

Exploring Spleen-Based Treatment Based on the Correlation between Intestinal Flora and Spleen Polycystic Ovary Syndrome

Xiaofan Li^{1,a}, Xia Liu^{2,b,*}, Xinchun Xiao^{2,c}

¹Shaanxi University of Chinese Medicine, Xianyang, 712046, Shaanxi, China

²Affiliated Hospital of Shaanxi University of Chinese Medicine, Xianyang, 712000, Shaanxi, China

^a2290139865@qq.com, ^b644701598@qq.com, ^cxxchsd2003@163.com

*Corresponding author

Abstract: Modern medicine believes that intestinal flora affects the development of polycystic ovary syndrome through five pathways: brain-gut axis, chronic inflammatory state, intestinal mucosal permeability, short-chain fatty acid metabolism, and bile metabolism. According to TCM, the key pathogenesis of polycystic ovary syndrome is spleen deficiency and phlegm obstruction, and it is mostly treated from the spleen. The intestinal flora and the spleen have many physiopathological correlations, and prescriptions for strengthening the spleen have a regulatory effect on the number and structure of intestinal flora, which provides a basis for treating polycystic ovary syndrome from the spleen and broadens the thinking of clinical treatment of polycystic ovary syndrome.

Keywords: intestinal flora; spleen; polycystic ovary syndrome; correlation

1. Introduction

Polycystic ovarian syndrome (PCOS) is a disease of endocrine and metabolic abnormalities that affects about 20-25% of women of reproductive age [1]. It affects approximately 20-25% of women of childbearing age. The main clinical features of PCOS are menstrual disorders or infertility caused by persistent anovulation, altered ovarian morphology, hyperandrogenemia, and an increased risk of metabolic syndrome and long-term complications due to the presence of obesity, insulin resistance and dyslipidemia [2]. External manifestations such as hirsutism, acne, and obesity due to endocrine disorders put PCOS patients in a state of chronic anxiety and depression, and these adverse psychological problems can cause abnormal endocrine stress [3], both of which interact and promote each other to worsen the condition. Therefore, PCOS is a clinical disease in which reproductive and metabolic problems coexist, seriously affecting the reproductive health and physical and mental health of women. In Chinese medicine, PCOS is classified as "late menstruation", "amenorrhea", "infertility" and "obstruction" [4]. The diagnosis and treatment of PCOS is mainly based on the dialectical evidence of the internal organs, blaming the liver, spleen and kidneys for its pathogenesis. The spleen in Chinese medicine has the name of "the source of the posterior sky" and "the source of biochemical energy and blood", and is involved in the transportation and absorption of water and grain essence; the intestinal flora is a complex ecosystem, involving human immunity, metabolism, nutrient absorption, and intestinal barrier. Modern medical research shows that intestinal flora is involved in the development process of PCOS. Therefore, this paper takes the correlation between spleen and intestinal flora as an entry point to discuss the treatment of PCOS from spleen theory.

2. Overview of intestinal flora

The intestinal flora is composed of a complex of microorganisms that reside in the human gastrointestinal tract and form an interdependent and mutually regulated micro-ecosystem. The intestinal flora is known as the "second human genome" because it has 150 times more genes than the host [5]. The composition, distribution and number of intestinal flora are dynamically adjusted according to the genetic, dietary, external environmental and bacterial factors of the host, so stability is the most significant characteristic of intestinal flora. Beneficial bacteria play an important role in maintaining the stability of the intestinal flora, mainly through the barrier effect on pathogenic bacteria, improving the barrier function of the intestinal mucosa, and regulating the immune function in three

ways^[6]. In addition, they prevent potentially harmful bacteria from entering the circulation, stimulate immunity and produce short-chain free fatty acids, and maintain the normal metabolism and immunity of the host intestinal barrier^[7]. The intestinal flora has a wide range of regulatory roles in human nutrient absorption, energy metabolism, immune defense, nervous system regulation and intestinal barrier. Recent studies have shown that imbalance of intestinal microbiota is closely related to many gastrointestinal diseases, metabolic diseases, cardiovascular diseases and tumors. Therefore, restoring the intestinal microecological balance is an important direction for human to overcome various difficult diseases.

3. Intestinal flora and PCOS

Gut flora disorders are an important cause of insulin resistance, hyperandrogenemia, and metabolic syndrome in PCOS patients. In the study by Yang et al.^[8], intestinal flora is a key factor in insulin resistance, which may promote disturbed glucose metabolism in PCOS through the anaphylatoxigenic - bile acid - intestinal FXR signaling pathway; Li^[9] et al. suggested that androgens could reshape the gut microbiota, which is a major regulator of androgen production and metabolism; Wang Cong^[10] et al. elaborated the relationship between gut flora and metabolic syndrome from the perspectives of obesity, diabetes, hyperlipidemia, and hypertension, respectively. Although the pathogenesis of intestinal flora and PCOS is not clear, we found that intestinal flora can affect PCOS through five pathways^[11]: (1) Decreased growth hormone-releasing peptide, a mediator of the brain-gut axis, leads to lower alpha-diversity and increased bacteriophage in PCOS patients, and the metabolic disorders in PCOS patients may be due to lower alpha-diversity leading to altered neurological function. (2) Chronic inflammatory state^[12]: Gut microbial disorders can increase lipopolysaccharide production and put the body in a state of insulin resistance. Long-term chronic low-grade inflammation can further aggravate high androgen levels and obesity in PCOS patients, preventing normal follicle development. (3) Intestinal mucosal permeability^[13]: Increased pro-inflammatory cytokines cause tight junction disassembly and increased intestinal permeability, leading to increased passage of endotoxins from gram-negative colonic bacteria into systemic circulation, resulting in chronic low release of pro-inflammatory factors in PCOS. (4) Short-chain fatty acid metabolism^[14-15]: A decrease in beneficial bacteria may lead to alterations in short-chain fatty acids that contribute to decreased insulin sensitivity and insulin resistance which in turn leads to excessive androgen production by the ovaries and increases free testosterone levels, thus promoting the development of PCOS. (5) Bile metabolic pathway^[16]: Gut microbes are involved in the biotransformation, metabolism, and absorption of bile acids, which decreases interleukin-22 and leads to insulin resistance, hyperandrogenemia, and ovarian dysfunction in PCOS.

4. Correlation between intestinal flora and spleen

The intestinal disorder of the mice in the model of spleen deficiency showed an increase in the number of aerobic bacteria such as *Escherichia coli* and a decrease in the number of anaerobic bacteria such as *Lactobacillus*, indicating a correlation between spleen deficiency and the imbalance of intestinal flora^[17]. Both the intestinal flora and the spleen, which is the hidden symbol of Chinese medicine, are more influenced by the acquired environment compared to the innate generation of genes^[18]. The two have similar roles in the physiological functions of nutrient absorption, energy metabolism, immune defense, nervous system regulation and intestinal barrier, and there are also similarities between spleen dysfunction and diseases caused by imbalance of intestinal flora.

4.1. *The spleen is responsible for the production of Qi and blood and the absorption of nutrients from the intestinal flora*

The essence of water and grain produced by the spleen and stomach can be transformed into Ying Qi and Wei Qi, of which Ying Qi is the material basis for the production of blood, so the spleen and stomach is the source of Qi and blood biochemistry. Zhou Xuehai "read medical essays - qi and blood spirit theory" said: "Ying qi, born in the spleen and stomach, to moisten the tendons, muscles, skin, full of nudge in the blood." Qi and blood provide nutrients for the body's organs and tissues, and play the role of internal nourishment of the five organs, external nourishment of the limbs and bones, skin and hair, thus maintaining the normal physiological function of the organs and bones. Modern research proves that intestinal flora can synthesize essential vitamins, amino acids, niacin, etc., and can also promote the absorption of a variety of mineral elements, and participate in the metabolism of sugar and

protein. The "Suwen symposium" said: "Now the spleen disease cannot for the stomach to move its essence, the limbs cannot endow water and grain gas, gas day to decline, the pulse is not conducive, tendons and muscles, are no gas to produce, so do not use". It shows that the spleen disease is a lack of source of water and grain essence production, resulting in a lack of qi and blood, which makes it difficult to moisten the limbs, and the muscles gradually atrophy. In the treatment of impotence, "Suwen - Impotence Theory" proposed the theory of "treating impotence by taking Yangming alone", while intestinal flora slowed the progression of muscular atrophy lateral sclerosis disease in mice by inhibiting the neurodegenerative microglia phenotype ^[19].

4.2. Spleen main transport and energy metabolism of intestinal flora

Suwen - meridians say: "drink into the stomach, overflowing essence, upward transmission in the spleen, spleen qi dispersed essence, up to the lungs, through the water channel, down to the bladder. Water essence four cloth, five parallel meridians." The absorption, transfer and transformation of various foods and water fluids are all done by the stomach, large and small intestines under the leadership of the main transport function of the spleen. The small intestine's function of receiving the chemical substances and secretion of the clear and turbid is actually the specific embodiment of the Spleen and Stomach's function of ascending the clear and descending the turbid, and the conduction function of the large intestine is also related to the circulation and descending of the gas and the transportation of the Spleen Qi. The intestinal flora can participate in the metabolic process of human body by providing various enzymes and pathways, which is known as "virtual metabolic organ" ^[20]. The intestinal flora can assist the body in digesting carbohydrates that it cannot digest by expressing enzymes. The "Yin Yang Ying Xiang Da Lun" says: "Clear in the lower, then the food and drink". If the spleen is not healthy, it will cause abnormal function of the large and small intestines, resulting in difficulty in defecation, diarrhea, and even incomplete grain, loose bowel movements, and other symptoms. Some studies ^[21] have shown that the subtypes of irritable bowel syndrome caused by different flora imbalance are different and are divided into diarrhea type, constipation type and alternating type.

4.3. Spleen as a defense and intestinal flora immune defense

In the Jin Kui Yao, it is suggested that "a strong spleen is not subject to evil in all seasons", and it is believed that a strong spleen is the key for the body to resist the attack of external evil in all seasons. The intestinal flora, together with intestinal mucus, secretory immunoglobulins, intestinal mucosal epithelium, bile salts, gastric acid, intestine-related lymphoid tissue and hormones, constitute the intestinal mucosal barrier ^[22]. It can prevent harmful substances in the intestine from moving to tissues and organs outside the intestinal cavity and prevent the organism from being attacked by parasitic bacteria and toxins.

4.4. Spleen in Zhiwei Si and intestinal flora regulation of the nervous system

The Suwen - painful theory of lifting" cloud: "thinking out of the heart, and the spleen should be" "thinking then the heart has some storage, the gods have returned, the right qi stay and not work, so the qi knot". Thinking is the will of the spleen, and it is also related to the heart, which is the master of the mind. Excessive thinking or inappropriate thinking will lead to depression of the heart and spleen, resulting in depression, indifference and emotional disturbance. As some studies have shown that intestinal flora is considered to be an important regulator of brain-gut interaction ^[23]. It can be involved in the regulation of the central nervous system through neural, immune and metabolic pathways. Gut flora can affect neurotransmitters such as 5-hydroxytryptamine, norepinephrine, dopamine, glutamate and gamma-aminobutyric acid, which can cause mood disorders such as depression ^[24].

4.5. The spleen governs the blood and the intestinal flora regulates the blood system

The Golden Horoscope says: "the blood of the five viscera and six bowels, all rely on the spleen regulating." Spleen qi is healthy, the water and grain essence source is sufficient, qi is also abundant, qi is strong so that the blood travels in the veins and does not overflow. If the spleen qi weakness, qi on the blood regulating function is weakened, so that the blood does not follow the normal path, resulting in a variety of bleeding disorders. The intestinal flora can maintain hematopoietic homeostasis, which is closely related to its function of synthesizing hematopoietic materials and maintaining the activity of hematopoietic cells ^[18]. If the intestinal flora disorder causes the lack of hematopoietic material and the

inactivity of hematopoietic cells, then the hematopoietic function loses its homeostasis, which also leads to various hemorrhagic diseases.

4.6. Soil congestion and intestinal flora liver lesions

If the spleen is not healthy, water and dampness will stop inside, dampness will trap the spleen and Yang, and dampness will turn into heat and fumigate the liver and gallbladder, resulting in loss of drainage of the liver and overflow of bile, which will lead to liver and gallbladder diseases such as dullness, loose stools, chest distension and pain, vomiting, or even jaundice. Intestinal flora disorders can lead to a large number of bacteria and bacterial metabolites into the liver and intestinal circulation, resulting in liver inflammation, fatty degeneration, fibrosis, which can develop into liver disease, such as alcoholic liver disease, viral hepatitis, fatty liver disease, cirrhosis, liver tumors, etc. [25].

4.7. Internal injury to the spleen and stomach and multi-system lesions of the intestinal flora

Su Wen Yu Ji Zhen Zang Lun" cloud: "the spleen pulse is also earth, orphaned organs to fill the four sides also", "Ling Shu Ben Shen" cloud: "spleen qi deficiency, then ... five organs restless". If the spleen qi is deficient, the other organs are deprived of the moistening of water and grain, resulting in the inability to harmonize the functions of the five organs and the development of various diseases, so there is a theory that "internal injury to the spleen and stomach, all diseases are caused by". Modern research [26] proves that the modern research proves that the dysbiosis of intestinal flora is involved in the occurrence and development of metabolic, immune, endocrine, cardiovascular and cerebrovascular diseases, cancer, etc.

5. Spleen-strengthening formula and intestinal flora

(1) Chinese herbal monomers Clinically, Chinese herbal medicines such as Astragalus, Radix Codonopsis and Atractylodes are mainly used to strengthen the spleen and benefit the qi for the treatment of spleen deficiency. Some studies [17] have shown that saponins, polysaccharides, volatile oils and flavonoids are the main effective components for the treatment of spleen deficiency, and polysaccharide herbal monomers can regulate the structure of intestinal flora [27-28]. Zhang Jingnan et al. [29] found that Astragalus polysaccharides increased the relative abundance of Bacillus phylum and Bifidobacterium phylum, decreased the relative abundance of Bacillus phylum and decreased the level of lipopolysaccharide. Meng Jing Yi [30] showed that Radix Codonopsis polysaccharide could improve gastrointestinal absorption, qi and blood biochemical functions and body immunity in mice with spleen deficiency, thus maintaining homeostasis of gastrointestinal hormones. He Han et al. [31] found that Atractylodes macrocephala polysaccharide could inhibit the growth of harmful bacteria and improve the intestinal flora of rats with spleen deficiency and diarrhea by regulating the abundance of beneficial bacteria.

(2) Chinese herbal compounding Ginseng and Baijusan and Sijunzi Tang are classical prescriptions for the treatment of spleen deficiency evidence, and Ou Guoshen et al. [32] found that the number of probiotic bacteria such as intestinal Bacillus mimicus and Lactobacillus increased, while harmful bacteria such as Clostridium faecalis and Escherichia coli decreased in mice with functional diarrhea model after treatment with Ginseng Ling Bai Zhu San. After treatment with Si Jun Zi Tang, the intestinal flora of rats showed an increase in the abundance of the phylum Phylum Thicket and a decrease in the abundance of the phylum Bacteroides; at the genus level, the abundance of the genera Lactobacillus and Bacillus anaerobicus increased and the abundance of the genus Muribaculaceae_norank decreased [33].

6. Summary

In today's society, women's work pressure has increased dramatically, sitting at the desk for a long time, easy to overwork and overthink, but also like to enjoy fat, sweet and thick taste, resulting in the weakness of the spleen and stomach, the loss of power of transportation and transformation, water and liquid into phlegm, blocking the punch, blood flow is not smooth, cannot be monthly menstruation followed by closed and not, and even infertility. The "Fu Qing master of female medicine - seeds" cloud: "obesity of the wet, not external evil is the spleen and earth within the disease ... and do not urgently replenish the spleen and stomach Qi, then Yang does not flourish, wet phlegm does not go".

Therefore, Chinese medicine believes that PCOS patients are the signs of deficiency, the main blame for the spleen deficiency of water and fluid stagnation, and the collection of phlegm and damp water and drink, the flow of Qi and blood is blocked, and the shape of their fat, body fat overflow, phlegm and damp Qi and blood for the zhengjiao, so that the ovaries are polycystic change-like changes^[34]. The result is polycystic change in the ovaries. Therefore, the treatment of PCOS clinical prescriptions from the spleen, and the spleen disease, poor must and kidney, resulting in deficiency of the spleen and kidney. The treatment of PCOS should be based on strengthening the spleen, dispelling dampness and phlegm, complemented by tonifying the kidneys, draining the liver and activating blood circulation to resolve blood stasis.

The relationship between intestinal flora, polycystic ovary syndrome and spleen is complex. Currently, the effects of spleen-strengthening prescriptions on intestinal flora are based on the extraction of active ingredients in spleen-strengthening drugs and the combined effects of drugs in spleen-strengthening formulae to observe their effects on the quantity and structure of intestinal flora, but it is not clear through which mechanism they work. The unique therapeutic advantages of TCM with multiple targets and pathways are compatible with the diversity of intestinal microecology and the high heterogeneity of patients with polycystic ovary syndrome, and whether the intestinal flora can be regulated by using the spleen-strengthening formula to treat polycystic ovary syndrome remains to be studied.

Acknowledgement

Xianyang City Key R&D Program Project (2021HZDYF-SF-0032).

References

- [1] Bruni V, Capozzi A, Lello S. *The Role of Genetics, Epigenetics and Lifestyle in Polycystic Ovary Syndrome Development: the State of the Art*[J]. *Reprod Sci*, 2022, 29(3):668-679.
- [2] Krentowska A, Kowalska I. *Metabolic syndrome and its components in different phenotypes of polycystic ovary syndrome* [J]. *Diabetes Metab Res Rev*. 2022, 38(1):3464.
- [3] Collée J, Mawet M, Tebache L, et al. *Polycystic ovarian syndrome and infertility: overview and insights of the putative treatments* [J]. *Gynecol Endocrinol*, 2021, 37(10):869-874.
- [4] Zhu YH, Deng AL, Deng CH, et al. *Study on quantitative diagnosis method of spleen deficiency, phlegm and dampness evidence in polycystic ovary syndrome*[J]. *Journal of Traditional Chinese Medicine*, 2020, 61(12):1080-1084.
- [5] Anon. *A framework for human microbiome research*[J]. *Nature*, 2012, 486(7042):215-221.
- [6] Tian Y, Mai XD, Ma K, et al. *Intestinal flora regulates the occurrence and development of metabolic diseases* [J]. *Chinese Journal of Science*, 2021, 66(13):1602-1613.
- [7] Lu K-N, Lin H-M. *Research progress on the involvement of intestinal flora and inflammatory factors in the pathogenesis of polycystic ovary syndrome and the intervention of traditional Chinese medicine* [J]. *Chinese Journal of Traditional Chinese Medicine*, 2022, 40(3):186-190.
- [8] Yang YL, Zhou WW, Wu S, et al. *Intestinal Flora is a Key Factor in Insulin Resistance and Contributes to the Development of Polycystic Ovary Syndrome*[J]. *Endocrinology*, 2021, 162(10):118.
- [9] Li X, Cheng W, Shang H, et al. *The Interplay between Androgen and Gut Microbiota: Is There a Microbiota-Gut-Testis Axis*[J]. *Reprod Sci*, 2022, 29(6). 1674-1684.
- [10] Wang C, Zhou J. *Correlation between intestinal flora and metabolic syndrome*[J]. *Henan TCM*, 2021, 41(9):1315-1318.
- [11] Liu R, Zhang C, Shi Y, et al. *Dysbiosis of gut microbiota associated with clinical parameters in polycystic ovary syndrome* [J]. *Front Microbiol*, 2017, (8):324.
- [12] Belani M, Deo A, Shah P, et al. *Differential insulin and steroidogenic signaling in insulin resistant and non-insulin resistant human luteinized granulosa cells—a study in PCOS patients*[J]. *Steroid Biochem Mol Bio*, 2018, 178: 283-292.
- [13] Zhang D, Zhang L, Yue F, et al. *Serum zonulin is elevated in women with polycystic ovary syndrome and correlates with insulin resistance and severity of anovulation*[J]. *Eur J Endocrinol*, 2015, 172(1):29-36.
- [14] Insenser M, Murri M, Del CR, et al. *Gut microbiota and the polycystic ovary syndrome: influence of sex, sex hormones, and obesity* [J]. *Clin Endocrinol Metab*, 2018, 103(7):2552-2562.
- [15] Fruzzetti F, Perini D, Russo M, et al. *Comparison of two insulin sensitizers, metformin and myo-inositol, in women with polycystic ovary syndrome (PCOS)*[J]. *Gynecol Endocrinol*, 2017, 33(1):

39-42.

- [16] Guo J, Shao J, Yang Y, et al. Gut Microbiota in Patients with Polycystic Ovary Syndrome: a Systematic Review[J]. *Reprod Sci*, 2022, 29(1):69-83.
- [17] Feng Hui, Zhu Xinyi, Wang Changsong. Research progress on the mechanism of action of spleen strengthening herbs on intestinal microecology[J]. *Chinese Journal of Traditional Chinese Medicine Information*, 2018, 25(10):137-140.
- [18] Guo WX, Wang Q, Guo G, et al. Exploring "the spleen as the basis of the postnatal life" based on human intestinal flora [J]. *Chinese Journal of Traditional Chinese Medicine*, 2021, 36(9): 5165-5168.
- [19] Cox LM, Calcagno N, Gauthier C, et al. The microbiota restrains neurodegenerative microglia in a model of amyotrophic lateral sclerosis [J]. *Microbiome*, 2022, 10(1):47.
- [20] Li SH, Chen GD, Hong B, et al. Exploring the relationship between the theory of "Tu Cong Mu Yu" and the development of chronic hepatitis B based on intestinal flora dysbiosis[J]. *Chinese Journal of Traditional Chinese Medicine*, 2021, 36(6):3129-3132.
- [21] Zhao C.W., Wang J. Research progress of Chinese herbal medicine based on intestinal flora for irritable bowel syndrome[J]. *Clinical Research in Chinese Medicine*, 2022, 14(1):141-144.
- [22] Wei YJ, Li XQ, Ji Boyang, et al. Analysis of intestinal flora-host relationship and progress of intestinal flora regulation/synthesis research[J]. *Chinese Journal of Science*, 2022, 52(2):249-265.
- [23] Du Caifeng, Zhao Y, Liu Hongqi, et al. Exploring the essence of perimenopausal insomnia based on the "intestinal flora-intestine-brain" axis of heart-kidney disconnection [J]. *Chinese Journal of Traditional Chinese Medicine*, 2021, 36(12):6975-6978.
- [24] Wang KX, Dong XM, Su YP, et al. Research progress on the relationship between intestinal flora and depression [J]. *Journal of Jilin University*, 2022, 48(4):1094-1100.
- [25] Li ZC, Sun PF, Li L, et al. Progress of research on the relationship between intestinal flora and liver diseases [J]. *Chinese Journal of Cancer Control*, 2021, 28(19):1433-1437.
- [26] Zhang J, Wang X L, Zhou Y, et al. Research progress on the correlation between intestinal flora and disease [J]. *Basic Medicine and Clinics*, 2020, 40(2):243-247.
- [27] Lin Bebe, Huang Hongli, Xia Yanqiu, et al. Exploring Chinese medicine interventions for polycystic ovary syndrome based on intestinal flora[J]. *Journal of Chinese Medicine*, 2021, 36(272): 89-93.
- [28] Yang Yijiao, Ni Xiaorong, Yang Ling. The relationship between polycystic ovary syndrome and intestinal flora and the current status of research on the prevention and treatment of Chinese medicine [J]. *Chinese Journal of Microecology*, 2022, 34(1):97-101.
- [29] Zhang Jingnan, Yuan Hong, Ma Chunli, et al. Astragalus polysaccharide suppresses intestinal inflammatory response in mice on high-fat diet by regulating intestinal flora[J]. *Journal of Food and Biotechnology*, 2022, 41(4):19-24.
- [30] Meng J.I. Study on the spleen tonic effect of Radix Codonopsis polysaccharide based on bitter-cold diarrhea in a mouse model of spleen deficiency [D]. Shanxi: Shanxi Medical University, 2021: 43-73.
- [31] He Han, Dan Linwei, Wang Qiaozhen, et al. Effects of aqueous decoction and polysaccharides of *Atractylodes macrocephala* before and after bran-frying on intestinal flora of rats with spleen deficiency and diarrhea based on 16S rRNA high-throughput sequencing[J]. *Chinese Pharmacology and Clinics*, 2022, 38(2):136-140.
- [32] Ou G. S., You D. S., Zhang L. H., et al. Exploring the intestinal microecological mechanism of Ginseng and *Atractylodes macrocephala* in the treatment of functional diarrhea with spleen deficiency [J]. *Journal of Guangzhou University of Traditional Chinese Medicine*, 2020, 37(11): 2232-2236.
- [33] Lu YK, Chen YY, Zhuang XM, et al. Study on the mechanism of Si Jun Zi Tang intervention in heart failure rats based on the regulation of intestinal flora imbalance [J]. *Chinese Journal of Traditional Chinese Medicine Information*, 2021, 48(4):81-87.
- [34] Xie Pang Pang, Zeng Lei, Yu Jing Wei, et al. Effect of adding and subtracting Cangfu Guiding Phlegm Tang on metabolism and conception in polycystic ovary syndrome with spleen deficiency and phlegm-dampness evidence [J]. *Chinese Journal of Experimental Formulary*, 2021, 27(14):87-92.