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Research Progress on Pharmacological Effects of Guizhi Fuling Pill

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Abstract: ***Guizhi Fuling Pill is a classic formula from Zhang Zhongjing's "Synopsis of the Golden Chamber". The whole formula has the effects of promoting blood circulation and removing blood stasis. In recent years, Guizhi Fuling Pill has been widely used in clinical practice in China. It can not only treat gynecological diseases such as uterine fibroids, ovarian cysts, polycystic ovary syndrome, endometriosis, pelvic inflammatory disease, and adenomyosis, but also play a positive therapeutic role in diseases such as prostate hyperplasia, coronary heart disease, chronic obstructive pulmonary disease, and hyperlipidemia. Pharmacological studies have confirmed that Guizhi Fuling Pill has anti-inflammatory, analgesic, anti-tumor, blood rheology improving, endocrine and lipid metabolism regulating effects. This article aims to systematically review and elucidate the pharmacological mechanisms and clinical effects of Guizhi Fuling Pills, providing reference for further research and clinical applications.***

Keywords: Guizhi Fuling Pill, Clinical application, Pharmacological effects, Research progress, Synopsis of the Golden Chamber, Gynaecology**.**

1. Introduction

Guizhi Fuling Pill (GFP) is derived from Zhang Zhongjing's book "Jin Kui Yao Lue - Treatment of Women's Pregnancy Diseases with Pulse Syndrome and Disease Part 20" during the Eastern Han Dynasty. Zhang Zhongjing believed that "women are prone to illness, and if their menstrual cycle is interrupted for less than three months and the fetus continues to leak, it is a chronic disease. If the fetus moves on the navel during the first three months of pregnancy, the fetus will be affected. If there is bleeding during the first three months of the menstrual cycle, the blood will not disappear after three months. Therefore, if the blood is not stopped, it will not disappear. Currently, Guizhi Fuling Pill is the main one." Guizhi Fuling Pill is composed of Guizhi, Fuling, Taoren, Chishao, and Mudan skin. Its main functions are to promote blood circulation, remove blood stasis, and alleviate symptoms. It can be used for women with symptoms, blood stasis and amenorrhea, abdominal pain during menstruation, and incomplete postpartum lochia. In the formula, Guizhi warms and promotes blood circulation, while Fuling permeates and benefits the heart and spleen qi. It not only helps to promote blood stasis, but also helps to stabilize the fetus, making it the main medicine; If there are symptoms of stagnation, it can often transform heat. Therefore, it is also combined with peony bark, red peony, and peach kernel to transform blood stasis and clear blood stasis and heat, making it an adjuvant medicine; Using honey as a pill, and also taking its ability to alleviate various blood stasis medicines, it has a soothing effect and is used as a remedy. The combination of various medicines can promote blood circulation, remove blood stasis, and alleviate symptoms. The ancient recipe for Guizhi Fuling Pills: Grind into fine powder, refine honey and pills, take 1 pill before meals daily, and add up to 3 pills if ineffective. Nowadays, on the basis of the past, our formula can be boiled in water or ground into powder and refined into honey to make large honey pills for consumption. In recent years, with the development of clinical experimental research, the clinical application and applicability of GFP have been widely expanded. Nowadays, GFP can effectively treat various diseases, including but not limited to internal medicine, surgery, and gynecological diseases. Advanced pharmacological research has shown that GFP has positive therapeutic effects such as anti-inflammatory, anti-tumor, analgesic, improving hemodynamics, regulating endocrine and lipid metabolism. These findings further confirm the importance of GFP in the medical field and bring broader prospects for its application. This article aims to systematically review and elucidate the pharmacological mechanisms and clinical effects of GFP, providing reference for further research and clinical applications. By delving into its pharmacological effects and clinical indications, we can better understand the therapeutic mechanism and value of GFP. At the same time, this article also aims to explore the potential uses of GFP in different fields, in order to provide guidance and inspiration for clinical doctors and researchers.

2. Pharmacological Research

2.1 Anti Inflammatory

Studies have shown that GFP plays a positive anti-inflammatory role in treatment. Wu Ruihua [1] After treating pelvic inflammatory masses with GFP, the levels of CRP and fibrinogen (Fib) involved in body coagulation decreased. Animal experiments have shown that GFP can reduce the levels of serum interleukin-1 β (IL-1 β), IL-6, and TNF - α in rats with chronic pelvic inflammatory disease, increase the expression of caspase-3 and caspase-8, thereby reducing inflammatory infiltration of rat uterine tissue [2]; Another animal experiment used GFP to intervene in pelvic inflammatory disease model rats, and observed a significant decrease in matrix metalloproteinase-9 (MMP-9) in the rat uterus and ovary tissues, effectively inhibiting chronic inflammatory fibrosis [3]. The effective drug components in GFP, such as quercetin, kaempferol, β - sitosterol, catechins, etc., reduce the occurrence of inflammatory reactions by regulating targets such as IL-6, IL1 β, tumor necrosis factor (TNF), chemokine ligand 2 (CCL2), and cell tumor antigen (TP53) [4]; The components contained in GFP, such as

cinnamaldehyde, paeoniflorin, and cinnamon oil, can effectively inhibit the growth of Staphylococcus aureus, Escherichia coli, and other viruses, demonstrating a wide range of antibacterial effects [5].

2.2 Anti Tumor

Xing Lei and his team [6] A successful experimental model of ovarian cancer transplantation in nude mice was constructed. The study found that the serum IL-2 level of ovarian cancer transplantation tumors in the GFP group increased, while the levels of FSH, LH, CA125, and IL-6 decreased. The expression of survival protein (Survivor) was downregulated, while the expression levels of cysteine protease (Caspase-3) and p21waf/cip protein increased. All of these can promote tumor cell apoptosis and achieve the goal of anti-tumor treatment. Other studies have shown that GFP can inhibit the proliferation and invasion of human breast cancer cell MCF-7 by reducing the protein expression of EGFR, cyclin A2 and cyclin dependent protein kinase 2 [7]. Yang Guang [8] Using GFP to intervene in cervical cancer Hela cells, it was found that GFP could dose dependently upregulate PTEN protein expression, inhibit AKT protein phosphorylation, and reduce the ability of cervical cancer Hela cells to proliferate, invade, and migrate. The main active ingredients of GFP, such as quercetin, can upregulate the TP53 gene and inhibit multiple signaling pathways such as PTK, PKC, MAPK, etc; β - sitosterol can inhibit tumor cell adhesion, invade the basement membrane, and prevent cancer cell metastasis; Shanna phenol can activate the p53 pathway to induce apoptosis in ovarian cancer cells, and bind to estrogen receptors to exert tumor suppressive effects; Ivy saponins can break down the activity of tumor cell membranes and promote tumor cell apoptosis; Epicatechins help enhance the sensitivity of cancer cells to platinum based drugs and reduce the production of MMP2 and MMP9; Tannic acid can prevent the binding of carcinogens to DNA, thereby reducing drug resistance in cancer cells, lowering ATP levels in cancer cells, and hindering the cell's reproductive cycle; Bean sterol derivatives have the ability to inhibit the growth of ovarian cancer cells; Phellinin can inhibit heat shock protein 90 and affect tumor cell growth through the Wnt/β - catenin pathway, indicating that GFP has the ability to regulate various cytokines such as IL-6, VEGFA, CCL2, TNF, MMP9, and affect multiple signaling pathways, thereby achieving the therapeutic effect of treating ovarian cancer [9].

2.3 Analgesia

The generation of pain is closely related to components such as potassium ions, serotonin, acetylcholine, bradykinin, histamine, etc. in the tissue, and prostaglandins in the damaged area can further enhance the pain effects of these components. Research has found that an increase in prostaglandins (PG) is the main cause of PD, with the release of PGF2 α causing strong uterine contractions. Additionally, an increase in COX-2 expression catalyzes the synthesis of PG from arachidonic acid, exacerbating the pain of uterine contractions. Nuclear factor kappa B (NF - κ B) is a key transcription factor regulating COX-2 synthesis [10]. Liu Canwen and others [10] Observing the therapeutic effect of GFP on uterine tissue of rats with primary dysmenorrhea, it was found that GFP can inhibit the NF - κ B/COX-2/PGF2 α pathway, reduce endometrial peeling and edema in rats, and effectively alleviate dysmenorrhea. Chen Jiao and others [11] Using GFP to treat EMT rat models, it was found that GFP increases the thermal radiation pain threshold of EMT rats; Improve the damage of DRG neurons (dorsal root ganglia, primary neurons that transmit pain sensation) in EMT rats; Dose dependent decrease in the density of NF200 (nerve cells) in tissues; Inhibiting the expression of NGF receptors and phosphorylation levels of Erk in the NGF/Erk signaling pathway (which triggers chronic inflammatory pain and neuropathic pain) effectively alleviates pain.

2.4 Improving Blood Rheology

Hemorheology consists of several indicators such as whole blood viscosity, whole blood reduced viscosity, plasma viscosity, erythrocyte sedimentation rate, and red blood cell deformability. It is a reflection of changes in blood fluidity, coagulation, and blood viscosity. Zheng Shunjie and others [12] The combination of GFP and mifepristone in the treatment of elderly patients with uterine fibroids showed a significant decrease in HBV, LBV, and PV (P<0 05), effectively alleviate the symptoms of uterine fibroids caused by blood stasis. Wang Huabin [13] 120 patients with chronic pelvic inflammatory disease (CPID) were selected as the study subjects. The control group was treated with metronidazole, while the observation group was treated with metronidazole combined with GFP. It was found that both groups had a decrease in venous blood LBV, HBV, hematocrit (HCT), and fibrinogen (Fib). The observation group was lower than the control group, and the difference was statistically significant (P<0.05). Ye Zhihui [14] Observing the effect of mifepristone combined with GFP in the treatment of uterine fibroids patients, the results showed that the HBV, LBV, PV, and PAR in the observation group were significantly lower than those in the control group (P<0.05). Related studies have shown that GFP achieves the goal of promoting blood circulation and removing blood stasis by downregulating the expression of VEGF, reducing plasma viscosity, increasing wall permeability, increasing blood flow, and improving microcirculation [15].

2.5 Regulating Endocrine and Lipid Metabolism

The occurrence of PCOS is related to abnormal regulation of the hypothalamic pituitary ovarian axis and adrenal dysfunction. Li Yin and others [16] Establishing a PCOS rat model and observing the therapeutic effect of GFP intervention in the rat model, it was found that GFP can reduce the body weight of PCOS rats, promote follicle formation and increase the thickness of follicular granulosa cell layer, reduce serum T and LH levels, increase E2 levels, and upregulate the PI3K/Akt/mTOR signaling pathway to improve the endocrine disorder environment of PCOS rats. You Pingping [17] In the treatment of 60 patients with diabetes, it was found that the fasting blood glucose, 2-hour postprandial blood glucose and glycosylated hemoglobin in the treatment group were lower than those in the control group (P. Zhao Qiusheng [18] Treat 35 PCOS model rats with GFP. Compared with the control group, the FBG, FINS, androgen (ADG), and HOMA-IR levels in the GFP group rats were significantly reduced (P<0.05), while the adiponectin (APN, insulin sensitizing hormone) value was significantly increased

($P<0.05$), indicating that GFP may regulate insulin resistance and lipid metabolism abnormalities by reducing the levels of FBG, FINS, and ADG in PCOS rats, correcting hypolipidemia.

3. Conclusion

Guizhi Fuling Pill, as a classic formula for promoting blood circulation and removing blood stasis in the "Synopsis of Jin Kui", is widely used in gynecological diseases such as uterine fibroids, ovarian cysts, pelvic inflammatory disease, polycystic ovary syndrome, etc. Due to its remarkable efficacy and few adverse reactions, this formula is also applied to male diseases, cardiovascular and cerebrovascular systems, respiratory systems, and other diseases according to the principle of "treating different diseases with the same treatment" in traditional Chinese medicine, fully utilizing the characteristics of multi-component, multi pathway, and multi-target regulation. Modern pharmacological research has shown that GFP has anti-inflammatory, analgesic, anti-tumor, endocrine and lipid metabolism regulating, and blood rheology improving effects. However, clinical studies have mostly focused on the treatment of gynecological diseases such as pelvic inflammatory disease and uterine fibroids. Clinical studies on cardiovascular and cerebrovascular systems, respiratory systems, tumor suppression, and other aspects are mostly focused on efficacy observation and preliminary mechanism exploration. Experimental studies are mainly conducted on animals, lacking cell experiments. In addition, some case reports and analyses lack unified diagnostic standards and systematic treatment plans, and there are relatively few studies on the correlation between effective drug components and efficacy in formulas. In the future, modern experimental research needs to be deeply applied to fully explore the pharmacological mechanisms and broaden the scope of clinical applications.

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