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Analysis and research progress on the anticancer effects of Scutellaria barbata

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Abstract. The most common anti-cancer therapy is to use chemotherapy drugs, but this drug has huge side effects on the patient's body, so some doctors want to study whether there are other natural drugs that can fight cancer and have fewer side effects. And Scutellaria barbata is one of the natural drugs studied by doctors. Scutellaria barbata is often used in traditional Chinese medicine to assist in inhibiting the growth of cancer cells, hoping to reduce the harm of cancer cells to patients. In the database, current doctors have "dissected" the effective ingredients of Scutellaria barbata into five categories. This article analyzes three of them, including flavonoids, polysaccharides and alkaloids. This article analyzes the research on Scutellaria barbata in anti-cancer, and obtained many clinically effective case results and some proven effective ingredients. This article can provide some useful references for future research ideas, but there is still a research gap on how to extract the effective anti-cancer ingredients of Scutellaria barbata and study drugs that can effectively inhibit cancer. Future research can focus on the direction of chemical components of Scutellaria barbata.

Keywords: Scutellaria barbata, alkaloids, anticancer effects, flavonoids.

1. Introduction

Cancer is a serious disease that cannot be solved by current medical technology. According to statistics from the World Health Organization, nearly 20 million people worldwide suffer from this disease each year, and nearly 9.7 million people die from cancer. Cancer causes one in nine male and one in twelfth female deaths [1]. Conventional chemotherapy and physical surgery have limited effects on cancer treatment, and their toxicity and side effects on normal cells cannot be ignored.

After long-term development, traditional Chinese medicine has been clinically proven to have significant therapeutic effects on various types of cancer. Therefore, medical scientists have thought of using Chinese medicinal materials as an auxiliary to inhibit tumor factors. For example, Scutellaria barbata is a medicinal material often used in traditional Chinese medicine to treat cancer. Barbata barbata belongs to the Lamiaceae family, and Scutellaria baicalensis is a perennial plant. One plant can reach 55 cm. The leaves are short-stalked or nearly sessile, and the leaves are triangular and oval. shape. Studies have shown that it contains many chemical components that have anti-tumor, heat-clearing and detoxifying, antibacterial, and anti-inflammatory effects. In recent years, this drug has been not only used in traditional Chinese medicine but also in Western medicine. It plays a role in various cancer treatments, such as colorectal cancer, ovarian cancer, cervical cancer, etc. Some studies have shown that Scutellaria barbata contains flavonoids, terpenes, alkaloids, volatile oils, polysaccharides and other

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chemicals, and some of them can effectively provide help in anti-cancer work. For example, the main anti-cancer components of flavonoids include scutellarin, apigenin, Luteolin, baicalin, and wogonin inhibit tumor growth and promote tumor cell apoptosis through thirteen cancer-specific pathways and nine general pathways [2]. Because the mechanism of action of Scutellaria barbata in treating tumors has not yet been clarified, and it is difficult to analyze and develop the effective anti-cancer components of Scutellaria barbata, it is difficult to develop drugs or treatments made from Scutellaria barbata. Planning remains a big problem. However, many studies have shown that Scutellaria barbata can assist in the treatment of cancer diseases and some possible mechanisms of action have been described.

This study will analyze the effective ingredients in Scutellaria barbata for cancer treatment, possible mechanisms of action, the results of Scutellaria barbata tests on breast cancer, colon cancer and esophageal cancer, and analyze the problems that still exist in using Scutellaria barbata to treat cancer. It is hoped that theoretical ideas can be provided for the application of Scutellaria barbata in cancer treatment to help further develop more effective treatment methods, bring new ideas and thoughts to medical scientists studying cancer treatment, and benefit more cancer patients.

2. Analysis of active ingredients

2.1. Analysis of flavonoid components

According to the extraction experiment, the effective anti-cancer ingredients of Scutellaria barbata include flavonoids, and flavonoids are most useful for making anti-cancer drugs and treating cancer. First, it can intervene in the growth and apoptosis of cancer cells through multiple targets and pathways. Second, flavonoids mainly include flavones, flavonols, dihydroflavones, isoflavones, flavanols, flavanone alcohols, flavanones, and saturated chalcones. Flavonoids have multiple pharmacological effects such as antioxidant, anti-mutagenic, antibacterial, anti-inflammatory, anti-allergic, and anti-cancer [2]. In addition, flavonoids and drugs do not have the side effects of traditional treatments that damage normal cells, so they are deeply loved by scientists and doctors. Among the main anti-cancer ingredients of flavonoids, baicalin is chemically named 4', 5, 6-trihydroxyflavone-O-β-D glucuronide. It is a flavonoid compound mainly composed of peptidoglycan, heteropolysaccharide and glucan. It is also known as scutellarin, scutellarin, homobaicalin, baicalin, apigenin, and ginseng. Its molecular formula is C21H18O12. Apigenin has multiple mechanisms of action, including anti-inflammatory, anti-oxidative stress, anti-fibrosis, regulation of proteases and anti-proteases, and influence on tumor cell proliferation [3,4]. Luteolin is a flavonoid compound that mainly exists in the form of glycosides. Studies have shown that luteolin has strong anti-inflammatory, anti-diabetic, and cardioprotective functions [5].

2.2. Polysaccharide composition analysis

Polysaccharides are a class of high molecular polymers, usually formed by the polymerization and dehydration of 10 or more monosaccharides through glycosidic bonds such as α (1, 4), α (1, 2), β (1, 3) and β (1, 6). They are widely present in various natural products as medicinal active ingredients [6]. Polysaccharides with complex structures have strong biological activities and are often used in clinical practice for human immune function regulation, antiviral, anti-tumor, antioxidant and hypoglycemic effects. The main types of polysaccharides in Scutellaria barbata are acidic polysaccharides and neutral polysaccharides. Ning Xin et al. used hot water extraction and DEAE-cellulose ion exchange column fractionation to obtain the acidic sugar fraction WSBP-A of Scutellaria barbata with a yield of 20.2%. The main monosaccharides and their molar ratios are GlcA∶Glc∶Man∶Ara∶GalA∶Gal∶Rha = 14.7∶11.4∶16.9∶8.0∶21.1∶18.8∶6.2; the main monosaccharides and their molar ratios in the acidic sugar fraction are GlcA∶Man∶Ara∶GalA∶Gal∶Rha = 17.2∶20.3∶5.4∶27.5∶18.8∶5.9. Kong Mingli et al. used distilled water extraction and DE-52 cellulose column chromatography to obtain acidic polysaccharide SPS II. The hydrolyzed product contained arabinose, mannose, fructose, and galactose [7]. Ning Xin et al. fractionated the polysaccharides of Scutellaria barbata and obtained the neutral sugar fraction WSBP-N with a yield of 50.8%. The monosaccharides with the highest content were Glc, Gal, and Ara. Because

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this method does not require expensive instruments and equipment, such as gel filtration chromatographs, ion exchange chromatographs, etc., nor does it require the purchase of expensive consumables such as ultrafiltration membranes. This greatly reduces the cost of grading, and the hot water boiling method is relatively mild, and the damage to the polysaccharide structure is relatively small, which is conducive to subsequent research. Kong Mingli and others used distilled water extraction and DE-52 cellulose column chromatography to obtain neutral polysaccharide SPS I. The hydrolyzed product contains rhamnose, ribose, xylose, and glucose. The DE-52 cellulose column chromatography method can separate different substances according to their affinity for cellulose. The target substance can be effectively separated, the purity of the extract can be improved, and the success of the research experiment can be improved. Wang Zhiyuan et al. used water extraction, polysaccharide gel and ion exchange column chromatography to obtain polysaccharide from Scutellaria barbata, which contained monosaccharides and their molar ratios of rhamnose: fucose: arabinose: xylose: mannose: glucose: galactose = 1.00: 0.13: 0.80: 0.10: 0.34: 0.56: 3.04 [8]. Although polysaccharide gel and ion exchange column chromatography are more expensive than water extraction, they have the advantages of good repeatability and reliability. Water extraction method helps to maintain the biological activity and natural characteristics of the extract, and increase the accuracy and correctness of the experiment.

3. Possible mechanisms of action (pathways, targets, changes in the tumor microenvironment)

3.1. Flavonoids

The main anti-cancer components of flavonoids include baicalin, apigenin, and luteolin [9]. Among them, baicalin can cause mitochondrial-mediated apoptosis of liver cancer cells through the STAT3 pathway in the field of anti-cancer [3]. Apigenin is a flavonoid compound that has anti-inflammatory, antioxidant and immune cell activity regulating effects. Apigenin can inhibit the proliferation, migration and invasion of HEC-1-B cells by inhibiting the activation of the PI3K/AKT signaling pathway [8]. Luteolin can reduce the expression levels of PI3K, pPI3K, Akt, and p-Akt to a certain extent, and down-regulate the expression levels of PI3K, Akt, and p-PI3K mRNA, regulate the PI3K/Akt signaling pathway, thereby inhibiting the proliferation rate and migration ability of cervical cancer HeLa cells, promoting HeLa cell apoptosis, and achieving the effect of improving and treating cervical cancer [9].

3.2. Polysaccharides

Polysaccharides have anti-cancer biological effects. In the study of colon cancer, it was found that Scutellaria barbata polysaccharide can inhibit the migration of tumor cells by reversing the EMT process of tumor cells through the Smad pathway. It can also inhibit the growth and proliferation of colon cancer HT29 cells by inhibiting the activation and activation of the PI3K/Akt pathway, inducing cell apoptosis and blocking the EMT process [9]. Second, Scutellaria barbata polysaccharide can inhibit lung cancer by inhibiting the expression of VEGF and EGFR in tumor tissues and upregulating the expression level of the nm23 gene. It can also inhibit the growth of 95-D tumor cells by downregulating the phosphorylation level of c-Met and blocking the p-AKT and p-ERK pathways [9]. Li et al. studied the effect of Scutellaria barbata polysaccharide on antagonizing the invasion and migration of HT-29 colon cancer cells induced by TGF-β1. They started this study by using TGF rats as the stimulating factor of EMT. The experimental results showed that Scutellaria barbata polysaccharide can reverse the EMT process of tumor cells with the help of the Smad pathway, thereby inhibiting the migration of tumor cells. Pengda Sun et al. confirmed that Scutellaria barbata polysaccharide can inhibit the growth and proliferation of colon cancer HT29 cells by inhibiting the activation of the PI3K/Akt pathway, inducing cell apoptosis and blocking the EMT process, thereby effectively treating colon cancer [9].

In terms of cervical cancer, Scutellaria barbata polysaccharide can inhibit cervical cancer by downregulating the expression of AMFR in tumor cells [9]. Scutellaria barbata polysaccharide can also inhibit the activity of gastric cancer cell SGC-7901. The higher the dose, the stronger the inhibitory effect. It inhibits cancer cell proliferation by upregulating the P53 gene [9]. Finally, Scutellaria barbata

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polysaccharide can also treat liver cancer through multi-target regulation, but the amino acid sequence of the related protein needs further research and confirmation [9].

Li et al. observed the effects of Scutellaria barbata polysaccharide on the expression of VEGF, EGFR, and nm23 in Lewis lung cancer mice, and confirmed that Scutellaria barbata polysaccharide can inhibit the expression of VEGF and EGFR in tumor tissues and upregulate the expression level of nm23 gene to inhibit lung cancer. Xiaokun Yang et al. also proved that Scutellaria barbata polysaccharide can inhibit the growth of 95-D tumor cells by downregulating the phosphorylation level of c-Met and blocking the p-AKT and p-ERK pathways, thereby achieving the purpose of treating lung cancer [10].

3.3. Alkaloids

Alkaloids can be extracted from Scutellaria barbata by acid extraction and alkali precipitation [11]. Hao Xiaoshan and others isolated cinchlor-type diterpene alkaloids from Scutellaria barbata that can inhibit P-glycoprotein and reverse tumor drug resistance and inhibit the proliferation of glioma U251 cells [10]. Experiments have found that barbataline B (SBT-B) has 6 effects in the treatment of glioma. The first is that SBT-B can inhibit the viability of U251 cells. Second, SBT-B inhibition can significantly reduce the rate of EdU-positive cells in U251 cell proliferation during the experiment. Third, SBT-B induces DNA double-strand breaks in U251 cells, based on the fact that the number of γ-H2AX foci and protein expression increased significantly during the experiment. Fourth, SBT-B can promote U251 cell apoptosis because the number of apoptotic cells significantly increased in the experiment, and the cleavage of PARP, caspase-8 and caspase-9 was significantly promoted. The last one is that SBT-B will activate the MAPK signaling pathway because the phosphorylation levels of ERK1/2, p38 MAPK and JNK1/2 were found to be significantly increased in experiments. Li et al. studied the inhibitory effect of barbataline on the growth of human osteosarcoma cells and its mechanism of action [11]. First, their colony formation experiments showed that SBT could inhibit the colony formation of 143B cells and reduce the number of cell colonies formed. The second Horchest 33258 staining results showed that SBT could induce apoptosis in 143B cells, and the nuclei showed high fluorescence phenomena such as pyknosis, fragmentation, and chromatin aggregation. The results of Western blotting showed that after SBT treatment, the protein level of the apoptosis molecule BAD increased, the protein level of the apoptosis inhibitory molecule BCL2 decreased, and the protein level of cleaved caspase 3, the active form of the apoptosis executor caspase 3, increased, which shows that SBT can promote 143B Apoptosis. Third, SBT can inhibit the migration and invasion of 143B cells. The results of scratch experiments show that SBT inhibits the migration of 143B cells and delays scratch healing. Transwell chamber experiment results show that SBT can inhibit the invasion of 143B cells and reduce the number of cells passing through the chamber. The fourth SBT can inhibit the activation of Wnt/β-catenin signaling pathway in 143B cells. The luciferase reporter gene experiment showed that TopLuc luciferase activity was reduced after SBT treatment. Western blot analysis confirmed that after SBT treatment, the protein level of β-catenin was down-regulated, and the protein levels of its downstream target molecules C-myc and Cyclin D1 were also reduced accordingly. At the same time, SBT can also inhibit the phosphorylation level of Ser9.

4. Progress in clinical application

In traditional Chinese medicine, Scutellaria barbata is often used as a cancer treatment drug. There are many clinical examples in traditional Chinese medicine that can prove the effectiveness of this drug. Luo Yi proposed that in the process of treating gastric cancer, it is necessary to strengthen the spleen and stomach, supplemented by the methods of clearing away heat and detoxifying, eliminating carbuncle and dispersing knots, and running through the whole process [12]. Wang Xiaomin believes that the use of 30g of lotus tongue medicine pair can have the effect of clearing heat and detoxifying [13]. Liu Weisheng believes that the lotus tongue medicine pair can achieve good results in clinical treatment of tumors when combined with tonic medicine, attacking and supplementing at the same time [14]. For patients in the early and middle stages with good physical fitness, the lotus tongue medicine pair is used at 20-30g each; for patients in the late stage or the elderly and weak, the dosage is reduced, and the usual

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dosage is 15-20g. This medicine pair is often used after chemotherapy, which can reduce the toxic and side effects of chemotherapy and improve the quality of life of gastric cancer patients. It has a unique advantage in improving the efficacy of late-stage gastric cancer. Shi et al. used Qishen Yiwei Decoction (including 10g of each lotus and tongue herb pair) to relieve gastric mucosal inflammation, block intestinal epithelial hyperplasia, improve chronic gastritis with precancerous symptoms, and treat both the symptoms and the root cause of gastric precancerous lesions. As mentioned above, Scutellaria barbata can help doctors provide better medical treatment for patients [15].

5. Conclusion

This article collects and summarizes the effective anti-cancer ingredients of Scutellaria barbata in many databases, including flavonoids, polysaccharides and alkaloids. The effective ingredients of flavonoids and polysaccharides are analyzed; combined with literature analysis, the possible mechanisms of action of polysaccharides, flavonoids and alkaloids are summarized. Through analysis, although there are few studies on Scutellaria barbata in anti-cancer, many literatures all reveal that Scutellaria barbata will play a huge role in anti-cancer treatment, benefiting more cancer patients and giving them a healthy body. In this article, the alkaloids of Scutellaria barbata are mentioned, which can inhibit the growth of cancer cells and promote apoptosis of cancer cells in many aspects and dimensions, and have lower side effects than normal drugs or therapies, such as the most common therapy now-chemotherapy. This article can provide some inspiration and ideas for future research on the use of Scutellaria barbata to treat cancer. However, since there are still few studies on Scutellaria barbata, it is still unknown whether some ingredients have an effect, and some mechanisms of action are still hypothetical, and no research has confirmed that this mechanism of action is true.

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