

# Exploring the Mechanisms and Research Progress of Traditional Chinese Medicine in the Treatment of Ulcerative Colitis from the Perspective of the Gut Microbiome

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**Abstract:** *Ulcerative colitis (UC) is one of the major types of inflammatory bowel disease (IBD). It is characterized by a prolonged course, a tendency to recur, and the need for long-term management. In recent years, dysbiosis of the gut microbiota and the resulting damage to the mucosal barrier, immune and inflammatory dysregulation, and metabolic abnormalities have become key factors that cannot be overlooked in explaining the onset and progression of UC. Traditional Chinese medicine (TCM) treatment for UC is characterized by holistic regulation that addresses both internal and external factors, and by the synergistic action of multiple components. It has demonstrated potential to improve clinical symptoms, regulate the intestinal microbiome, promote mucosal repair, and reduce the risk of recurrence. Research on interventions such as TCM compound formulas, active ingredients of TCM, TCM enemas, and the combination of acupuncture and herbal medicine suggests that these methods may exert their effects by modulating the microbial community structure, influencing metabolites such as short-chain fatty acids and bile acids, improving intestinal epithelial barrier function, and alleviating excessive inflammatory responses. However, current evidence largely comes from animal experiments, small-sample clinical studies, and systematic reviews, and significant differences remain among studies in syndrome classification, intervention protocols, outcome measures, and mechanisms of action. This study focuses on the gut microbiota to review the pathogenesis of UC, the limitations of Western medical treatment, and research progress in TCM—particularly TCM enemas—with the aim of providing more targeted guidance for the comprehensive treatment of UC and future research.*

**Keywords:** Ulcerative colitis, Gut microbiota, Traditional Chinese medicine, Herbal enema, Intestinal mucosal barrier, China Library Classification: R259, Document Type Code: A.

## 1. Introduction

Ulcerative colitis (UC) is a chronic, recurrent disease primarily characterized by persistent inflammation of the rectal and colonic mucosa. Clinically, it is mainly manifested by symptoms such as diarrhea, mucoid, purulent, and bloody stools, abdominal pain, and tenesmus [1]. The prevalence of UC is on the rise in China and worldwide, increasing the disease burden on patients and significantly impacting their quality of life [1,2]. With changes in lifestyle, increased environmental exposure, and continuous improvements in disease diagnosis, this condition has become one of the more common and important diseases of the digestive system requiring long-term management. Current Western medical treatments primarily include 5-aminosalicylic acid, glucocorticoids, immunosuppressants, biologics, and small-molecule targeted drugs. Clinical stratified treatment regimens have become relatively well-established; however, some patients still experience primary or secondary treatment failure, adverse drug reactions, difficulties with long-term maintenance, and relapse following discontinuation of medication [3]. Against this backdrop, balancing symptom control, mucosal repair, relapse prevention, and long-term safety remains an ongoing challenge in the comprehensive management of UC. In recent years, the role of the gut microbiota in the pathogenesis of UC has received increasing attention. Research suggests that dysbiosis, abnormal metabolic products, damage to the mucosal barrier, and an imbalance in the immune response are not independent changes but rather key factors that collectively contribute to

persistent intestinal inflammation [2,4]. This perspective has also become a new approach for the treatment of UC with traditional Chinese medicine (TCM). Both internal and external treatments in TCM emphasize holistic regulation and syndrome differentiation; they may play a complementary and synergistic role in the comprehensive treatment of UC by regulating the gut microbiota, improving the local environment, and promoting mucosal repair [5,6]. However, existing reviews remain inadequate; modern research has not sufficiently clarified the relationship between the pathogenesis of TCM and microbial dysbiosis, and there are still shortcomings in the integration of mechanisms of action and the stratification of evidence for distinctive therapies such as Chinese herbal enemas. Against this backdrop, this paper reviews the pathogenesis of UC and advances in TCM treatment to explore new approaches for the comprehensive management of UC.

## 2. Pathogenesis of UC and Gut Microbiota Imbalance

### 2.1 TCM Understanding of the Etiology and Pathogenesis of UC

Traditional Chinese Medicine does not recognize the term “ulcerative colitis.” Clinically, it is often classified into categories such as “dysentery,” “bloody stools,” or “resting dysentery” based on symptoms including recurrent abdominal pain, diarrhea, mucus- and pus-tinged bloody stools, and tenesmus. The current consensus holds that UC is localized to

the large intestine and is closely associated with the spleen, stomach, liver, and kidneys. Its core pathogenesis is often summarized as “deficiency at the root and excess at the branch,” with spleen and kidney deficiency serving as the root and pathogenic factors such as dampness, heat, toxins, and blood stasis serving as the branch [5,7]. In the early stages of the disease, the condition often manifests as an “excess” pattern. Patients frequently experience impaired spleen function and internal retention of dampness and turbidity due to irregular diet, emotional imbalances, invasion by external pathogenic factors, or constitutional spleen deficiency. When dampness and turbidity accumulate over time and transform into heat, the pathogenic factors of damp-heat and toxin stagnate in the intestines and blood vessels, scorching the blood vessels and resulting in bloody, purulent stools. As the disease progresses, the condition often shifts from excess to deficiency, with a mixture of both, and the pathological location further involves the spleen and kidneys. Consequently, patients exhibit recurrent episodes and a protracted, intractable course [8,9]. The pathogenesis in Traditional Chinese Medicine is not a simple substitute for modern scientific explanations, but there is a certain connection between the two. Impaired spleen function and the internal generation of dampness and turbidity can be linked to an imbalance in the intestinal microenvironment; damage to the intestinal collaterals and the lingering of pathogenic toxins can be linked to a compromised mucosal barrier and persistent local inflammation; the recurrence of symptoms even during remission aligns with the characteristic of “pathogenic factors lurking in the intestinal collaterals,” suggesting that UC does not reach a state of pathological stability once symptoms subside. It is possible that issues such as an unrestored microbial niche, a persistent local pro-inflammatory environment, and insufficient repair of the epithelial barrier still exist [10]. Reinterpreting the pathogenesis of Traditional Chinese Medicine from the perspective of the gut microbiota helps bridge the gap between traditional theory and modern research findings.

## 2.2 The Role of Gut Microbiota Dysbiosis in UC

The gut microbiota serves as a crucial foundation for maintaining host metabolic homeostasis, mucosal barrier integrity, and immune balance. Under normal conditions, maintaining the stability of the intestinal microecology requires the collective participation of gut microorganisms in processes such as nutrient metabolism, vitamin synthesis, pathogen antagonism, and immune education [4,11]. Once the structure and richness of the microbiota are persistently disrupted, the intestine may experience problems such as damage to the epithelial barrier, an imbalance in metabolic products, and abnormalities in mucosal immunity, which in turn drive the continuous amplification of inflammatory responses [2,4]. Patients with UC often exhibit characteristics such as a reduction in beneficial commensal bacteria, an increase in opportunistic pathogens, and a decline in microbiome diversity [2]. These changes are not merely coincidental; they may also contribute to disease onset and progression through multiple pathways. Microbial dysbiosis reduces the production of short-chain fatty acids such as butyrate, thereby compromising the energy supply to and barrier function of the colonic epithelium. The proliferation of pathogenic bacteria enhances inflammatory signals such as

lipopolysaccharides (LPS), leading to abnormal activation of pattern recognition receptors (PRRs) such as TLRs and amplifying the local inflammatory response [12]. Abnormalities in the microbiota and its metabolism also affect the Th17/Treg balance, the integrity of the mucus layer, and the expression of tight junction proteins, leading to increased intestinal mucosal permeability and further exacerbation of immune dysregulation [4,11]. Thus, UC is not a disease driven by a single inflammatory factor, but rather the result of the combined effects of abnormalities in multiple pathways, including the microbiota, the intestinal barrier, the immune system, and metabolism. For Traditional Chinese Medicine (TCM) to demonstrate its advantages in treating this disease, its value lies primarily in the synergistic regulation of these multiple pathways.

## 3. Current Status of Western Medical Treatment and the Practical Basis for TCM Intervention

Western medicine has established a relatively mature stepwise treatment protocol for UC. 5-ASA is a key component of baseline therapy for patients with mild to moderate disease; glucocorticoids have a well-established role in inducing remission during periods of moderate to severe activity; and immunosuppressants, biologics, and small-molecule targeted drugs play important roles in the treatment of refractory, recurrent, or moderate-to-severe cases [3,13]. These treatment strategies are highly valuable for rapidly controlling inflammation, alleviating symptoms, and promoting mucosal healing in some patients; therefore, Western medicine remains an important component of modern UC treatment. However, from the perspective of long-term management, current treatments still have shortcomings. Some patients exhibit primary or secondary non-response to traditional medications or biologics; long-term use of glucocorticoids can lead to adverse reactions; and immunosuppressants and biologics also involve practical issues such as infection risk, immunogenicity, and financial burden [3,13]. Even after symptoms have subsided, some patients may still experience residual damage to the mucosal barrier and an imbalance in the microbiome, which can increase the risk of relapse after discontinuing medication. Although Western medicine has clear advantages in controlling active inflammation, there is still room for improvement in long-term microbiome restoration, individualized syndrome regulation, and comprehensive rehabilitation management. It is inappropriate to view traditional Chinese medicine (TCM) as an alternative to Western medical treatment; rather, it is better suited to a complementary and synergistic role in comprehensive management [14,15]. It is particularly suitable for use during the consolidation phase of remission, for the long-term care of patients with mild to moderate disease, in cases where symptom improvement is insufficient, or when patients wish to reduce the risk of recurrence. If TCM interventions can improve the gut microbiota, promote mucosal repair, and enhance quality of life without affecting standard treatment, they would have significant clinical value. Therefore, when discussing the value of TCM in treating UC, we should consider it within the framework of modern standard treatment, rather than simplistically framing it as a dichotomy between the merits of TCM and Western medicine.

#### **4. The Primary Mechanisms of Traditional Chinese Medicine in Treating UC Through Gut Microbiota Intervention**

Research on TCM treatment for UC is gradually shifting from simple observation of symptoms to a multifaceted understanding involving the microbiome, the intestinal barrier, the immune system, and metabolism. TCM may exert its effects on UC-related pathological changes through the synergistic regulation of multiple components, pathways, and levels, unlike some modern drugs that primarily target a single mechanism [5,6]. Overall, its mechanisms of action can be broadly summarized as follows.

##### **4.1 Restoring the Gut Microbiome Structure and Inhibiting the Proliferation of Pathogenic Bacteria**

An imbalance in the gut microbiota is a key underlying factor in the pathogenesis of UC. Multiple studies have shown that intervention with TCM formulations can reduce the abundance of opportunistic pathogens and inflammation-associated bacteria, while simultaneously promoting the recovery of beneficial bacteria such as *Lactobacillus*, *Bifidobacterium*, and *Prevotella* [16,17]. For example, the “Intestinal Cleansing and Dampness-Resolving Formula” can inhibit the proliferation of *Escherichia coli* and pathogenic *Proteobacteria*, while improving gut microbiota structure and short-chain fatty acid metabolism [16]; the “Zhuli Decoction” can inhibit the TLR4/NF- $\kappa$ B/NLRP3 inflammatory pathway by regulating the microbiota and related metabolites [17]; Studies on Wu Mei Wan also suggest that it helps increase the abundance of beneficial bacteria and corrects microecological imbalances [18,19]. These results suggest that the role of traditional Chinese medicine in UC is not limited to anti-inflammatory effects; it may also weaken the basis for sustained inflammation by reshaping the gut ecosystem. It should be noted that current research on the microbiota-modulating effects of TCM remains primarily based on animal studies. Different studies employ varying modeling approaches, sequencing platforms, intervention durations, and analytical indicators; therefore, the reproducibility and stability of microbiota changes require further validation. Microbiota improvement can be regarded as an important clue for TCM treatment of UC, but it will take some time for these changes to translate into definitive clinical benefits.

##### **4.2 Modulating Microbial Metabolites to Improve the Intestinal Environment**

The impact of the gut microbiota on host health is reflected not only in changes in microbial composition but also at the functional molecular level of its metabolites; both aspects are of critical importance. Substances such as short-chain fatty acids, bile acids, and tryptophan metabolites can directly participate in intestinal epithelial energy metabolism, the maintenance of immune balance, and the regulation of inflammatory responses. Current research suggests that TCM formulas and certain active ingredients may exert their effects by improving the microbial metabolic profile [16,17]. For example, the “Clearing the Intestines and Resolving Dampness” formula and related formulations can promote the restoration of short-chain fatty acid metabolism [16,18]; Berberine can reduce the risk of colonitis-associated

tumorigenesis by reshaping the gut microbiota and regulating short-chain fatty acid metabolism [20,21]. These findings suggest that Traditional Chinese Medicine (TCM) interventions do not merely adjust static structures—such as increasing beneficial bacteria and reducing harmful bacteria—but are more likely to further improve the local microecology of ulcerative colitis (UC) by influencing the metabolic environment, manifested as promoting the formation of beneficial metabolites and inhibiting the development of an inflammatory metabolic environment. However, current research on the relationship between bile acid and tryptophan metabolism and TCM syndromes is still in its infancy [22]. Most studies have small sample sizes, and no consistent conclusions have yet been reached regarding metabolic markers across different syndrome patterns. Therefore, conducting higher-quality research on the relationship among syndrome differentiation, gut microbiota metabolite profiles, and treatment response remains an important direction for future in-depth studies.

##### **4.3 Repairing the Intestinal Mucosal Barrier and Reducing Epithelial Permeability**

Damage to the intestinal mucosal barrier is a key pathological basis for the persistent inflammation and recurrent flare-ups in UC. Dysbiosis not only reduces the production of protective metabolites but also impairs the mucus layer and tight junction structures, making it easier for bacterial products to penetrate the epithelium and activate the mucosal immune response. Traditional Chinese medicine (TCM) has established a solid research foundation in improving barrier function. Experimental studies have shown that certain TCM formulas or preparations can upregulate the expression of tight junction proteins such as ZO-1 and occludin, thereby improving intestinal epithelial permeability and promoting the repair of damaged mucosa [23,24]. Topical preparations such as the TCM Qingchang Suppository have a positive effect on the expression of tight junction proteins in the colonic mucosa [24]; Studies on Shaoyao Decoction also suggest that it can improve fluid metabolism and intestinal epithelial permeability by regulating signaling pathways [23]. From a clinical perspective, one of the key advantages of traditional Chinese medicine over purely anti-inflammatory treatments may be barrier repair, as symptom relief does not necessarily equate to complete recovery of the mucosa and microbiome, and promoting barrier reconstruction may be associated with a reduced risk of recurrence and improved long-term prognosis. However, most of the existing evidence on barrier repair comes from animal studies and surrogate markers; high-quality clinical studies with outcomes such as endoscopic healing and mucosal repair scores remain scarce. Therefore, a cautious approach is still warranted.

##### **4.4 Modulating the Immune-Inflammatory Network to Achieve Multipathway Synergistic Intervention**

The persistence of UC inflammation is closely related to factors such as abnormal activation of the innate immune system, imbalance in the adaptive immune system, and amplification of inflammatory signaling pathways. Existing research suggests that traditional Chinese medicine may play a role in inhibiting inflammatory pathways such as TLR4/NF- $\kappa$ B/NLRP3, regulating Th17/Treg imbalance, and

promoting the expression of anti-inflammatory factors [12,17]. For example, Zhuli Decoction can inhibit the activation of the TLR4/NF- $\kappa$ B/NLRP3 pathway [17]; berberine can improve gut microbiota composition and alleviate inflammatory damage [25]; following combined acupuncture and herbal therapy, Bifidobacteria and Lactobacilli increased, while the Th17/Treg balance improved [26]. These findings suggest that the regulatory effects of traditional Chinese medicine on UC extend beyond the limited, single goal of anti-inflammation and may instead exert a holistic effect through the bidirectional interaction of gut microbiota remodeling and immune regulation. It should be emphasized that, although many current studies have observed that changes in the gut microbiota occur simultaneously with a decrease in inflammatory factors, there is still insufficient evidence to prove a strict causal relationship between the two. Therefore, one should avoid directly attributing all improvements in inflammation to gut microbiota mediation. When explaining the mechanisms of action of TCM, a key focus for future research should be distinguishing between correlated changes and proven key mediating mechanisms.

## 5. Advances in the Clinical Application of Traditional Chinese Medicine for the Treatment of UC

### 5.1 Internal Treatment with Traditional Chinese Medicine: From Empirical Formulas to In-Depth Mechanism Research

Compound TCM formulas remain the main focus of research on internal TCM treatment for UC. Existing studies suggest that formulas such as Qingchang Huashi Fang, Zhuli Tang, and Wumei Wan show potential in improving symptoms, regulating microbiota structure, alleviating inflammatory responses, and promoting mucosal repair [16,17]. These formulas typically do not target a single inflammatory factor or a specific type of microbiota; rather, they achieve multi-target intervention through syndrome differentiation and treatment, making them particularly well-suited to the complex and ever-changing nature of UC. In addition to compound formulas, active ingredients in traditional Chinese medicine, such as berberine, have gradually become a research focus. Their roles in modulating the microbiota, reducing inflammation, and regulating metabolism provide a relatively clear direction for modern research on traditional Chinese medicine [20,25]. However, based on current research, studies on TCM internal therapy still face challenges such as small sample sizes, significant variations in study protocols, inconsistent treatment durations, and high heterogeneity in outcome measures. Some studies focus on symptom scores, while others emphasize inflammatory markers or changes in the microbiome; however, studies that truly use recurrence rates, mucosal healing, and long-term prognosis as endpoints remain scarce. Therefore, although internal TCM therapy has a solid theoretical foundation and promising research prospects, higher-quality evidence-based data is still needed to substantiate its clinical value.

### 5.2 External TCM Therapy: Characteristics and Limitations of Chinese Herbal Enemas

Herbal enemas are one of the most widely used and

representative methods of external treatment for ulcerative colitis (UC) in traditional Chinese medicine (TCM). They offer particular advantages in the treatment of gastrointestinal diseases, as the medication acts directly on the affected area. Theoretically, this helps increase local drug concentrations, reduces the gastrointestinal irritation associated with some oral medications, and more directly alleviates local inflammation and improves the mucosal environment in the rectum and distal colon [27,28]. In terms of usage patterns, herbs such as *Anemarrhena asphodeloides*, *Coptis chinensis*, *Sanguisorba officinalis*, and *Bletilla striata* are frequently used in enema regimens for UC of the damp-heat pattern [28,29]; research findings suggest that TCM enemas may exert their effects by improving tight junction protein expression, alleviating local inflammatory responses, and promoting mucosal barrier repair [24]. Clinical studies and meta-analyses suggest that TCM enemas offer certain advantages in improving symptom scores, reducing certain inflammatory markers, and enhancing short-term efficacy when used in combination with mesalazine [27,30]. These findings indicate that TCM enemas are not merely an empirical treatment modality but are supported by a solid foundation of modern clinical research. Compared with oral administration of TCM alone, TCM enemas better embody the characteristics of “local administration—direct delivery to the site of disease—local environmental intervention”; therefore, they represent a treatment modality worthy of special attention in this discussion. However, research on TCM enemas also has notable shortcomings. There are significant variations across studies in terms of formula composition, enema temperature, retention time, treatment duration, and combination therapy regimens, which may affect the comparability of research findings; many clinical studies have limited sample sizes, and randomization and blinding are often inadequate; currently, many studies still use symptom improvement as the primary endpoint, while reports on endoscopic remission, mucosal healing, and long-term recurrence control remain relatively scarce [27,31]. The translational application of novel drug delivery methods, such as temperature-sensitive gels and nanodelivery systems, is also not yet fully developed [32,33]. Therefore, although TCM enemas represent a promising direction in the external treatment of UC, the strength of the evidence falls short of supporting their widespread, standardized adoption.

### 5.3 Acupuncture and Integrated Internal-External Treatment: The Potential of a Comprehensive Intervention Model

In addition to compound TCM formulas and TCM enemas, acupuncture and the combination of acupuncture and herbal medicine are also important components of comprehensive TCM treatment for UC. Existing research suggests that acupuncture may exert its effects by regulating the gut microbiota, improving brain-gut axis function, suppressing inflammatory responses, and modulating immune balance [34,35]. Some studies have shown that following combined acupuncture and herbal therapy, patients exhibit increased levels of Bifidobacteria and Lactobacilli, reduced levels of *Escherichia coli* and *Enterococcus*, and an improved Th17/Treg balance, suggesting that this approach offers certain advantages in terms of dual regulation of the microbiome and the immune system [26]. From the

perspective of Traditional Chinese Medicine's holistic view, the approach that best aligns with the characteristics of UC—including recurrent flare-ups, a protracted course, and a mixture of deficiency and excess patterns—is the simultaneous treatment of both internal and external factors [15]. Oral herbal formulas focus on overall regulation, while herbal enemas emphasize local intervention, and acupuncture exerts effects at the levels of neural and immune regulation; the combined use of these three modalities theoretically has the potential to produce complementary effects. Although this integrated approach has certain theoretical advantages, current research remains largely limited to single-center, small-sample clinical observations, with relatively limited data on standardized protocols, suitable patient populations, and long-term follow-up. Therefore, the integrated treatment of both internal and external factors can be regarded as an important future direction for TCM in the treatment of UC, but this approach still requires validation through more rigorous clinical studies.

## 6. Conclusion and Outlook

From the perspective of the gut microbiota, UC is not caused by a single inflammatory response but rather results from the combined effects of microbial imbalance, metabolic disorders, barrier disruption, and immune abnormalities. The advantage of TCM in treating UC does not lie in simply competing with modern standard therapies, but rather in its ability to implement multi-faceted, synergistic interventions targeting this complex pathological process. Existing research suggests that treatment modalities such as TCM compound formulas, active ingredients of TCM, TCM enemas, and the combination of acupuncture and herbal medicine may exert their effects by modulating gut microbiota composition, improving metabolic products such as short-chain fatty acids, promoting mucosal barrier repair, and regulating immune and inflammatory responses. Among these, TCM enemas—due to their characteristics of local administration, direct delivery to the site of the disease, and ease of combination with other therapies—have become one of the most distinctive and promising areas for translational research in external treatments. However, we must also clearly recognize that the current evidence remains significantly insufficient. While basic research is abundant, high-quality randomized controlled clinical trials remain scarce; there are also significant differences among studies in terms of models, syndromes, prescriptions, and outcome measures. Most studies are still limited to demonstrating that “changes in the microbiota occur simultaneously with therapeutic effects,” and strong causal evidence regarding whether the microbiota serves as a key mediating factor is lacking. Furthermore, a stable correspondence between syndrome stratification and microbiome phenotypes has not yet been established, which also limits the modern application of syndrome - differentiation - based treatment. Future research should establish an interlinked research pathway encompassing “syndrome — microbiota — metabolites — therapeutic efficacy” to strengthen the correspondence between TCM syndrome differentiation and modern biomarkers. Clinical studies should standardize treatment duration, dosing regimens, objective endpoints, and follow-up indicators, with particular emphasis on hard criteria such as mucosal healing, endoscopic remission, and recurrence rates. improve the

standardization of TCM enema prescriptions and operational procedures; explore more rational pathways for the integration of TCM and Western medicine based on modern standard treatments; and clarify applicable strategies for different disease stages and patient populations. Only by simultaneously advancing both mechanism-of-action research and high-quality clinical evidence can the practical value of TCM—particularly TCM enemas—in the comprehensive management of UC be elucidated in a more objective, comprehensive, and generalizable manner.

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