

# Research Progress in Chinese and Western Medicine Treatment of Ulcerative Colitis with Anxiety and Depression

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**Abstract:** By reviewing and summarizing the relevant literature and data, we systematically described the medical practice about ulcerative colitis with anxiety and depression recently. From the perspective of the therapeutic methods of Chinese medicine and Western medicine, we elaborated the treatment methods of Chinese medicine with evidence-based diagnosis and treatment, internal administration of proprietary Chinese medicine, Chinese medicine enema, acupuncture and moxibustion treatment and five-tone therapy, and summarized the application of some conventional treatment with Western medicine to provide clinicians with more options to reduce patients' pain and improve their quality of life as much as possible.

**Keywords:** Ulcerative colitis; Anxiety and depression; Chinese and Western medicine treatment; Chinese medicine

## 1. Introduction

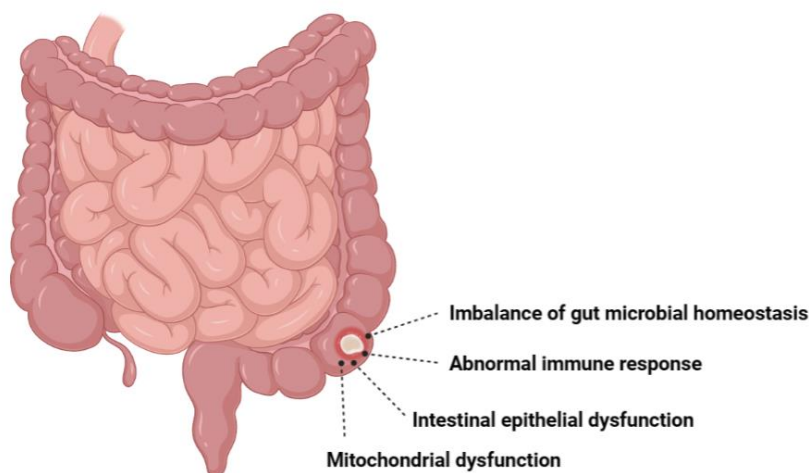


Figure 1: Pathogenesis of ulcerative colitis

Ulcerative colitis (UC) is an inflammatory bowel disease (IBD) based on continuous and diffuse inflammatory changes in the colonic mucosa. The most common symptoms are diarrhea, abdominal pain and mucopurulent blood, which may be accompanied by systemic symptoms such as urgency and weight loss, and may also involve other extra-intestinal tissues and organs, such as joints, skin and eyes, with other corresponding symptoms. According to our epidemiological data, it is clear that the number of consultations has been increasing rapidly in the last 20 years. Most scholars generally agree that the pathogenesis of UC is diverse and may be related to immune dysregulation, epithelial barrier dysfunction and genetic factors, as shown in Figure 1. The results of one study showed that the prevalence of anxiety in patients with IBD was approximately 20% and the prevalence of depression was approximately 15% [1]. The prevalence of anxiety and depression in patients increases the difficulty

of the disease in terms of treatment and prognosis to some extent. Therefore, in clinical treatment, we should not only focus on the treatment of the disease itself, but also on the psychological aspects of conditioning and treatment. In recent years, conventional therapeutic drugs in Western medicine have been developed in clinical work, but long-term use of these drugs may lead to the emergence of some toxic side effects, such as malignant hematological disease, bone marrow toxicity, and liver and kidney dysfunction [2]. Traditional Chinese medicine treatment as a complementary and alternative therapy is being used more and more widely in clinical practice due to its significant effect and low toxic side effects.

## 2. Western medical treatment

### 2.1. Basic treatment of ulcerative colitis

Aminosalicic acid preparations are mostly used clinically for the treatment of mild and moderate UC [3], mainly involving salazosulfapyridine and 5-aminosalicylic acid preparations. The best choice for the treatment of UC is the 5-aminosalicylic acid preparation due to their comparable effectiveness and the less toxic side effects compared to the 5-aminosalicylic acid preparation. Mesalazine significantly inhibits the inflammatory response of the intestinal mucosa [4] and has become a widely used first-line drug in the treatment of UC. After adequate doses of aminosalicic acid agents to treat UC, symptoms remain uncontrolled, especially in patients with relatively extensive lesions can be switched to hormonal therapy such as prednisone and methylprednisolone. Patients in whom hormones have become dependent or do not work can be treated with thiopurines. When hormone or immunotherapy is not effective or hormone dependence occurs and the organism cannot tolerate it, treatment can be switched to infliximab [5]. A study [6] pointed out that probiotics can improve the dysbiosis of the intestine, enhance the immunity of the body, increase the epithelial barrier function of the intestinal mucosa, and stimulate the body to secrete anti-inflammatory factors such as IL-10. A study [6] found that the effect of probiotics in UC patients with different conditions was significant, with the best effect of VSL#3. Fecal flora transplantation can increase the variety of beneficial intestinal bacteria and enhance the richness and diversity of intestinal microorganisms. (Figure 2)

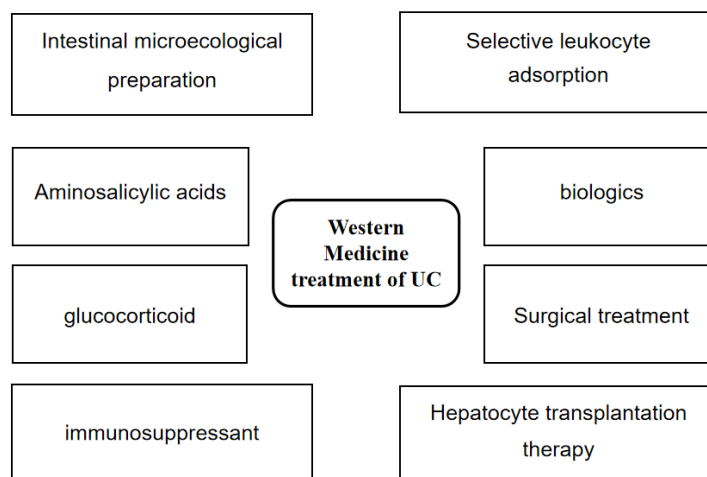


Figure 1: Western medical treatment of ulcerative colitis

### 2.2. Treatment of ulcerative colitis with anxiety and depression

#### 2.2.1. Paroxetine

Paroxetine, a selective 5-HT reuptake inhibitor, belongs to the 2nd generation of antidepressants and has more than 20 years of clinical application. It is the most widely used drug in China at this stage in terms of anti-anxiety and depression, and has good and stable effects in the treatment of anxiety, depression and obsessive-compulsive disorder, and the toxic side effects of paroxetine are not significant. Shen Hao et al. [7] found that the use of paroxetine combined with mesalazine was more advantageous than only mesalazine for the drug efficacy of elderly UC with anxiety and depression, and it had better safety.

### 2.2.2. Flupentixol melitracen

Dextran, a 5-HT reuptake inhibitor, is a combination of small doses of flupentixol (a thiazide neuroblocker) and melitracen (a biphasic antidepressant) in a 1:20 ratio. The two work together to increase the content of neurotransmitters such as DA and 5-HT in the synaptic gap, which can give full play to the anxiolytic and antidepressant effects [8], and also improve these gastrointestinal symptoms such as abdominal pain, bloating, and abnormal bowel movements in UC patients by regulating gastrointestinal nerve function and relieving visceral hypersensitivity [9]. One study concluded that Dextran plus conventional drugs is more effective than conventional drugs only in the treatment of UC patients with anxiety and depression [10], which broadens the idea of clinical treatment of UC with anxiety and depressive states.

## 3. Chinese medicine treatment

### 3.1. Chinese medicine dialectical treatment

According to the clinical symptoms of UC, it can be included in the Chinese medicine category of "intestinal diarrhea" and "prolonged dysentery". The onset of the disease is based on spleen deficiency, blamed on emotional and mental disorders, poor diet (clean), feeling external evil and so on. In the remission period, the disease is mostly due to the deficiency of the spleen and the failure of the spleen to transport and transform the dampness, which is a mixture of deficiency and reality [11]. The ancient medical doctors' understanding of the etiology of the disease: "Suwen" said: "those who do not eat and drink, and those who live and work from time to time ..... long for intestinal gas", that dietary disorder and external evil can be the etiology of the disease. It is pointed out in the "Treatise on the Classical Evidence" that "damp steam and heat congestion in the stomach and internal organs leads to condensation of Qi and blood ..... and pus and blood injection", suggesting the pathogenesis of this disease.

The Chinese medicine can be divided into large intestine damp-heat evidence, liver depression and spleen deficiency evidence, spleen deficiency and damp obstruction evidence, spleen and kidney Yang deficiency evidence, stasis and obstruction of intestinal ligaments evidence, cold and heat mixed evidence, heat poison incandescence evidence, as shown in Table 1. They were treated with Paeoniae Tang, Painful Diarrhea Essential Formula combined with Si Wei San, Ginseng Ling Bai Zhu San, Li Zhong Tang combined with Si Shen Wan, Shao Abdominal Expelling Blood Stasis Tang, Wu Mei Wan, and Bai Tou Weng Tang with addition and subtraction, respectively [12]. Studies have shown that the most commonly used formula is Bai Tou Weng Tang, followed by Ginseng Ling Bai Zhu San, Peony Tang, Tonic Zhong Yi Qi Tang, and Painful Diarrhea Remedy. Moreover, in clinical practice, about 26.3% of these prescriptions were often combined with western drugs, such as salazosulfapyridine and mesalazine. It was also concluded that the most commonly used herbal medicine was Huang Lian, followed by Bai Zhu, Gan Cao, Bai Shao, and Bai Tou Wu [13]. The Qing dynasty physician Shen Jinao wrote a book called "Miscellaneous Diseases Source Stream Rhinoceros Turbidity", which contains a formula of Shen's Dayu Tang for the treatment of liver depression and acid vomiting, with a reduced formula consisting of 10 g each of Chai Hu, Orange leaf, Sheng Ma, Mulberry Bai Pi, Chuanxiong, and Roasted licorice, 15 g each of Xiang Shen, and 30 g each of Bai Shao and Tribulus terrestris. Zhang Xueying et al. [14] applied Shen's Dayu Tang with a reduced formula combined with Wu Yin therapy and Chen Yahui et al. [15] used Shen's Dayu Tang with a reduced formula supplemented with auricular acupressure to treat UC patients with anxiety and depression, and the results proved its ability to alleviate the patients' TCM clinical symptoms and depressive state.

Table 1: Identification of ulcerative colitis in Chinese medicine

Syndrome type	Prescription
Dampness-heat syndrome of large intestine	Shaoyao decoction
Syndrome of liver depression and spleen deficiency	Tongxie Yaofang and Sini San
Syndrome of spleen deficiency and dampness obstruction	Shenling Baizhu San
Spleen-kidney Yang deficiency syndrome	Lizhong Decoction and Sishen pills
Syndrome of stasis of intestinal collaterals	Shao Fu Zhu Yu Decoction
Syndrome of mixed cold and heat	Wumei pills
The syndrome of heat toxicity	Plus or minus Radix anemone Decoction

### 3.2. Internal administration of proprietary Chinese medicines

In the clinical treatment of UC, proprietary Chinese medicines are considered to be a non-negligible part: for example, Xiang Lian Wan and Hu Di Enteric Capsules can be used for the evidence of damp-heat in the large intestine. Ginkgo baijiao san is indicated for the evidence of spleen deficiency and dampness obstruction. Wu Mei Wan is indicated for the evidence of cold and heat misalignment. Spleen and Intestine Pill and Gu Ben Yi Intestine Tablet can be used for evidence of spleen and kidney yang deficiency. Dragon Blood Dried Tablets are used for the evidence of stasis obstruction of intestinal ligaments <sup>[12]</sup>. Kangfu Xin Liquid, a biological preparation developed by Professor Li Shunan in 1985, is widely used clinically to promote ulcer surface repair. It is obtained from the dried body of the American cockroach and can promote blood circulation, nourish yin, and promote muscle growth <sup>[16]</sup>. It is mainly used in patients with mild to moderate depression. Xue Zhiping <sup>[17]</sup> treated UC with anxiety-depressive state with liver detoxification capsule combined with mesalazine with higher efficacy than mesalazine alone, and also the anxiety-depression in the group applying the drug combination was improved after treatment. Wu Ling capsule is refined from Wu Ling ginseng by modern technology, which has anti-anxiety-depression, sedative-hypnotic and cognitive function improvement effects. Mo Dayu et al. <sup>[10]</sup> showed that Wu Ling capsule combined with Mesalazine and Delixin can reduce the symptom expression of active UC with anxiety and depression state and reduce the adverse effects of the disease on patients' daily life, and the safety is not low. (Table 2)

Table 2: Traditional Chinese medicine for ulcerative colitis

Syndrome type	Chinese patent medicine
Dampness-heat syndrome of large intestine	Xianglian pills, Hudi enteric-soluble capsules
Syndrome of spleen deficiency and dampness obstruction	Shenling Baizhu San
Syndrome of mixed cold and heat	Wumei pills
Spleen-kidney Yang deficiency syndrome	Invigorating spleen Yichangpills, Guben Yichang tablets
Syndrome of stasis of intestinal collaterals	Dragon's Blood
Syndrome of liver depression and spleen deficiency	Shugan Jieyu Capsule

### 3.3. Traditional Chinese medicine external treatment methods

#### 3.3.1. Chinese medicine enema treatment

Enema can make the medicine reach the lesion directly, make full contact between the medicine and the intestine, promote the ulcer surface of the peptic tract to repair itself and improve blood circulation, and also can avoid the destruction of the medicine by gastric acid in the process of oral medicine <sup>[18]</sup>. He Zongqi et al. <sup>[19]</sup> used the enema of Huangkui astringent formula for the treatment group, which consisted of 30 g each of Dijinxu, Fenugreek, and Yellow Marshmallow flower, 5 g each of Wu Bei Zi, and 15 g each of Comfrey and Cyperus, and enema using mesalazine enema solution as the control group. The results showed that the clinical efficacy of the two groups of UC patients was similar after enema treatment, and the probability of adverse reactions in the group using the enema with Huangkui astringent formula was much lower than that in the group using mesalazine enema solution. Yang Weiwei <sup>[20]</sup> used Chinese herbal enemas (15 g each of septoria, dahurian, and ziziphus, 6 g each of betel nut, wuxia, and baihe, and 10 g each of peony bark, mullein, red peony, bitter ginseng, and yuanhu) combined with oral administration of salazosulfapyridine, with oral administration of salazosulfapyridine alone as the control, and the results suggested that the efficacy of the combined group was significantly higher than that of the control group.

#### 3.3.2. Acupuncture and moxibustion therapy

Acupuncture and Moxibustion Zisheng Jing said, "Fuyao is the main intestinal stool pus and blood ..... Guan Yuan treats dysentery." It suggests that we can select acupuncture points according to the nature and concurrent evidence of dysentery. The "Treatise on the Origin of Diseases - Dysentery" was written by Chao Yuan Fang of the Sui Dynasty, which states that "all dysentery is due to deficiency of Rong Wei and weakness of the intestines and stomach", and that the root of dysentery is deficiency of Rong Wei and weakness of the intestines and stomach <sup>[21]</sup>. Gong Yanyan et al. <sup>[22]</sup> analyzed the frequency of acupoints involved in 37 groups of main acupuncture point prescriptions, and the top six acupoints were Tianshu, Shang Juxu, Zhonggui, Feosanli, Qihai, and Guangyuan, which

were used as the base prescriptions, and then supplemented with Quchi, Neiting, and Hegu acupoints for the treatment of damp-heat in the large intestine or with Yinlingquan and Spleen Yu for the treatment of spleen deficiency and dampness. Zhu Peipei et al. [23] randomly grouped 68 patients with ulcerative colitis with spleen deficiency and dampness, and then treated them with or without thunder fire moxibustion during the open time of Gong Sun acupuncture point as the treatment group and the control group according to the theory of the eight methods of Ling Gui, and the results clearly showed that thunder fire moxibustion treatment during the open time of Gong Sun acupuncture point was more effective than avoiding thunder fire moxibustion treatment during the open time of Gong Sun acupuncture point in treating UC, and also reduced the anxiety state of these patients to some extent. The results clearly showed that Leihuo moxibustion treatment during the open time of Gong Sun acupoint was more effective in treating UC than avoiding the open time of Gong Sun acupoint, and also reduced the anxiety of these patients to some extent.

### 3.3.3. Acupuncture Point Applying Therapy

Based on the holistic concept and the meridian theory, acupuncture point application can fully absorb the medicinal power through the skin of human body, and stimulate the relevant meridian acupoints to regulate the corresponding meridian system to promote the healing of diseases, which can achieve good results in disease treatment. The commonly used acupuncture point patches are mainly made of ground white mustard seeds, dogwood, Yuanhu, spleen tablet, and cinnamon, and are applied to acupuncture points such as Shenqu, Great Intestine Yu, Spleen Yu, and Foot Sanli. A study [24] found that acupuncture point compresses can regulate the distribution of microflora in the intestinal tract and the expression of inflammatory immune cytokines in the body, repair the intestinal mucosa, and also enhance autoimmunity. Mo Yaoding [25] set the control group to take only oral salazosulfapyridine, while the observation group used oral salazosulfapyridine combined with acupressure of intestinal healing cream, made of 60 g of rhubarb, 120 g each of cinnamon, Huang Lian, and red peony, and 240 g of Astragalus, etc. The two groups of acupressure points, Shen Que, Foot San Li, Spleen Yu, and Tian Shu, Middle Epigastric, and Large Intestine Yu, were selected and applied alternately.

### 3.3.4. Five Tones Therapy

The five tones correspond to the five elements, the five organs and the five wills. Suwen-Zangxiang" cloud: "Liver, in sound is horn, in will is anger ....." Suwen - Yin and Yang Yingxiang Da Lun (The Great Treatise on Yin and Yang Yingxiang), cloud: "The horn tunes the wood sound, which is also tuned and straight ....." [26]. Li Haiyan et al. [27] selected 80 cases of UC patients and randomly divided them into two groups, the control group used conventional treatment, and the test group used conventional treatment with "Gong Tune" in the Five Tones Therapy, the results showed that conventional treatment with "Gong Tune" was more effective than the control group. The results showed that the effect of conventional treatment with "Gong Tune" was more significant than that of the control group, and the anxiety state of the patients in the experimental group improved significantly after treatment compared with that of the control group. (Figure 3)

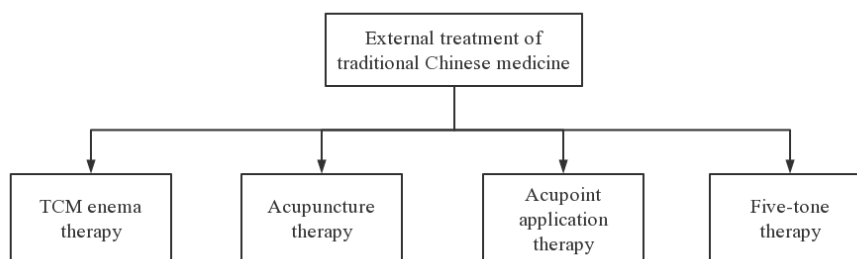


Figure 3: External Chinese medicine treatment for ulcerative colitis

## 4. Summary

In recent years, with the continuous development of medical level and scientific research, people have increasingly found that psychological issues have become the accompanying symptoms or aggravating factors of many diseases in the context of the continuous improvement of material life. Because ulcerative colitis is difficult to cure and easy to relapse, it brings double financial and psychological burden to patients. Therefore, patients with UC are often accompanied by anxiety and

depression. The state of anxiety and depression can cause ulcerative colitis to deteriorate further, which will lead to a vicious circle and greatly increase the difficulty of disease treatment. Therefore, we should not only treat the disease itself in clinical work, but also pay attention to psychological guidance, which may help patients to reduce symptoms, improve quality of life and reduce recurrence. In recent years, clinical workers have increasingly found that the therapeutic effects that can be achieved by purely Western medical treatment are limited, and the advantages of Chinese medicine characteristic treatment have gradually come to the fore as a complementary and alternative treatment method, which has also achieved good therapeutic effects, attracting more clinicians to keep digging for innovation in this field.

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