/β-catenin pathway. *Gynecological Endocrinology* 2023; 39(1): 2181637.

[45] Wang C, Yu J, Ding C, et al. CangFu Daotan decoction improves polycystic ovarian syndrome by downregulating FOXK1. *Gynecological Endocrinology* 2023; 39(1): 2244600.

[46] Hu P, Li J, Liu D, et al. Exploring the mechanism of Cangfu Daotan Wan in treating polycystic ovary syndrome based on network pharmacology. *Journal of Hainan Medical University* 2021; 27(12): 918-924.

[47] Xia Y, Zhao Y, Chen W, et al. Research on the Molecular Mechanism of Cangfu Daotan Wan in Treating Polycystic Ovary Syndrome Based on Network Pharmacology and Bioinformatics. *World Science and Technology - Modernization of Traditional Chinese Medicine* 2021; 23(05): 1368-1377.

[48] Vaez S, Parivr K, Amidi F, et al. Quercetin and polycystic ovary syndrome; inflammation, hormonal parameters and pregnancy outcome: A randomized clinical trial. *American Journal of Reproductive Immunology* 2023; 89(3): e13644.

[49] Ma C, Xiang Q, Song G, et al. Quercetin and polycystic ovary syndrome. *Frontiers in Pharmacology* 2022; 13: 1006678.

[50] Mihanfar A, Nouri M, Roshangar L, et al. Therapeutic potential of quercetin in an animal model of PCOS: Possible involvement of AMPK/SIRT-1 axis. *European Journal of Pharmacology* 2021; 900: 174062.

[51] Wang Z, Zhai D, Zhang D, et al. Quercetin Decreases Insulin Resistance in a Polycystic Ovary Syndrome Rat Model by Improving Inflammatory Microenvironment. *Reproductive Sciences* 2017; 24(5): 682-690.

[52] Zheng S, Chen Y, Ma M, et al. Mechanism of quercetin on the improvement of ovulation disorder and regulation of ovarian CNP/NPR2 in PCOS model rats. *Journal of the Formosan Medical Association* 2022; 121(6): 1081-1092.

[53] Kang G, Jing Z. Shannaifen Relieves Ox-LDL-Mediated Endothelial Cell Injury by Regulating the AMPK/Nrf2/HO-1 Signaling Pathway. *Chinese Journal of Immunology* 2018; 34(04): 525-530.

[54] Chen D. Study on the Anti-inflammatory and Analgesic Effects of Shannaifen and Its Mechanisms. Master's Degree. Nangjing University of Chinese Medicine: Nanjing, China, 2021.

[55] Zhang L, Han Y, Zhang X, et al. Luteolin reduces obesity-associated insulin resistance in mice by activating AMPKα1 signalling in adipose tissue macrophages. *Diabetologia* 2016; 59(10): 2219-2228.

[56] Yu Q, Wu G. Research Progress on the Anti-inflammatory Mechanism of Luteolin. *Pharmaceutical Research* 2019; 38(02): 108-111, 119.

[57] Huang Y, Zhang X. Luteolin alleviates polycystic ovary syndrome in rats by resolving insulin resistance and oxidative stress. *American Journal of Physiology-Endocrinology and Metabolism* 2021; 320(6): E1085-E1092.

[58] Li X, Guo C. Pharmacological Activity Research of Luteolin. *China Pharmacy* 2007; 18(18): 1421-1424.

[59] Lan X, Zhao B, Zhang B, et al. Effects of β-Sitosterol on In Vitro Maturation of Porcine Oocytes and Embryo Development. *Journal of Animal Husbandry and Veterinary Medicine* 2024; 55(04): 1629-1637.

[60] Zhang P, Liu N, Xue M, et al. Anti-Inflammatory and Antioxidant Properties of β-Sitosterol in Copper Sulfate-Induced Inflammation in Zebrafish (Danio rerio). *Antioxidants (Basel)* 2023; 12(2): 391.

[61] Yuan C, Zhang X, Long X, et al. Effect of β-sitosterol self-microemulsion and β-sitosterol ester with linoleic acid on lipid-lowering in hyperlipidemic mice. *Lipids in Health and Disease* 2019; 18(1): 157.

[62] Yu Y, Cao Y, Huang W, et al. β-Sitosterol Ameliorates Endometrium Receptivity in PCOS-Like Mice: The Mediation of Gut Microbiota. *Frontiers in Nutrition* 2021; 8: 667130.

[63] Wang Y, Zeng K, Yu X, et al. Naringenin Regulates the Expression of miR-29b Affecting the IRS-1/AKT/GLUT4 Signaling Pathway in Insulin Resistance Models of HepG2 and 3T3-L1 Cells. The 13th China Western Nutrition and Health Summit Forum: Chengdu, China 2018.

[64] Xu J, Shen L, Qu Q. Exploring the Mechanism of Naringenin in Improving Insulin Resistance in Polycystic Ovary Syndrome Rats Based on the PI3K/AKT Pathway. *Tianjin Medicine* 2022; 50(03): 270-275.

[65] Xiang Y, Wang M, Yu G, et al. Naringenin alleviates the excessive lipid deposition of polycystic ovary syndrome rats and insulin-resistant adipocytes by promoting PKGIα. *American Journal of Reproductive Immunology* 2023; 90(6): e13795.

[66] Wang L. The Protective and Hormonal Regulatory Effects of Naringenin on Ovaries in Polycystic Ovary Syndrome Model Rats. *Journal of China's Eugenics and Genetics* 2023; 31(04): 721-725.

[67] Wu Y, Yang X, Han B, et al. Naringenin regulates gut microbiota and SIRT1/PGC-1α signaling pathway in rats with letrozole-induced polycystic ovary syndrome. *Biomedicine & Pharmacotherapy* 2022; 153: 113286.

[68] Yang J, Li M, Qin Y, et al. Research Progress on the Pharmacological Activity of Nobiletin. *Journal of Traditional*

Chinese Medicine 2023; 38(04): 719-725.

[69] Vajdi M, Farhangi M. Citrus peel derived poly-methoxylated flavones (PMF). *International Journal for Vitamin and Nutrition Research* 2023; 93(3): 252-267.

[70] Xue F, Wang J. Research Progress on the Pharmacological Effects and Related Mechanisms of Dehydrocarvedilol. *World Latest Medical Information Abstracts* 2017; 17(95): 58-60.

[71] Lai K, Lu G, Huang Z, et al. Research Progress on the Plant Sources and Pharmacological Effects of Medizitan. *Guangxi Medical Journal* 2023; 45(01): 92-97, 106.

[72] Teng D, Luan X. Research Progress on the Pharmacodynamics of Icariside. *Journal of Traditional Chinese Medicine* 2016; 28(04): 593-596.

[73] Bao Q, Li M, Huang R, et al. Mechanism of Icariside Regulating AKT-FOXO1 Pathway to Improve Insulin Resistance in HepG2 Cell Glucose Metabolism. *Food Industry Technology* 2020; 41(23): 320-324.

[74] Lu J, Zheng Z, Xu Z, et al. Research Progress on the Mechanism of Plant Sterols in Lowering Blood Lipids. *Chinese Journal of Traditional Chinese Medicine* 2019; 44(21): 4552-4559.

[75] Liu Y, Li L, Sun W, et al. Research Progress on the Anti-inflammatory Effects of Plant Sterols. *China Oils and Fats* 2022; 47(05): 93-99.

[76] An F. Clinical Observation on the Treatment of Infertility with Polycystic Ovary Syndrome of Phlegm-Dampness Internal Obstruction Type by Modified Danggui Liuhuang Decoction Combined with Cangfu Daotan Pill. *Practical Journal of Chinese Medicine* 2021; 37(08): 1394-1395.

[77] Yao F. Clinical Observation on the Treatment of Infertility with Polycystic Ovary Syndrome of Spleen Deficiency and Phlegm-Dampness Type by Modified Cangfu Daotan Pill Combined with Acupuncture. *Practical Journal of Chinese Medicine* 2024; 40(04): 623-626.

[78] Zhang L. Effects of Cangfu Daotan Pill Combined with Acupoint Embedding on Pregnancy Rate and Gut Flora in Patients with Obese Polycystic Ovary Syndrome. *Chinese Modern Drug Application* 2020; 14(03): 211-213.

[79] Zhang L, Jiang X. Effects of Cangfu Daotan Pill Combined with Acupoint Embedding on Pregnancy Rate and Vaginal Flora in Patients with Obese Polycystic Ovary Syndrome. *Chinese Modern Drug Application* 2020; 14(04): 193-194.

[80] Xie C, Qian P. Discussion on the Clinical Efficacy of Modified Cangfu Daotan Pill Combined with Acupoint Embedding in the Treatment of Obese Polycystic Ovary Syndrome. *Medical Theory and Practice* 2020; 33(24): 4153-4154.

[81] Peng X, Xiao S, Cao J. Observation on the Efficacy of Acupoint Embedding Combined with Traditional Chinese Medicine Modified Cangfu Daotan Pill in Treating Obese Polycystic Ovary Syndrome. *Chinese Community Physician* 2020; 36(13): 93-94.