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Research methods and evaluation of antipyretic prescriptions

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ABSTRACT. *In recent years, traditional Chinese medicine (TCM) has been widely used in the treatment and rehabilitation of cancer patients, all of which benefit from its prominent efficacy of synergy and detoxification. TCM holds that when blood meets heat coagulation, burning is phlegm，phlegm, turbidity, Qi and blood can block meridians and viscera, coalesce into tumors. It can be seen that one of the most important causes leading to tumors is heat toxicity. Although the method of clearing away heat and detoxification belongs to the treatment of attacking pathogens, it also has a wide range of regulating effects on the body, making it different from the pure drug of attacking pathogens. Therefore, the author reviews the general treatment of cancer patients by prescriptions, drugs and active ingredients with heat-clearing and detoxifying effects, as well as the mechanism of influencing the metabolism of cancer cells and enhancing the immunity of the body. It is concluded that Qingre Jiedu recipe can not only promote the apoptosis of tumor cells, inhibit the proliferation and invasion of tumors, but also have significant effects in regulating immune anti-tumor and multi-drug resistance.*

KEYWORDS: *Heat-Clearing And Detoxification; Traditional Chinese Medicine; Anti-Cancer; Mechanism Of Action; Review;*

1. Introduction

Although cancer research is in full swing at present, it has not fundamentally revealed the true cause of cancer. The overall concept of traditional medicine and dialectical treatment are simplified. It is concluded that heat toxicity is an important factor in the occurrence and development of tumors. The key to the surgical mind of the medical professor Jinjian is recorded in the proof of loss of pride (i.e. thyroid nodules or thyroid cancer): "The proof of loss of pride is formed by anger, melancholy, depression, blood rebellion and fire coagulation." It is said that thyroid nodules and thyroid cancer may be caused by the patient's excessive mood and depression. In addition, based on the pathogenesis of fire pathogen in Su Wen, Liu Hejian, a doctor of Jin and Yuan Dynasties, expounded the category of Fire-heat syndrome and established the frontier view that "all six Qi are from cremation". Its treatment theory is summarized as follows: "Fa should be treated with hard cold

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medicine, heat dissipation. Or the heat stagnation knot can not be opened, the law should be under the hard cold medicine, knot heat dissipation and no depression knot. [1] Heat toxicity can form tumors, blood coagulates together when it meets heat, Jin burn is phlegm, Qi, blood and phlegm can obstruct meridians and viscera, and coalesce into tumors. Therefore, we can often see in the clinical, some, especially in patients with advanced cancer, local mass burning pain, five upset fever, red stool thirst, yellow tongue coating, pulse string number and other toxic heat or local or overall signs of evil heat stasis poisoning. To sum up, clearing away heat and detoxification is an important principle in the treatment of cancer.

Through consulting the literature, we can find that the use of heat-clearing and detoxification prescriptions in the treatment of cancer mainly includes the following research forms:

2. To study the therapeutic effect of prescriptions with clearing away heat and detoxifying effect on a disease or symptom.

Ren Junze et al. [2] Based on the network pharmacology research, we found that the active ingredients of Baitouweng Decoction had significant effects on 54 GO biological processes, including cell proliferation, migration, apoptosis, protein phosphorylation regulation and ERK1, ERK2 cascade reaction, which were important factors affecting the occurrence and development of tumors. Further enrichment analysis of KEGG signaling pathway revealed that the active ingredients of Baitouweng Decoction were even associated with 57 tumor-related pathways, such as TNF, PI3K-Akt. The above results predicted that Baitouweng Decoction may affect the proliferation, migration, apoptosis, angiogenesis, protein phosphorylation and other processes of cancer cells through the above pathways, thus playing a role in the treatment of gastrointestinal, respiratory and endocrine system tumors. Many studies have confirmed that the four drugs in Baitouweng Decoction have strong anti-tumor activity. Among them, beta-sitosterol, quercetin, saponins of Baitouweng, berberine and berberine play an anti-tumor role through a variety of signaling pathways, which is consistent with the results of network pharmacology research, thus further verifying the classics of traditional Chinese medicine. Accuracy of prescriptions for ancient prescriptions.

Hou Junming et al. measured the proliferation of SW480 cells by MTT assay. [3] Flow cytometry showed that Ehuang decoction could inhibit the proliferation of SW480 cells, suggesting that Ehuang Decoction might prevent cells from entering G2/M phase, and the specific time of action might be S phase.

3. To explore the effects of antipyretics and their effective extracts on cell metabolism by affecting specific proteins or pathways:

Yang Tao et al. [4] found that rhubarb extract could significantly inhibit the proliferation of HSC at the dose of EC50 of 10.4 ug/ml, and promote the apoptosis of (LX-2) cells at the same time. At the concentration of 2 ug/ml, rhubarb extract

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had no adverse effect on cell cycle. Therefore, rhubarb extract can promote the apoptosis of HSC and has potential anti-hepatic fibrosis activity.

Zhouzhen et al. [5] MTT assay and flow cytometry showed that baicalein could significantly inhibit the proliferation of hepatocellular carcinoma cells and promote the growth of hepatocellular carcinoma cells to stagnate in G0/G1 phase, and showed time-and dose-dependent tolerance. When As2O3 was combined with baicalein, the inhibition was stronger. The synergistic effect of As2O3 5 micromol/L and baicalein 20 micromol/L for 48 hours was the most obvious. At the same time, the expression of caspase-3, caspase-6, caspase-9 protein and mRNA in HCCLM9 and MHCC97L cells treated with baicalein at 20 micromol/L and AS2O3 at 5 micromol/L for 48 hours were significantly increased. The apoptotic effect of baicalein combined with As2O3 on hepatocellular carcinoma cells was also detected by Tunel.

Li Sheng and others divided the extract of Paris polyphylla into different dosage groups to act on SW480 cells. The proportion of cells in S phase decreased significantly, the distribution of cells in G0-G1 phase and G2/M phase increased ($P < 0.05$), and the expression of SCF increased ($P < 0.05$). It is worth mentioning that its mechanism of action may also be unrelated to SCF. [6]

Chen Boyi et al. [7] In recent years, basic experimental studies have found that andrographolide can inhibit the expression of Akt and p38 proteins and induce apoptosis and autophagy of cancer cells by regulating the expression of p53 in JNK1/2 pathway. It can also regulate the mitochondrial apoptosis pathway of cholangiocarcinoma cells and inhibit cholangiocarcinoma by reducing the expression of BCl-2. Cell proliferation promotes apoptosis of cholangiocarcinoma cells. Andrographolide can also promote the apoptosis and inhibit the activity of breast cancer cells. The mechanism may be related to its ability to inhibit the abnormal activation of NF-kappa B and regulate the activation of NF-kappa B.

Liu Ying et al. [8] Telomerase activity of Hela cells treated with Hedyotis diffusa was detected by immunohistochemical method. The expression of hTERT gene was determined by immunofluorescence method. The results showed that the extract of Hedyotis diffusa with a certain concentration could induce apoptosis of Hela cells. With the increase of drug concentration, it could induce apoptosis of Hela cells. With the prolongation of time, the Telomerase activity of Hela cells decreased, the apoptotic rate of tumor cells increased, and the expression of hTERT specific gene decreased. This suggests that Hedyotis diffusa may play an anti-tumor role by down-regulating the expression of hTERT gene.

Gao Chao et al. [9] By studying the effects of Hedyotis diffusa on cell cycle, apoptosis and Telomerase activity of human cervical cancer cells, we concluded that Hedyotis diffusa might have the ability to further reduce its Telomerase activity by changing cell cycle distribution and inducing apoptosis, thus achieving anti-tumor effect. At the same time, the mitochondrial transmembrane potential (MTP) of leukemia cells treated with the extract of Hedyotis diffusa decreased significantly, suggesting that the inhibition of leukemia cell proliferation may be through reducing the mitochondrial transmembrane potential and improving the permeability of cell

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membrane, thus activating Caspase or destroying chromatin by releasing Bax family proteins from cells to induce cell proliferation. Apoptosis.

4. Effective extracts of some antipyretic and detoxicating drugs can improve the immune function of the body.

Lu Pingcheng et al. [10] found that Scutellaria barbata polysaccharide could promote the transformation of spleen lymphocyte induced by Con A in vitro. After percutaneous injection, the positive rate of esterase staining in peripheral blood lymphocyte of mice was significantly increased, and the delayed hypersensitivity induced by DNSB occurred earlier. However, when the dosage was too high, the polysaccharide of Scutellaria barbata had no effect on spleen index, only inhibited thymus index of mice.

Wang Hongqi et al. [11] By comparing the effects of Chinese herbs for tonifying and clearing away heat and detoxification on hepatocellular carcinoma H22 cells and the experimental study of immunological mechanism, we found that the mechanism of hepatocellular carcinoma H22 cells necrosis and apoptosis induced by Scutellaria barbata polysaccharides may be related to the effective improvement of cellular immune function of Scutellaria barbata polysaccharides.

Other studies have found that shikonin exerts its anti-tumor effect mainly by regulating the immune function of the organism. Yuexin et al. [12] studied that shikonin may have the opportunity to become a new sensitizer for choriocarcinoma chemotherapy. Shikonin can reverse the drug resistance of JAR/MTX cells by down-regulating the expression of Survivin and BCl-2 genes. Shikonin can not only directly damage ovarian cancer HO-8910 cells, but also stimulate the maturation of dendritic cells and activation of tumor antigen-specific T cells by exposing calcium reticulin on the surface of HO-8910 cell membrane, and ultimately enhance the immunogenicity of apoptotic tumor cells. [13]

According to the latest data released by the International Health Organization, more than 8 million people die of cancer every year, but compared with the significant decline in cancer incidence in the United States in recent years, China's figure is growing steadily. [14] It is precisely because the continuous development of traditional Chinese medicine in the field of cancer research and clinical use can significantly improve the overall situation of patients, reduce cancer pain, delay or reverse drug resistance, reduce adverse reactions to chemotherapy and other effective ways to improve the quality of life of cancer patients, more and more researchers choose traditional Chinese medicine as the research goal. In recent years, the research methods of network pharmacology and systematic evaluation have developed vigorously, effectively gathering the previous research results of traditional Chinese medicine, and using data to show the authenticity of the therapeutic effect of traditional Chinese medicine. On this basis, we also found some facts that had been neglected before. It was confirmed by experiments that Qingre Jiedu Prescription can promote apoptosis of cancer cells, inhibit proliferation and invasion of cancer, and has remarkable effect in multidrug resistance and regulating

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immune and anti-tumor, although it is not enough to deal with chemotherapy. Drugs or targeted drugs are comparable, but as adjuvant therapy, they are far better than western medicine. In conclusion, the anti-tumor properties of Chinese herbal medicine for clearing away heat and detoxification make it have great potential in the application of anti-cancer, which is worth further exploring.

Fund projects

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2. The special scientific research program of Shaanxi Provincial Department of education, 18jk0230, the effect of Zehuang enema on the growth and HIF-1 α - uPA, uPAR pathway of human rectal cancer sw837 transplanted tumor;
3. Xianyang Science and Technology Achievement Promotion Program, 2018KT-43.Through high-throughput sequencing technology to study the effect of Zedoary enema on intestinal flora and intestinal mucosal barrier function of rectal cancer rats;

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