

Application of Guizhi Fuling Pill in Gynecology

Gang LI¹, Mingchen ZHU^{2*}

1. Hubei University of Chinese Medicine, Wuhan 430000, China; 2. Shiyan Hospital of Chinese Medicine Affiliated to Hubei University of Chinese Medicine, Shiyan 442012, China

Abstract This paper reviews the research progress of Guizhi Fuling Pill in the clinical application of gynecology, such as the treatment of uterine leiomyoma, ovarian cyst, infertility and dysmenorrhea, in order to provide further research ideas for clinical researchers.

Key words Guizhi Fuling Pill, Gynecological diseases, Synopsis of Golden Chamber, Research progress

1 Introduction

Guizhi Fuling Pill first appeared in *Synopsis of Golden Chamber: Twentieth Treatment of Women's Pregnancy Diseases and Pulse Syndrome* written by Zhang Zhongjing, a medical sage in Han Dynasty. It is recorded that a woman has a history of chronic disease, which occurs after less than three months of menopause, and the fetal movement is located on the navel, which is caused by lump in the body. Fetal movement with normal menstruation in the three months before pregnancy is normal movement. Menstruation is out of balance in the first three months before menopause, blood stasis is seen three months after menopause, and the blood clot is purple-black. The reason for the bleeding is that the intra-abdominal lump has not gone away, so it should be removed and treated with Guizhi Fuling Pill. The composition and usage of this prescription are as follows: Cinnamomi Ramulus, Poria cocos and Moutan Cortex, Persicae Semen, and Paeoniae Radix Alba are ground into powder, and made into pills as large as rabbit excrement. One pill is taken on an empty stomach, and three pills can be taken if efficacy is not so good. It has the functions of promoting blood circulation, removing blood stasis and relieving disease, and is mainly used for treating uterus blood stasis syndrome. With the continuous in-depth research and combined treatment with Western medical drugs, it has been widely used in obstetrics and gynecology diseases such as uterine fibroids, infertility, hyperplastic mass diseases, endocrine and metabolic diseases, circulation and vascular diseases, *etc.*, with good curative effect. In view of this, this article reviewed the clinical application of Guizhi Fuling Pill in gynecology research progress in the recent five years, in order to provide further research ideas for clinical researchers.

2 Gynecological diseases

2.1 Uterine fibroids In traditional Chinese medicine, "uterine fibroids" falls into the category of "abdominal mass"^[1]. In Western medicine, the conservative treatment methods of uterine fibroids are generally using gonadotropin-releasing hormone agonists, mifepristone, tamoxifen, tonorgestrel intrauterine slow release system, uterine artery embolization, radiofrequency abla-

tion, high intensity focused ultrasound and other drugs or surgical treatment^[2].

Tao Meng^[3] treated 25 patients with uterine fibroids with Sijunzi Decoction combined with Guizhi Fuling Pill, with a total effective rate of 96%, which can effectively reduce the incidence of adverse reactions, recurrence rate, tumor marker level and hormone level, and improve the quality of life of patients. Wang Wenjie *et al.*^[4] treated 53 patients with uterine fibroids with Guizhi Fuling Pill combined with mifepristone, with a total effective rate of 96.23%. The effect is good, and it has a good effect on regulating immunity, hemorheology and improving sex hormone level. Wang Chunhong^[5] treated 71 patients with uterine fibroids with Sijunzi Decoction and Guizhi Fuling Pill, with a total effective rate of 92.26%, suggesting that the combination of Sijunzi Decoction and Guizhi Fuling Pill had better clinical effect on uterine fibroids, can improve its immune function and hormone level, and can also reduce the expression level of carbohydrate antigen 125 (CA125) and vascular endothelial growth factor (VEGF), having certain clinical application value. Pan Qingjie *et al.*^[6] used acupuncture combined with Guizhi Fuling Pill to treat 40 patients with uterine fibroids, with a total effective rate of 97.5%. Studies have shown that Guizhi Fuling Pill can significantly reduce serum VEGF and HIF-1 α levels, inhibit the formation of neovascularization, significantly reduce the metastasis, proliferation, shedding and differentiation of endometrium, improve the clinical treatment effect and speed up the recovery of patients.

2.2 Ovarian cyst Ovarian cyst falls into the categories of "abdominal mass" and "lump in the abdomen" in traditional Chinese medicine. The conservative treatment of ovarian cyst in Western medicine is mainly to use tamoxifen, gestrinone, mifepristone and other drugs, or to use non-conservative treatment such as surgical treatment^[7].

Yang Qiuji *et al.*^[8] used Guizhi Fuling Pill combined with Jiawei Xiaoyao Pill to treat 39 patients with polycystic ovarian cyst, with a total effective rate of 94.87%, which can obviously improve the clinical efficacy, regulate the level of sex hormones and reduce the recurrence rate. Wang Fei *et al.*^[9] used Fuke Qianjin Capsule combined with Guizhi Fuling Pill to treat 53 patients with ovarian cyst, with a total effective rate of 94.34%, which can improve ovarian function and hemorheological indexes

of patients and reduce the level of inflammatory factors. Peng Huangqing *et al.*^[10] used Guizhi Fuling Pill combined with Dahuang Zhechong Pill to treat 30 patients with ovarian cyst, with a total effective rate of 83.33%, which was significantly higher than in the treatment group with conventional drugs for promoting blood circulation and removing blood stasis (60.00%). The incidence of adverse reactions in the study group (6.67%) was significantly lower than that in the control group (30.00%), and the curative effect was better, which can reduce the focus volume, quickly relieve symptoms and improve sex hormone levels.

2.3 Infertility Western medicine believes that ovulation disorder, fallopian tube factors, uterus, vulva and other factors are the female factors causing infertility. Western medicine often considers gynecological diseases such as polycystic ovary syndrome, endometriosis and pelvic inflammatory disease sequelae in the treatment of infertility, and usually adopts correcting pelvic organic diseases, inducing ovulation and using assisted reproductive technology^[11].

Wang Wenjuan *et al.*^[12] used Guizhi Fuling Pill, ozone injection combined with mechanical dredging to treat 52 cases of infertility caused by fallopian tube obstruction, with a total effective rate of 76.92%, which was higher than that of the control group (57.69%). The fallopian tube dredging rate and pregnancy rate of patients in the observation group were significantly higher than those in the control group, which can improve the fallopian tube dredging rate and pregnancy rate, reduce the fallopian tube re-occlusion rate, improve the TCM syndrome and hormone level of patients, and reduce the inflammatory factor level of the body. Xu Yugui *et al.*^[13] used Guizhi Fuling Capsule combined with hysteroscopic surgery to treat 41 patients with pelvic inflammatory infertility. The short-term total effective rate of patients in the combined group was 95.12%, which was higher than that of patients in the operation group (80.49%). After 2 months of treatment, the TCM symptom scores of patients were lower than those before treatment, and the scores for patients in the combined group were significantly lower than those in the operation group, which can improve the serum sex hormone level of patients and was of great significance for improving pregnancy rate. Fu Jing *et al.*^[14] treated 60 cases of infertility with phlegm and blood stasis with Kaiyu Erchen Decoction and Guizhi Fuling Pill. The serum hormones were improved and the TCM syndromes were relieved, which was helpful to improving the psychological state of patients and promoting ovulation and pregnancy. Yang Zhiyuan^[15] used Bushen Huoxue Egg-promoting Prescription combined with Guizhi Fuling Pill to treat 48 patients with irregular menstruation infertility. After 1, 3 and 6 months of treatment, the TCM syndrome scores of patients in the study group were significantly lower than those in the control group, and the incidence of adverse reactions in the study group was 6.3%, which was significantly lower than that in the control group (25.0%). After treatment, the intimal thickness and follicle diameter of the two groups were significantly larger than those before treatment, and the intimal thickness and fol-

licle diameter in the study group were significantly larger than those in the control group.

2.4 Dysmenorrhea In Western medicine, dysmenorrhea is mainly treated by drugs, including oral prostaglandin synthase inhibitors such as ibuprofen, ketoprofen and diclofenac, and oral contraceptives.

Li Cuiyun^[16] used Xionggui Jiaoai Decoction combined with Guizhi Fuling Pill to treat 28 patients with adenomyosis dysmenorrhea. The total effective rate was 96.43%, which was higher than that of the control group (71.43%). The recurrence rate and side effect rate were 3.57% and 7.14%, respectively, which were lower than those of the control group (32.14% and 39.29%). The effect was good and can reduce the pain degree. Some scholars^[17] have found that Guizhi Fuling Pill can significantly relieve the pain degree of primary dysmenorrhea due to blood stasis and fever, and there is no obvious adverse reaction. Wang Yujie *et al.*^[18] used Wenjing Huayu Decoction combined with Guizhi Fuling Capsule to treat 48 patients with primary dysmenorrhea, with a total effective rate of 93.75% and remarkable analgesic effect. Its mechanism may be related to regulating the expression of PGF2 α , P and E₂ in patients' serum, and high medication safety.

2.5 Hyperplasia of mammary glands Hyperplasia of mammary glands falls into the category of "mammary lump" in traditional Chinese medicine. Hyperplasia of mammary glands is commonly treated in Western medicine by oral tamoxifen, vitamins, Danazol and other drugs^[19-20] and surgical or physical microwave external therapy^[21]. Although Western medicine can control the disease, it can't cure it. Long-term use of hormone drugs can easily induce adverse reactions such as endometritis and alopecia, and some patients have drug dependence^[22].

Lin Yicen *et al.*^[23] treated 43 patients with hyperplasia of mammary glands with acupuncture combined with Guizhi Fuling Pill, with a total effective rate of 97.67%, which can effectively relieve breast pain and negative emotions, reduce breast lumps and improve their quality of life. Cui Genrong^[24] used Xiaoyaosan Prescription combined with Guizhi Fuling Pill to treat 25 patients with hyperplasia of mammary glands, and the clinical treatment effect was good. Yan Zhibo^[25] treated 70 patients with hyperplasia of mammary glands with Rupixiao Tablet combined with Guizhi Fuling Pill, with a total effective rate of 91.43%. Yang Bin *et al.*^[26] used Guizhi Fuling Pill combined with tamoxifen citrate tablets to treat 61 patients with hyperplasia of mammary glands, with a total effective rate of 88.52%, which was higher than in the control group only taking tamoxifen citrate tablets (73.77%), and the incidence of adverse reactions (11.48%) was significantly lower than that in the control group (31.15%), which can effectively improve the clinical symptoms of patients with hyperplasia of mammary glands, subside breast masses, improve endocrine level, improve treatment efficiency and have higher safety.

2.6 Pelvic inflammatory diseases There is no name of "pelvic inflammatory disease" in ancient Chinese medicine books, and it can be put into the categories of "leukorrhoeal diseases" and

"abdominal mass" according to its symptoms. The commonly used Western medicine treatments are metronidazole and aminoglycoside antibiotics, ultrashort wave, microwave physiotherapy, TDP therapy machine and other physiotherapy methods, as well as surgical treatment and interventional therapy^[27].

Si Qingchen *et al.*^[28] used Guizhi Fuling Pill combined with microwave therapeutic instrument to treat 47 patients with chronic pelvic inflammatory disease of qi stagnation and blood stasis, with an effective rate of 95.74%. The disappearance time of symptoms such as fever, mass, abdominal pain and abnormal secretion of patients was shorter than that of patients under conventional treatment, and the clinical curative effect was obviously improved, which can improve symptoms, and reduce the level of inflammatory factors, with better safety. Wang Lingling *et al.*^[29] used thunder-fire moxibustion combined with Guizhi Fuling Pill to treat 51 patients with chronic pelvic inflammatory disease. The total effective rate was 92.2%, which was significantly higher than that of Western medicine group (76.5%). It can inhibit the activation of TGF- β 1/Smads pathway, relieve symptoms and inflammatory reaction, improve hemorheology and imaging indexes, and improve the curative effect, and the medication was safe and reliable. Dong Yanshuang *et al.*^[30] used Guizhi Fuling Capsule combined with azithromycin to treat 148 patients with pelvic inflammatory disease, with a total effective rate of 94.59%, which was significantly higher than that of Western medicine treatment group (85.14%). The clinical effect was definite, and it can improve ovarian hemodynamics, improve patients' antioxidant capacity, reduce inflammatory reaction and had high safety.

2.7 Endometriosis There is no record of "endometriosis" in ancient Chinese medicine books, which can be classified as "dysmenorrhea", "abdominal mass" and "menorrhagia" according to its clinical manifestations. The commonly used methods in Western medicine for endometriosis are surgical treatment and taking oral contraceptives, anti-progesterone, gonadotropin-releasing hormone agonists, and progesterone such as medroxyprogesterone acetate, norethindrone acetate or levonorgestrel acetate^[31].

Wu Yuhua *et al.*^[32] treated 33 patients with endometriosis with Guizhi Fuling Pill combined with Digestrol Acetone, with a total effective rate of 96.97%, which was higher than that in the treatment group with Digestrol Acetone Tablets alone (75.00%). The clinical effect was good, and it can more effectively reduce the level of sex hormones, inhibit the proliferation of endometrial cells, reduce the recurrence rate of diseases, improve the pregnancy rate and have higher safety. Chen Shunxia^[33] found that Guizhi Fuling Pill combined with levonorgestrel intrauterine sustained-release system and gonadotropin-releasing hormone agonist can not only improve the quality of life of patients with moderate and severe blood stasis endometriosis, but also meet the needs of patients to preserve uterus and fertility under certain conditions, with a certain clinical practical value. Huang Chunsheng^[34] found that Guizhi Fuling Pill combined with goserelin acetate sustained-release implant can obviously improve the ovarian function of pa-

tients with endometriosis, reduce the expression levels of serum CA125, VEGF and TNF- α , and had good clinical effect, with a certain popularization and application value.

In addition, some scholars have found that Guizhi Fuling Pill can induce apoptosis of ectopic endometrial stromal cells by promoting the stability of VPS53 protein^[35].

2.8 Irregular menstruation Irregular menstruation, also known as menstrual disorder, mainly refers to the abnormal menstrual period, cycle and menstrual volume of women^[36]. In treating menstrual disorders, Western medicine generally gives patients appropriate sex hormone drugs to adjust their menstrual cycle and improve their clinical symptoms^[37].

Zhou Weiwei^[38] used Guifu Dihuang Pill combined with Guizhi Fuling Pill to treat 50 patients with irregular menstruation, which can improve the clinical symptoms of patients with irregular menstruation, increase the levels of estrogen and progesterone, improve the level of serum hormones, reduce the incidence of adverse reactions, and have high safety. Chejian *et al.*^[39] used *Leonurus heterophyllus* granules combined with Guizhi Fuling Pill to treat 24 patients with irregular menstruation, with a total effective rate of 95.83%, which was significantly higher than that of the treatment group only using Mudanpi granules. It shows that Mudanpi granules combined with Guizhi Fuling Pill can effectively regulate patients' menstruation, protect female endometrium, dissipate stagnation, dredge channels and promote blood circulation, improve hemostatic effect, improve patients' normal menstrual cycle and menstrual blood volume, accelerate patients' menstrual recovery speed, and have high safety. Liu Fang^[40] used Guifu Dihuang Pill combined with Guizhi Fuling Pill to treat 23 patients with irregular menstruation due to kidney deficiency and blood stasis, and achieved good results. Guo Mingyan^[41] used Guizhi Fuling Pill combined with Taibao Capsule to treat 63 patients with irregular menstruation, with a total effective rate of 94%, which was higher than that of pure Western medicine treatment group (81%). It can quickly improve their clinical symptoms, help stabilize their menstrual time, menstrual volume and menstrual cycle, improve their dysmenorrhea symptoms, and significantly improve their quality of life, having positive significance for ensuring their disease recovery and improving their pregnancy rate.

2.9 Polycystic ovary syndrome There is no name for this disease in traditional Chinese medicine, and it can be classified as "infertility", "amenorrhea" and "hypomenorrhea" according to its symptoms. At present, the commonly used treatment methods in Western medicine are oral contraceptives and symptomatic treatment^[42].

According to experiments^[43], Guizhi Fuling Pill can inhibit autophagy of granulosa cells in rat polycystic ovary syndrome model, promote follicular development, and alleviate ovulation disorder in rat polycystic ovary syndrome model, which is related to the activation of PI3K/AKT/mTOR signaling pathway. In another study^[44], the rat model of polycystic ovary syndrome was established by injection of dehydroepiandrosterone, and Guizhi Fuling

Pill combined with rosiglitazone was given. The results showed that the combined treatment inhibited the weight and ovarian weight of rats with polycystic ovary syndrome, reduced fasting blood glucose and fasting insulin, inhibited total cholesterol, triglyceride, low density lipoprotein, enhanced high density lipoprotein, improved oestrous cycle, ovarian histological changes and follicular development, and alleviated ovarian dysfunction in rats with polycystic ovary syndrome, which may be related to PI3K/AKT/NF- κ B, Nrf2/HO-1 pathway. Li Jiannan *et al.*^[45] treated 46 patients with polycystic ovary syndrome with Guizhi Fuling Pill combined with Western medicine, with a total effective rate of 93.02%, which was significantly higher than that of Western medicine group. The study showed that Guizhi Fuling Pill combined with Western medicine can improve the curative effect, promote ovulation, regulate sex hormone level and insulin resistance. Wang Yun *et al.*^[46] used Guizhi Fuling Pill, Erchen Decoction and conventional Western medicine to treat 41 patients with polycystic ovary syndrome, with a total effective rate of 87.80%, which can improve clinical efficacy, improve ovarian function and sex hormone level, and reduce insulin resistance, with relatively good safety.

3 Other diseases

Lan Haili *et al.*^[47] used modified Guizhi Fuling Pill to treat 33 cases of chronic radiation proctitis of damp-heat stasis type, and achieved good results, which can reduce intestinal inflammatory reaction, improve clinical symptoms and improve patients' quality of life. Yan Zhenguo *et al.*^[48] used Guizhi Fuling Pill and earthworm to treat 53 patients with minimal brain lesions, with a total effective rate of 88.46%, which can reduce the levels of glycosylated hemoglobin and total cholesterol in patients with minimal brain lesions, and reduce the occurrence of minimal brain lesions. Liu Ying *et al.*^[49] used Linggan Wuwei Jiangxin Decoction and Guizhi Fuling Pill to treat 37 patients with acute exacerbation of chronic obstructive pulmonary disease of cold fluid and blood stasis type, which can effectively improve the clinical symptoms and lung function of patients, reduce the level of serum inflammatory factors and improve the quality of life of patients. Some studies have inferred that Guizhi Fuling Pill may be used as a therapeutic drug to alleviate liver fibrosis^[50]. Zheng Yunpeng *et al.*^[51] used Chaihu Guizhi Ganjiang Decoction and Guizhi Fuling Pill to treat 30 elderly patients with diabetic skin pruritus, which can reduce the index level of serum inflammatory factors in patients, stabilize the blood sugar level, and accelerate the disappearance of skin pruritus symptoms, and the treatment safety was relatively high. Liu Yunlin *et al.*^[52] used Mufangji Decoction and Guizhi Fuling Pill to treat 40 patients with acute exacerbation of pulmonary heart disease (heart, lung and kidney yang deficiency syndrome), with a total effective rate of 95.00%, which can effectively improve patients' lung function, relieve patients' clinical symptoms, reduce patients' blood viscosity and reduce the number of attacks in acute exacerbation, with definite curative effect.

4 Conclusion

Guizhi Fuling Pill is created by Zhang Zhongjing to treat women with concretion lumps and blood stasis. In the prescription, Cinnamon Ramulus is used to warm and dredge blood vessels, to achieve the effect of reducing stasis, and to take the role of monarch medicine. Persicae Semen is "a special medicine for blood stasis and blood occlusion", which is used as adjuvant medicine. Moutan Cortex and Paeoniae Radix Alba can be used to cool blood, remove blood stasis and relieve pain; Poria can be used to remove dampness and phlegm to help eliminate the lump and strengthen the spleen, benefit the stomach and calm the heart to strengthen the qi, all of which are used as adjuvant medicines. Pills coated with white honey are sweet and moist, and it can be used as conductant medicine to alleviate the effect of various medicines. This prescription is a common prescription for the syndrome of blood stasis blocking the uterus, and it is also the representative prescription for relieving the lumps. Later doctors took Guizhi Fuling Pill as the basic prescription, or combined it with other prescriptions, and used TCM syndrome differentiation thinking to treat various gynecological diseases caused by lumps and blood stasis. Women's Prescription changed its name to Death Pill to treat pregnant women with cold sweat and shortness of breath when they have a miscarriage and the fetus died in the womb; Synopsis of Treating Women's Diseases changed it to decoction, and changed its name to Cuisheng Decoction, which can cure abdominal pain, low back pain and hasten parturition. Nowadays, doctors flexibly combine Guizhi Fuling Pill with Western medicine or other therapies, and bring into play a greater role of Guizhi Fuling Pill in treating various kinds of diseases in addition to women's diseases, which promotes the combination of Chinese medicine and Western medicine to a certain extent, and promotes doctors to explore Guizhi Fuling Pill in a deeper level, so that Chinese medicine can continuously develop and innovate.

Although the research of Guizhi Fuling Pill in treating women's diseases and other diseases has made great progress, it is thought that there is still room for improvement. One is that Guizhi Fuling Pill in treating diseases caused by blood stasis has unique Chinese medicine characteristics, but it is not effective for some diseases such as uterine fibroids with large tumor body, so it can be further combined with Western medicine therapy to make clinical research, and to expand the research scope of Guizhi Fuling Pill in treating related diseases on the premise of ensuring patient safety, in order to obtain qualitative and quantitative standards. Furthermore, at present, they are mostly clinical observations of combined Western medicine therapy, and there is still a lack of pharmacological analysis on the effective components and mechanism of action of the acting drugs, and the related research on whether the use of drugs combined with Western medicine will change the mechanism of action of Guizhi Fuling Pill is insufficient. In order to identify the main effective components of the drugs, the related pharmacological mechanisms of combined drugs can be further studied in the future. Third, we should actively

carry forward the tradition of seeking root causes and syndrome differentiation of traditional Chinese medicine, and focus on the possibility of Guizhi Fuling Pill to cure the root cause.

The aforementioned research in this paper shows the clinical application of Guizhi Fuling Pill, but we can still make a study continuously to expand the research scope as much as possible, increase the experimental samples to improve the credibility without losing precision, and further explore the feasibility of treating other diseases with this prescription. At the same time, we should explore the deep mechanism and principle of this prescription combined with Western medicine or other therapies, so as to control the application range of Guizhi Fuling Pill more accurately in clinic.

References

- [1] TAN Y. Gynecology of traditional Chinese medicine (4th edition for the new century) [M]. Beijing: China Press of Traditional Chinese Medicine, 2016: 253–259. (in Chinese).
- [2] CHEN YJ, LIU GH. Current status of research on conservative treatment of uterine fibroids in Western medicine[J]. Modern Medicine and Health Research, 2020, 4(14): 108–111. (in Chinese).
- [3] TAO M. Clinical effect observation of Sijunzi decoction combined with Guizhi Fuling pills in treatment of uterine fibroid[J]. Chinese Community Doctors, 2023, 39(23): 74–76. (in Chinese).
- [4] WANG WJ, YANG JH, YAN KK. Clinical study on the curative effect of Guizhi Fuling pills combined with mifepristone in the treatment of uterine fibroids[J]. Systems Medicine, 2023, 8(12): 186–189. (in Chinese).
- [5] WANG CH. Clinical study on Sijunzi decoction combined with Guizhi Fuling pill in the treatment of hysteromyoma[J]. Shanghai Medical & Pharmaceutical Journal, 2022, 43(9): 23–26. (in Chinese).
- [6] PAN QJ, SU WW, CHEN MZ, *et al.* Efficacy of acupuncture combined with Guizhi Fuling pills in the treatment of uterine fibroids and its effect on the expression of serum VEGF and HIF-1 α [J]. Inner Mongolia Journal of Traditional Chinese Medicine, 2021, 40(7): 128–129. (in Chinese).
- [7] DONGARUHAN. Recent advances of ovarian cyst[J]. Chinese Journal of Ethnomedicine and Ethnopharmacy, 2016, 25(20): 57–59. (in Chinese).
- [8] YANG QJ, LU WZ, WANG LX. Clinical efficacy of Guizhi Fuling pills combined with Jiawei Xiaoyao pills in the treatment of polycystic ovarian cysts and its effect on sex hormone and recurrence rate[J]. The Journal of Medical Theory and Practice, 2021, 34(24): 4313–4314. (in Chinese).
- [9] WANG F, CHENG J, ZHANG W. Clinical efficacy of gynaecological Qianjin capsule combined with Guizhi Fuling pills on patients with ovarian cyst [J]. Chinese Traditional Patent Medicine, 2021, 43(10): 2928–2930. (in Chinese).
- [10] PENG HQ, BIAN QH, CHEN RR. Clinical efficacy of Guizhi Fuling Pills combined with Dahuang Zhechong pills in the treatment of ovarian cyst[J]. Laboratory Medicine and Clinics, 2023, 20(3): 383–386. (in Chinese).
- [11] XIE X, KONG BH, DUAN T. Obstetrics and gynaecology (9th ed.) [M]. Beijing: People's Health Publishing House, 2019: 361–365. (in Chinese).
- [12] WANG WJ, JIAO SF, LI JJ. Clinical observation of Guizhi Fuling pills and injection of ozone combined with mechanical dredging in the treatment of tubal obstructive infertility[J]. China Pharmaceuticals, 2022, 31(14): 108–111. (in Chinese).
- [13] XU YG, LUO CL, ZHUANG F, *et al.* Clinical effect of Guizhi Fuling capsule combined with hysterolaparoscopic surgery in the treatment of pelvic inflammatory infertility[J]. Chinese Journal of Clinical Rational Drug Use, 2022, 15(29): 142–145. (in Chinese).
- [14] FU J, ZHU GL, WANG NM. Study on the efficacy of Kaiyu Ercheng Tang combined with Guizhi Fuling pills in treating infertility with phlegm and stasis mutual conjugation[J]. Shaanxi Journal of Traditional Chinese Medicine, 2019, 40(3): 341–343. (in Chinese).
- [15] YANG ZY. Analysis of Chinese medicine evidence points and safety of tonifying kidney and activating blood to promote ovulation formula combined with Guizhi Fuling pills in treating menstrual dysfunction type infertility[J]. Electronic Journal of Practical Gynecological Endocrinology, 2021, 8(1): 62–64. (in Chinese).
- [16] LI CY. Study on the effect of Xionggui Jiaoai decoction combined with Guizhi Fuling pills in the treatment of dysmenorrhoea in adenomyosis [J]. Practical Gynaecological Endocrinology Electronic Journal, 2021, 8(36): 57–59. (in Chinese).
- [17] LUO YN, MAO P, CHEN PP, *et al.* Effect of Guizhi Fuling Wan in primary dysmenorrhea: A randomized controlled trial [J]. Journal of Ethnopharmacology, 2023(307): 116247–116247.
- [18] WANG YJ, SHI YP. Analgesic effect of Wenjing Huayu decoction combined with Guizhi Fuling capsule in the treatment of primary dysmenorrhoea and its effect on the levels of sex hormone and prostaglandin F2 α [J]. Hebei Journal of Traditional Chinese Medicine, 2019, 41(11): 1670–1673, 1679. (in Chinese).
- [19] KONG XJ. Clinical studies of tamoxifen combined with low-dose danazol in the treatment of breast hyperplasia in middle-aged women[J]. Journal of China Prescription Drug, 2020, 18(7): 135. (in Chinese).
- [20] SONG DF, SHI XJ, LI CJ, *et al.* Effect of vitamin D3 on hyperplasia of mammary glands in experimental rats [J]. Gland Surgery, 2022, 11(1): 136–146.
- [21] DONG XJ, YU P, ZHANG YL, *et al.* Efficacy of traditional Chinese medicine paste method combined with breast disease therapeutic instrument in the treatment of acute mastitis and its effect on patients' prognosis[J]. Contemporary Medical Symposium, 2020, 18(17): 220–221. (in Chinese).
- [22] ZHAO LP, HAN X. Progress of adverse reactions of tamoxifen and its disposal countermeasures [J]. Shanxi Medical Journal, 2013, 42(9): 1018. (in Chinese).
- [23] LIN YC, HE D. Clinical effect of thumbtack needle combined with Guizhi Fuling pills for hyperplasia of mammary glands[J]. New Chinese Medicine, 2022, 54(24): 158–161. (in Chinese).
- [24] CUI GR. Clinical observation on the treatment of mammary gland hyperplasia by combining with Guizhi Fuling pills with additional subtractions of Xiaoyaosan[J]. Electronic Journal of Practical Gynecological Endocrinology, 2020, 7(36): 50–51. (in Chinese).
- [25] YAN ZB. Clinical efficacy observation of breast fetish elimination tablets combined with Guizhi Fuling pills in the treatment of breast hyperplasia [J]. Inner Mongolia Journal of Traditional Chinese Medicine, 2018, 37(8): 24–25. (in Chinese).
- [26] YANG B, WANG YJ, LIANG F, *et al.* Efficacy and safety of Guizhi Fuling pills combined with tamoxifen citrate tablets in the treatment of breast hyperplasia[J]. Clinical Research and Practice, 2018, 3(8): 129–131. (in Chinese).
- [27] LIU ZH, FAN CW. Study on clinical progress of traditional Chinese and Western medicine treating chronic pelvic inflammatory disease [J]. Modern Diagnosis and Treatment, 2021, 32(15): 2384–2385, 2417. (in Chinese).
- [28] SI QC, YE YT, GU HH. Effects of Guizhi Fuling pills combined with microwave therapeutic apparatus on clinical efficacy, symptom improvement and inflammatory factor levels in patients with Qi stagnation and blood stasis type chronic pelvic inflammatory disease[J]. Clinical Research, 2023, 31(7): 78–81. (in Chinese).
- [29] WANG LL, ZHANG X. Effect of thunder fire moxibustion combined with Guizhi Fuling pills for treating patients with chronic pelvic inflammatory disease and its influence on the TGF- β 1/Smads pathway [J]. Chinese Journal of Family Planning, 2023, 31(3): 515–521. (in Chi-

- nese).
- [30] DONG YS, WEI ZP, ZHAO HX. Observation on the therapeutic effect of Guizhi Fuling capsule combined with azithromycin on patients with pelvic inflammatory disease[J]. *Maternal and Child Health Care of China*, 2023, 38(1): 30–33. (in Chinese).
- [31] SUN MZ, HUANG WQ. Research advances on pathogenesis and clinical diagnosis and treatment of endometriosis[J]. *International Journal of Laboratory Medicine*, 2023, 44(16): 2017–2022. (in Chinese).
- [32] WU YH, LUO SQ, TONG ZQ. Clinical efficacy and safety of Guizhi Fuling pills combined with dydrogesterone in the treatment of endometriosis[J]. *Chinese Journal of Clinical Rational Drug Use*, 2023, 16(6): 131–133. (in Chinese).
- [33] CHEN SX. Clinical effect of Guizhi Fuling pill combined with LNG-IUS and GnRH-a on patients with moderate and severe blood stasis emt[D]. Hefei: Anhui University of Traditional Chinese Medicine, 2023. (in Chinese).
- [34] HUANG CS. Application effect of activating blood stasis method in treating endometriosis[J]. *Chinese Journal of Urban and Rural Enterprise Hygiene*, 2022, 37(2): 156–158. (in Chinese).
- [35] ZHANG ZY, LIU FY, XU YY, *et al.* GZFLW induces apoptosis of ectopic endometrial stromal cells via promoting VPS53 protein stability [J]. *Evidence-based Complementary and Alternative Medicine : eCAM*, 2018(2018):1293630.
- [36] LI ZY. Factors associated with menstrual irregularities[J]. *World Latest Medicine Information*, 2019, 19(68): 171. (in Chinese).
- [37] REN C. Analysis of the effect of treating menstrual disorders with gynaecological rejuvenation capsule[J]. *Contemporary Medical Symposium*, 2016, 15(15): 139–140. (in Chinese).
- [38] ZHOU WW. Clinical effect of Guifu Dihuang pills combined with Guizhi Fuling pills in treating menstrual disorders [J]. *Chinese Baby*, 2023 (16): 64–66. (in Chinese).
- [39] CHE J, LIU H. Application effect of Yimucao Keli combined with Guizhi Fuling pills in the treatment of menstrual disorders[J]. *Electronic Journal of Practical Gynecological Endocrinology*, 2020, 7(26): 58, 63. (in Chinese).
- [40] LIU F. Clinical observation of Guifu Dihuang pill combined with Guizhi Fuling pill in treating menstrual disorders of kidney deficiency and blood stasis type[J]. *China Health Care & Nutrition*, 2021, 31(12): 242. (in Chinese).
- [41] GUO MY. Clinical application analysis of Guizhi Fuling pills combined with Embryo capsule in the treatment of menstrual disorders [J]. *Chinese Remedies & Clinics*, 2018, 18(1): 85–86. (in Chinese).
- [42] GU JQ, YU SH, XU F, *et al.* Progress of research related to adolescent polycystic ovary syndrome (PCOS) in Chinese and Western medicine [J]. *Journal of Practical Traditional Chinese Internal Medicine*, 2023, 37(4): 4–7. (in Chinese).
- [43] LIU M, ZHU HQ, ZHU Y, *et al.* Guizhi Fuling Wan reduces autophagy of granulosa cell in rats with polycystic ovary syndrome via restoring the PI3K/AKT/mTOR signaling pathway[J]. *Journal of Ethnopharmacology*, 2021(270): 113821.
- [44] YE YJ, ZHOU WM, REN YF, *et al.* The ameliorating effects of Guizhi Fuling Wan combined with rosiglitazone in a rat ovarian model of polycystic ovary syndrome by the PI3K/AKT/NF-κB and Nr2f2/HO-1 pathways. [J]. *Gynecological Endocrinology : The Official Journal of the International Society of Gynecological Endocrinology*, 2023, 39(1): 2254848.
- [45] LI JN, YU FY, SHEN HH, *et al.* Efficacy of Guizhi Fuling pills combined with western medicine in the treatment of PCOS and its regulatory effect on PI3K/AKT/mTOR pathway[J]. *Journal of Molecular Diagnostics and Therapy*, 2023, 15(2): 197–200, 204. (in Chinese).
- [46] WANG Y, WANG JJ. Clinical study on Guizhi Fuling pill and erchen decoction combined with routine Western medicine for polycystic ovary syndrome[J]. *New Chinese Medicine*, 2023, 55(1): 40–43. (in Chinese).
- [47] LAN HL, SHI Y, WU S, *et al.* Clinical effect of modified Guizhi Fuling pills in treatment of chronic radiation-induced proctitis with stagnant dampness-heat;An analysis of 33 cases[J]. *Hunan Journal of Traditional Chinese Medicine*, 2023, 39(9): 1–4. (in Chinese).
- [48] YAN ZG, CAO H, CHEN J, *et al.* Clinical efficacy of Guizhi poria pills and cadelorol on intracerebral microlesions[J]. *Chinese Journal of Integrative Medicine on Cardio-Cerebrovascular Disease*, 2023, 21(18): 3444–3448. (in Chinese).
- [49] LIU Y, YUN B, ZHOU JH. Observation on the clinical efficacy of modified Linggan Wuwei Jiangxin decoction combined with Guizhi Fuling pills in the treatment of acute exacerbation of chronic obstructive pulmonary disease of cold fluid and blood stasis obstruction type[J]. *Journal of Guangzhou University of Traditional Chinese Medicine*, 2023, 40(9): 2182–2189. (in Chinese).
- [50] XU BG, ZHENG JW, TIAN XX, *et al.* Antihepatofibrotic effect of Guizhifuling pill on carbon tetrachloride-induced liver fibrosis in mice [J]. *Journal of Traditional Chinese Medicine*, 2022, 42(5): 715–722.
- [51] ZHENG YP, MA CH. Observation on the clinical efficacy of Chaihu Guizhi Ganjiang decoction combined with Guizhi Fuling pills plus and minus on pruritus in elderly diabetes mellitus[J]. *The Journal of Medical Theory and Practice*, 2023, 36(17): 2959–2962. (in Chinese).
- [52] LIU YL, HAO XD, CHEN JH. Therapeutic efficacy of Mufangji decoction combined with Guizhi Fuling pills in the treatment of acute exacerbation of pulmonary heart disease (cardiopulmonary and renal Yang deficiency) [J]. *Journal of Emergency in Traditional Chinese Medicine*, 2023, 32(8): 1411–1414. (in Chinese).

(From page 50)

- [4] CHEN YL, XIA W, ZHU JF, *et al.* Clinical observation on panretinal laser photocoagulation combined with Mimenghua recipe in the treatment of diabetic retinopathy [J]. *Guangming Journal of Chinese Medicine*, 2021, 36(10): 1683–1685. (in Chinese).
- [5] LIU F, GUO YP, LIU B, *et al.* Isolation and identification of chemical constituents of ethyl acetate extraction layer from *Buddleja officinalis* Maxim [J]. *Journal of Kunming Medical University*, 2021, 42(8): 31–34. (in Chinese).
- [6] LONG ZH, LI BY, WANG QY, *et al.* A new hexenol glycoside from *Buddleja officinalis* [J]. *China Journal of Chinese Materia Medica*, 2021, 46(23): 6178–6184. (in Chinese).
- [7] XU C, SONG JT. Effect of modified Mimenghua decoction on the retinal thickness in macular area after cataract surgery in diabetic patients [J]. *China Journal of Chinese Ophthalmology*, 2020, 30(10): 719–722. (in Chinese).
- [8] CHEN YL, XIA W, ZHU JF, *et al.* Clinical observation on panretinal laser photocoagulation combined with Mimenghua recipe in the treatment of diabetic retinopathy [J]. *Guangming Journal of Chinese Medicine*, 2021, 36(10): 1683–1685. (in Chinese).
- [9] DONG SQ, YAN WW, XIAO CW. CBX2 regulates the proliferation and apoptosis of cervical cancer cells by Wnt/β-catenin signaling pathway [J]. *Journal of Youjiang Medical University for Nationalities*, 2023, 45(5): 731–735. (in Chinese).
- [10] LIU S, PENG LY, ZHU MY, *et al.* Screening of anti-tumor active components of *Solanum torum* Swartz extract in vitro and its mechanism of action [J]. *Journal of Youjiang Medical University of Nationalities*, 2016, 38(2): 157–159, 167. (in Chinese).