

# Research Progress of Shenlingbaizhu Powder in the Treatment of Malignant Tumor

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**Abstract:** *Traditional Chinese medicine considers that the deficiency of healthy qi and the disequilibrium of spleen and stomach are one of the basic pathogenesis of malignant tumor. Shenlingbaizhu Powder, as one of the classic representative prescriptions of invigorating spleen and invigorating qi, is widely used in the clinical treatment of malignant tumor. There are many literature reports on the mechanism of addition and reduction of Shenlingbaizhu powder in the treatment of malignant tumor. This article mainly reviews the research progress of Shenlingbaizhu powder in the treatment of malignant tumors from two aspects of clinical and experimental studies, in order to provide references for the clinical application of traditional Chinese medicine in the treatment of tumor and the development of new anticancer drugs.*

**Keywords:** Shenlingbaizhu Powder, Malignant tumor, Traditional Chinese medicine, Clinical experience.

## 1. Introduction

At present, the incidence and mortality of cancer continue to rise globally and is expected to become the leading cause of death in every country in the 21st century. At present, comprehensive treatment methods including surgery, radiotherapy, chemotherapy, targeted therapy and immunotherapy are mostly adopted for malignant tumors, which can cause different degrees of damage to the body and seriously affect the quality of life of patients. In recent years, traditional Chinese medicine has been widely used in the clinical treatment of malignant tumors, which can effectively prevent the occurrence of malignant tumors, reduce postoperative recurrence and metastasis, prolong survival time, and play a unique advantage in enhancing the effectiveness and attenuating the toxicity of radiotherapy and chemotherapy and improving the quality of life of patients. TCM believes that the formation and development of tumor is closely related to the disharmony of the spleen and stomach and the deficiency of healthy qi, and the treatment should focus on strengthening the healthy and consolidating the root, and the key to supporting healthy qi is strengthening the spleen. Shenling Baizhu Powder, as a representative prescription for strengthening spleen and supplementing qi, has significant clinical effect in the treatment or auxiliary treatment of malignant tumors. This article mainly summarizes the research progress of Shenling Baizhu Powder in the treatment of cancer, and provides reference for its clinical application and further study.

## 2. Experimental Research Progress of Shenlingbaizhu Powder in the Treatment of Malignant Tumors

### 2.1 Shenling Baizhu Powder Inhibited the Proliferation of Cancer Cells and Promoted Apoptosis

Normal cells maintain dynamic balance under the bidirectional regulation of growth signal and growth inhibition signal, and carry out orderly growth and differentiation, while cancer cells can remove the growth

inhibition signal control through gene mutation, so that the cell cycle progression and cell growth disorder can be infinite proliferation. Song [1] et al. added 10% rat serum of Shenlingbaizhu powder into the medium of LPS-induced lung adenocarcinoma cell lines, and found that the drug-containing serum of Shenlingbaizhu powder could effectively inhibit the proliferation of lung adenocarcinoma cell lines promoted by LPS and down-regulate the mRNA expression level of Toll receptor 4 induced by LPS-induced. This indicated that soil cultivation and gold generation could inhibit the proliferation of tumor cells through Toll receptor-4 signaling pathway at the cellular level. Peng Ying [2] 's study found that Shenlingbaizhu powder combined with cyclophosphamide was more effective in slowing the tumor growth of H22 liver cancer transplant tumor chemotherapy model mice than Shenlingbaizhu powder or cyclophosphamide alone. Shenlingbaizhu powder and cyclophosphamide can synergistically promote the apoptosis of tumor cells, and the mechanism may be related to the regulation of the expression of PDGF-BB, VEGF, Ang-1, Ang-2 and other tumor apoptosis-related factors.

### 2.2 Shenlingbaizhu Powder Inhibited Tumor Cell Migration and Angiogenesis

Tumor angiogenesis is a key factor in tumor growth, metastasis, recurrence and prognosis. VEGF is a heparin-binding growth factor specific to vascular endothelial cells, which can induce angiogenesis and promote the growth of tumor tissue. AKT and VEGF are closely related in tumor angiogenesis, and the AKT signaling pathway plays an important role in the regulation of endothelial cells, vascular smooth muscle cells, macrophages and other vascular abnormal cells. AKT1 seems to be a major subtype that promotes the normal physiological function of endothelial cells. The expression of activated AKT1 allele in endothelial cells can block the formation of new endometrial lesions after arterial injury and induce pathological angiogenesis. In this [3,4] study, 45 mouse models of lung cancer with bone metastasis cancer pain were divided into 5 groups according to random number table method: Shenlingbaizhu powder supplemented high-dose, medium-dose and low-dose groups,

and rapamycin group. By detecting the protein expression of VEGF, mTOR, AKT and P70S6 in tibia of mice in each group, it was found that Shenlingbaizhu Powder supplemented compound may inhibit the expression of VEGF, mTOR, AKT and P70S6, thus affecting the formation of tumor blood vessels and tumor tissues, and play a role in the treatment of bone cancer pain.

### **2.3 ShenlingBaizhu Powder Regulates the Body's Immune Function Modern**

studies have found that Codonopsis polysaccharide can enhance the immune response of the body and has an immune-promoting effect. The water extract of Poria Cocos can increase the proportion of NK, CD4+ T cells and CD8+ T cells in spleen and enhance the activity of NK cells, so as to play the role [5] of immune regulation. Baizhu polysaccharide can improve the damage [6] of intestinal mucosal immune barrier in rats with severe acute pancreatitis by inhibiting the activation of related signaling pathways. Studies have found that the most commonly used combination of Codonopsis codonopsis, Poria codonta, combination of cold and warm in Baizhu and harmonization of liver and spleen can effectively regulate the levels of cytokines such as IL-6, tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), transforming growth factor- $\beta$ 1 (TGF $\beta$ 1), and have the effect [7] of inhibiting tumor growth and delaying tumor development.

### **2.4 Shenling Baizhu Powder Can Improve the Tumor Inflammatory Microenvironment**

Modern medicine believes that inflammation is reflected in all stages of malignant tumors, and sustained inflammation can promote the formation of inflammatory blood vessels to form an inflammatory microenvironment, in which tumor cells are more likely to proliferate and spread, significantly increasing the rate of tumor metastasis. At present, studies have shown that the proliferation of malignant tumor cells can be inhibited by inhibiting the inflammatory microenvironment. Zhang Yunting [8] et al. found that Shenlingbaizhu powder can downregulate the protein expression of inflammatory related factors TLR4 and MyD88, promote the protein expression level of Caspase-3, regulate the inflammatory response of tumor tissues, change the tumor microenvironment, and improve the tumor inhibition rate. Compared with cisplatin and Shenlingbaizhu powder alone, The tumor inhibition rate of Shenlingbaizhu powder combined with cisplatin could reach 44.51%.

### **2.5 Regulation of Intestinal Flora**

The gut microecosystem is often considered a "forgotten functional organ", but its relevance to human diseases has attracted increasing attention from scholars at home and abroad in recent years. Domestic scholars have analyzed the difference in intestinal microflora spectrum between cancer patients and healthy adults, and the results show that compared with healthy adults, the intestinal microflora of cancer patients is in an unbalanced state, the types and number of pathogenic bacteria have increased, while the types and number of probiotics have decreased significantly, indicating that the occurrence and development of cancer may be related to changes in intestinal microflora. Jingjiang Lai [9] et al.

showed that Shenlingbaizhu powder could potentially reduce the relative abundance of Escherichia coli, Helicobacter pylori and Enterobacteriaceae, and increase the relative abundance of Helicobacillaceae, Bacteriaceae and Lactobacillaceae, etc. Shenlingbaizhu powder could regulate the disturbance of microflora caused by pirlotinib, and significantly alleviate diarrhea in rat models of pirlotinib diarrhea. The therapeutic effect reached 66.7%. Wang Shuyun [10] et al. found that chemotherapy drugs could damage the intestinal mucosal barrier in mice to a certain extent, and the damage of intestinal mucosal barrier would lead to low intestinal immune function, imbalance of intestinal flora, and dysfunction of digestion and absorption, resulting in an increased incidence of intestinal inflammation. However, Shenlingbaizhu powder can significantly repair the histological arrangement of colorectal villi after chemotherapy, reduce the occurrence of inflammatory response, and significantly increase the expression levels of colonic tight junction protein closure protein, occluding protein and atretic zonolin-1 after chemotherapy. Compared with oxaliplatin, Shenlingbaizhu powder combined with oxaliplatin can alleviate the intestinal mucosal barrier damage and repair the intestinal mucosal barrier damage caused by chemotherapy to a certain extent. On the other hand, Shenlingbaizhu powder could increase the infiltration of CD8+ T cells in the tumor microenvironment.

## **3. Clinical Research Progress of Shenlingbaizhu Powder in the Treatment of Malignant Tumors**

### **3.1 The Synergistic and Toxic-reducing Effects of Shenlingbaizhu Powder on Radiotherapy, Chemotherapy and Targeted Therapy**

At the same time, chemotherapy drugs can damage the functions of the viscera, especially the functions of the spleen and stomach to different degrees, resulting in symptoms of weakness of the spleen and stomach, such as loss of appetite, abdominal distention, nausea and vomiting, thin loose stool, fatigue and other symptoms. Chemotherapy makes the body more vacuous, reduce the body immunity, often make the treatment can not be completed on schedule, and even suspend the treatment. Lai Yiqin [11] et al. collected 60 patients with spleen and stomach qi deficiency who were going to receive 5-FU/CF combined with paclitaxel dose intensive chemotherapy for stage IV gastric cancer. They were respectively treated with chemotherapy or chemotherapy combined with Shenlingbaizhu Powder Chinese herbal decoction. The results showed that Shenlingbaizhu powder could alleviate neutropenia and other toxic side effects caused by spleen and stomach qi deficiency type gastric cancer caused by intensive chemotherapy. It can improve the clinical symptoms of traditional Chinese medicine, improve the quality of life and cellular immune function of patients, and enhance the patient's tolerance to radiotherapy and chemotherapy, which can effectively ensure the successful completion of radiotherapy and chemotherapy, and finally obtain significant synergistic and toxic-reducing effects. Yu [12] Li et al. found that the clinical efficacy of Shenlingbaizhu powder combined with apatinib in the treatment of advanced gastric cancer was superior to that of Apatinib single drug, which could reduce the toxic side effects

of apatinib and improve the quality of life. Li Huan [13] et al. found that Shenling Baizhu combined with chemotherapy in the treatment of patients with spleen-deficiency and shi-sheng type esophageal cancer after three field radical surgery could reduce the incidence of bone marrow suppression and digestive system side reactions, improve patients' physique and improve patients' quality of life. Wang Lei [14] et al. found that Huaban Decoction combined with Shenlingbaizhu Powder had a good preventive effect on lung injury caused by cancer radiotherapy, and could reduce inflammation, improve immune function and lung function, and reduce the incidence of lung injury caused by radiation, the mechanism of which may be related to the inhibition of miR-17-5p and miR-7-5p expression.

### 3.2 ShenlingBaizhu Powder Regulates the immune Function of Patients with Malignant Tumors

Zhao Min [15] et al. retrospectively analyzed the medical records of 72 patients who underwent total mesenteric resection after neoadjuvant chemotherapy. The results showed that the Shenlingbaizhu powder combined with neoadjuvant chemotherapy group could improve the immune function of patients, increase the levels of cellular immune factors CD3+, CD4+, CD4+/CD8+, and decrease the levels of CD8+, and the KPS score was significantly improved compared with the chemotherapy group. The incidence of nausea and vomiting, abdominal pain, diarrhea, thrombocytopenia and leukopenia during chemotherapy were lower than those in chemotherapy group. Fan Zhijun [16] 's study found that Shenlingbaizhu powder combined with operation in the treatment of nasal inverted papilloma could regulate the levels of CD8T, CD3, CD4 and NK cells, improve the immune function of patients, and reduce the recurrence rate and malignant transformation of tumors.

### 3.3 ShenlingBaizhu Powder can Improve Tumor Cachexia

The mechanism of carcinogenic cachexia is very complex and still not fully understood. One of the main reasons is systemic metabolic disorders caused by tumor release of some cytokines (such as TNF- $\alpha$ , IL-1, IL-6, TWEAK, etc.) and related gene changes. Hu Chenglin [17] et al. found that the combination of ShenlingBaizhu Powder and nutritional support can improve the traditional Chinese medicine syndroms and physical condition of patients with tumor cachexia. Shenlingbaizhu powder may control the occurrence of tumor cachexia by reducing the expression of TNF- $\alpha$ , TWEAK and Fn14 in patients. Cancer-induced fatigue is a typical symptom of cancer patients, and the main treatment is symptomatic support treatment, but there are limitations in the treatment, which affects the compliance of patients. Zhang Hui [18] 's research found that compared with conventional Western supportive treatment, combined with Shenlingbaizhu powder for the treatment of cancer related fatigue syndrome of spleen and stomach weakness, the effective rate is high, the prognosis is good, and the quality of life of patients is improved, and it is worthy of application.

### 3.4 ShenlingBaizhu Powder can Regulate Intestinal Flora

Li [19] Hua et al. studied the regulatory effects of

Shenlingbaizhu powder on intestinal flora, intestinal barrier and immune function in patients with gastric cancer undergoing postoperative chemotherapy. It was found that compared with chemotherapy alone, the levels of Th17, Treg and Th17/Treg were lower, the proportions of lactobacillus, bifidobacterium and Bacillus/coccus were higher, and the numbers of Escherichia coli, Enterococcus, staphylococcus and peptostreptococcus were lower. These results indicated that Shenlingbaizhu powder may regulate the balance of human intestinal flora by maintaining beneficial bacteria and inhibiting pathogenic bacteria, and play a role in reducing adverse reactions of digestive tract and enhancing body immunity.

### 3.5 ShenlingBaizhu Powder can Improve the Postoperative Recovery of Tumor

Yang Zhao [20] observed the changes of body weight, albumin and barium meal of upper digestive tract in patients with gastric cancer treated with total gastrectomy and jejunal replacement. It was found that Shenling Baizhu Powder had obvious improvement effect on gastric function after total gastrectomy and jejunal replacement. Hou Ronghua [21] divided 120 patients with digestive system tumor into two groups. The control group was treated with routine oral morbuline for gastrointestinal dysfunction; The study group took Shenlingbaizhu powder with water decoction. Results It was found that the recovery time of gastrointestinal function in Shenling Baizhu Powder group was shorter than that of conventional mobutyl line treatment, and the clinical effect rate (90.0%) was higher than that of mobutyl line treatment (68.3%), indicating that Shenling Baizhu powder could significantly promote the recovery of gastrointestinal function in patients with postoperative digestive system tumor digestive dysfunction.

## 4. Summary and Prospect

Cancer belongs to the category of "accumulation syndrome" and "puffiness" in traditional Chinese medicine. The foundation of cancer is deficiency of positive qi. Doctors of all dynasties think that deficiency of positive qi is mainly caused by weakness of spleen and stomach in the acquired middle jiao. Clinical studies have also shown that spleen deficiency symptoms such as anorexia, weight loss and malnutrition are common in cancer patients, and are closely related to poor prognosis. Therefore, spleen deficiency can affect the prognosis of cancer patients. The experimental study of Tao Zhiguang et al. showed that the tumor grows more rapidly under the condition of spleen deficiency, which is consistent with the theory of "healthy qi deficiency leads to diagenesis" in TCM oncology.

Shenling Baizhu powder was originally published in "Taiping Huimin and prescription", in which ginseng greatly tonifies Qi, Fu pulse and gutuo, tonifying spleen and lung, Shengjin calming, Poria can strengthen spleen and ningxin, moistening water, stir-fried Baizhu spleen-dehumidifying, tonifying Qi and Qi, coix seed spleen-oozing dampness, Yams tonifying kidney Qi, tonifying spleen and stomach, stirfried lentils spleen-tonifying stomach, tonifying water and reducing swelling, sand Renren Qi, moistening and stopping vomiting, Platycodon platycodon suitable lung ventilation, expectorant

cough, swelling and drainage pus, liquorice flat taste sweet, can reconcile the drugs. The combination of all kinds of drugs to eliminate and supplement, qi and spleen, detoxification anti-cancer.

Traditional Chinese medicine believes that malignant tumor is caused by the dysfunction of zang-fu organs and the deficiency of healthy qi, and the treatment should be to strengthen spleen and stomach and support healthy qi. Shenlingbaizhu powder, as a representative prescription for strengthening spleen and benefiting Qi, has multiple effects such as enhancing immunity, anti-tumor and protecting the organs from the damage of harmful toxins, but its clinical application is mostly limited to the adjuvant chemotherapy, and there is a lack of large sample random double-blind controlled clinical trials.

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