

Mechanism of Morbidity Based on Ulcerative Colitis: A Review of Traditional Chinese Medicine Treatment of Ulcerative Colitis

Yan Huang¹, Zhuolin Ma², Xiaonan Xu¹, Zhaoxia Liu¹

¹First Affiliated Hospital, Heilongjiang University of Chinese Medicine, Harbin, Heilongjiang, 150000, People's Republic of China; ²Heilongjiang Eye Hospital, Harbin, Heilongjiang, 150007, People's Republic of China

Correspondence: Xiaonan Xu, First Affiliated Hospital, Heilongjiang University of Chinese Medicine, 26 Heping Road, Xiangfang District, Harbin City, Heilongjiang, 150000, People's Republic of China, Email 1509726765@qq.com; Zhaoxia Liu, First Affiliated Hospital, Heilongjiang University of Chinese Medicine, 26 Heping Road, Xiangfang District, Harbin City, Heilongjiang, 150006, People's Republic of China, Email hlj0451lx@163.com

Abstract: Ulcerative colitis (UC) is a chronic inflammatory disease of the colon and rectum that has become an increasing global health concern. Its pathogenesis is multifactorial, involving genetic susceptibility, environmental triggers, epithelial barrier dysfunction, gut microbiota imbalance, and immune dysregulation. Clinically, UC is characterized by bloody diarrhea, mucosal inflammation, and a relapsing-remitting course, with diagnosis typically confirmed by clinical, endoscopic, histological, and laboratory findings. Despite the increasing number of therapeutic options, including corticosteroids, immunosuppressants, and biologics, many patients still experience suboptimal responses or adverse events, and some ultimately require colectomy. In this context, Traditional Chinese Medicine (TCM) has attracted attention as a complementary approach due to its multi-target mechanisms and historical use in gastrointestinal diseases. This review summarizes recent evidence on the application of TCM in UC, including its theoretical foundations, active compounds, and modulation of key signaling pathways such as TLR4/NF- κ B, NLRP3, JAK/STAT3, PI3K/Akt, Notch, and AMPK/mTOR. Additionally, we highlight clinical data from randomized controlled trials (RCTs) evaluating TCM formulas either as monotherapy or in combination with conventional treatments. Some studies report improvements in symptom scores, inflammatory markers, and endoscopic healing when TCM is combined with agents like mesalazine. However, these findings must be interpreted with caution. Most RCTs are single-center with small sample sizes, lack placebo control, and show considerable heterogeneity in intervention protocols and outcome assessments, making quantitative comparisons to standard therapies, such as remission rates or adverse event frequencies relative to mesalazine or biologics, being limited. Therefore, while TCM demonstrates therapeutic potential in UC management, more rigorous evidence is needed to establish its comparative efficacy and safety. Future studies should include large-scale, multicenter, placebo-controlled RCTs with standardized endpoints, and consider integrating TCM syndrome differentiation with modern pathophysiological frameworks to enhance clinical relevance and translational value.

Keywords: ulcerative colitis, diarrhea, hematochezia, defecation difficulty, mucosal barrier, traditional Chinese medicine

Introduction

Ulcerative colitis (UC) is an inflammatory bowel disease characterized by chronic relapsing inflammation of the colonic mucosa, typically beginning in the rectum and extending proximally in a continuous manner. Its incidence has increased globally over recent decades, posing a substantial burden on healthcare systems and patients' quality of life.^{1,2} The pathogenesis of UC is multifactorial and involves a complex interplay between genetic predisposition, environmental triggers, immune dysregulation, gut microbiota alterations, and epithelial barrier dysfunction, with current treatment strategies aiming to induce and maintain clinical and endoscopic remission, using agents such as 5-aminosalicylic acid (5-ASA), corticosteroids, immunosuppressants, and biologics targeting cytokine pathways.³ Despite these advances, a subset of patients remains refractory to medical therapy and ultimately requires colectomy. Moreover, pharmacologic treatments may be associated with adverse effects and economic burdens, underscoring the need for additional therapeutic strategies.

Mesalazine is recognized as the primary treatment for mild-to-moderate UC, while topical and systemic corticosteroids are used for recurrent cases. For moderate to severe manifestations of the disease, immunosuppressants and biologics are used.⁴ Despite these advancements, remission rates remain relatively low, ranging from 20% to 30% in inductive clinical trials and from 30% to 60% in real-world settings.⁵ The direct and indirect costs associated with UC are estimated to be between €12.5 billion and €29.1 billion annually in Europe, and between \$2.1 billion and \$14.9 billion in the United States.⁶ Consequently, a subset of patients requiring surgical intervention for drug-refractory conditions remains. Although total proctectomy has the potential to resolve colonic inflammation, postoperative complications, particularly pouchitis and fecal incontinence, are common. Thus, UC management continues to present challenges. Traditional Chinese Medicine (TCM) has a long-standing history and extensive clinical applications in the treatment of UC, demonstrating certain levels of efficacy and safety. Within the framework of TCM, UC is often classified as a manifestation of “spleen-kidney deficiency” and “dampness-heat accumulation”.⁷ These traditional diagnostic constructs are based on symptom patterns rather than histopathological evidence, and their relevance to modern biomedical understanding remains a subject of translational interest. Nonetheless, there are growing efforts to bridge these paradigms by correlating TCM concepts with underlying biological mechanisms, such as immune imbalance, impaired mucosal integrity, and dysbiosis.

The use of TCM herbal compounds for UC is supported by empirical clinical practice and increasingly by experimental studies demonstrating anti-inflammatory, immunomodulatory, antioxidant, and barrier-protective effects, which are often mediated through modulation of signaling pathways, including TLR4/NF- κ B, NLRP3 inflammasome, JAK/STAT3, PI3K/Akt, and Notch.⁸ However, the rationale for selecting specific herbal interventions is often grounded in traditional use, with limited discussion of modern pharmacokinetic properties, optimal dosing strategies, or active constituent standardization. Moreover, few studies have addressed the comparative efficacy of these botanicals against standard-of-care therapies such as mesalazine or biologics. Existing meta-analyses suggest potential benefits of TCM interventions in combination with conventional treatment but also highlight methodological heterogeneity, small sample sizes, and insufficient data on long-term safety.⁹

Additionally, potential herb-drug interactions and the risk of hepatotoxicity associated with certain TCM formulations warrant careful consideration. The lack of regulatory standardization, variability in plant sourcing and extraction methods, and insufficient reporting of adverse events further complicate clinical translation. These issues highlight the importance of evaluating TCM interventions not only based on traditional use but also in accordance with modern pharmacological principles and clinical trial standards.

Based on these considerations, this review examines how TCM may contribute to the treatment of UC by summarizing recent findings from molecular studies, experimental research, and clinical trials. The discussion aims to relate TCM principles to known pathophysiological mechanisms of UC and to evaluate current evidence on efficacy and safety. In doing so, we aim to clarify the relevance of TCM in UC management and highlight existing challenges, such as limited pharmacokinetic data and regulatory variability, to guide future research.

Clinical Signs

In UC, the manifestation of symptoms typically occurs in a gradual manner and can persist for several weeks to months. Following the initial period of morbidity, if therapeutic interventions prove ineffective, the disease trajectory is marked by episodes of recurrent mucosal inflammation interspersed with periods of symptom remission.

Common clinical manifestations include diarrhea, hematochezia, and difficulties with defecation. The likelihood of UC diagnosis is heightened in patients with a prolonged history of bloody diarrhea and nocturnal bowel movements. UC is frequently associated with distal conditions, such as proctitis and proctocolitis, where patients may predominantly experience rectal bleeding, tenesmus, and defecation challenges. Notably, paradoxical constipation may occur in up to 10% of individuals with rectal or left-sided colitis.¹⁰

Acute weight loss is prevalent in pediatric populations; however, linear growth is often preserved, in contrast to Crohn's disease, which typically impairs linear growth.¹¹ Approximately 15% of patients present with severe UC at onset, which can be accompanied by systemic symptoms such as fever, weight loss, tachycardia, nausea, and vomiting.¹² Although toxic megacolon can develop initially, it is more frequently observed during disease recurrence. Clinically,

toxic megacolon is characterized by severe UC symptoms¹² and abdominal radiographic findings indicative of a dilated colon. This condition represents a surgical emergency owing to the associated risks of perforation and sepsis.

Approximately 30% of individuals diagnosed with UC exhibit extra-intestinal manifestations (EIMs).¹³ Among these, arthritis is the most prevalent, occurring in 21% of the patients. This form of arthritis may be classified as either axial or peripheral, affecting both small and large joints. The severity and prevalence of arthritis and arthralgia are frequently associated with the activity level of bowel diseases.¹⁴ EIMs can affect various organ systems, including the hepatobiliary system (eg, primary sclerosing cholangitis and autoimmune hepatitis), ocular system (eg, uveitis and epithelial scleroderma), oral cavity (eg, canker sores), integumentary system (eg, erythema nodosum, impetigo, and psoriasis), and hematological system (eg, thrombosis).¹⁵ Primary sclerosing cholangitis is observed more frequently in male patients, those with extensive lesions, and pediatric populations.^{16,17} Furthermore, patients with UC who present with dermatological manifestations are typically younger and predominantly female at the time of diagnosis.¹⁸ Erythema nodosum is generally associated with the activity of luminal disease, whereas pyoderma gangrenosum tends to follow an independent clinical course^{14,19} (See Figure 1).

Diagnosis

In the evaluation of UC, clinicians must establish a comprehensive differential diagnosis. A thorough medical history should be obtained, encompassing inquiries regarding travel history, medication use, including antibiotics and nonsteroidal anti-inflammatory drugs (NSAIDs), tobacco exposure, and recent hospitalizations.²⁰ The prevalence of *Clostridium difficile* infection (CDI) in patients with UC is significantly elevated, being three to four times greater than that observed in individuals with Crohn's disease and eight times higher than that in the general population.^{20,21} CDI can present with symptoms that mimic those of UC, which may contribute to an increased rate of misdiagnoses. In cases where CDI is identified, appropriate treatment should be administered; however, management of UC should continue, particularly if the symptoms persist. Clinicians should consider *Campylobacter* infections in patients with a history of travel. Cytomegalovirus (CMV) infection is another important consideration, especially in immunocompromised individuals.²² While latent CMV is found with similar frequency in patients with and without inflammatory bowel disease (IBD),²³ recent or reactivated CMV is more prevalent among those with IBD.²⁴ Notably, up to one-third of

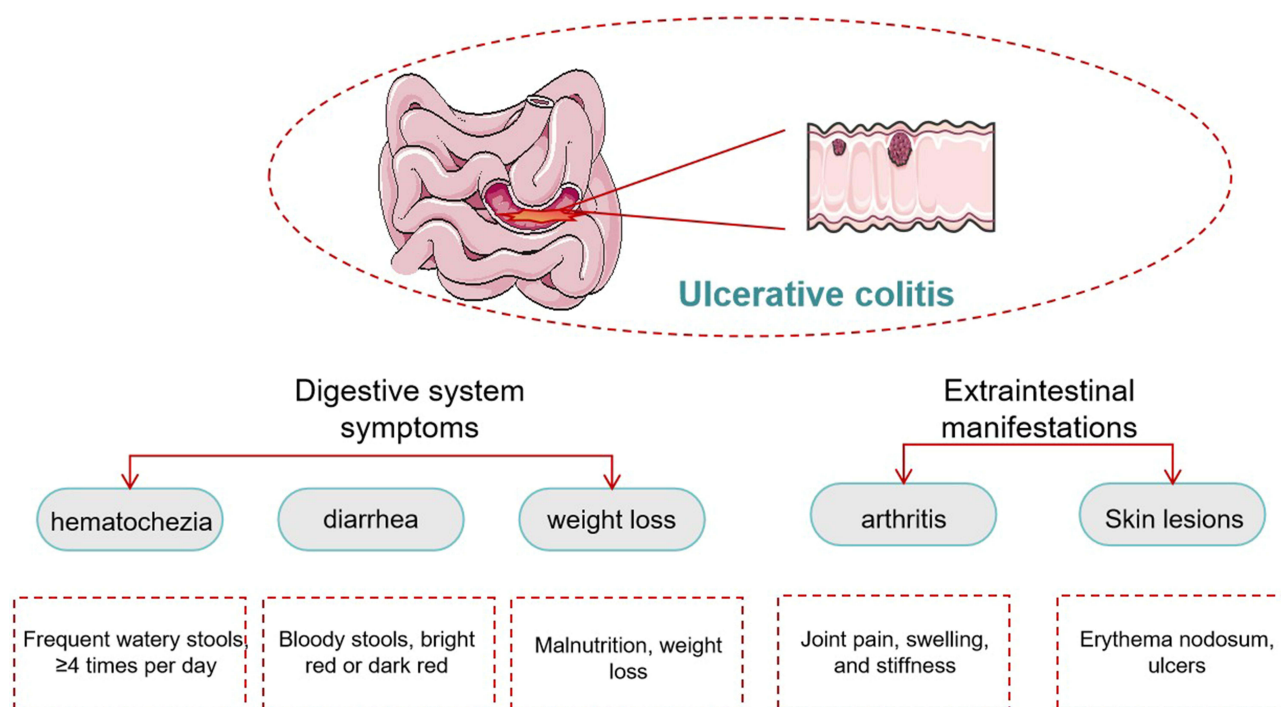


Figure 1 Clinical manifestations of UC.

patients with acute steroid-refractory UC may develop CMV infection.²⁵ The diagnosis of CMV infection should be confirmed through endoscopy and biopsy,²¹ using techniques such as hematoxylin and eosin staining, immunohistochemistry, or tissue polymerase chain reaction.^{25,26}

When evaluating patients exhibiting symptoms of UC, it is essential to consider additional conditions such as malignancy, bleeding hemorrhoids, rectal prolapse, vasculitis, and irritable bowel syndrome.¹² In younger patients, the presence of ischemic colitis should prompt consideration of factors such as coagulopathy, medication usage, and lack of vigorous physical activity.²⁰

Patients diagnosed with UC should undergo a comprehensive physical examination to evaluate extraintestinal manifestations associated with the condition. The presence of pallor may serve as an indicator of anemia.²⁰ Facial examination should be conducted to assess scleral abnormalities, episcleritis, and ulcerations of the oral mucosa. Patients with colitis may present with a normal abdominal examination or tenderness localized to the left side. Significant tenderness may be observed in cases of fulminant disease or toxic megacolon. A perianal examination may reveal findings indicative of Crohn's, such as skin tags or anorectal stenosis. Additionally, a hand examination may uncover digital spasms. Skin examination may identify lesions, such as erythema nodosum or pyoderma gangrenosum, typically located on the lower extremities. Furthermore, joint examinations may reveal signs of arthritis.

Preliminary laboratory assessments should encompass a comprehensive blood count, electrolyte levels, blood urea nitrogen, creatinine, liver function evaluations, iron studies, vitamin D concentrations, C-reactive protein (CRP), erythrocyte sedimentation rate, albumin levels, and stool analyses for microbial infections, with a particular emphasis on *Clostridium difficile*.²⁷ The presence of hypoalbuminemia (defined as albumin levels below 3.5 g/dL) at the time of ulcerative colitis diagnosis is correlated with an increased probability of requiring corticosteroids, thiopurines, or anti-TNF therapies.²⁸

Laboratory indicators have been investigated as potential markers for assessing the disease activity and severity. Notably, serum CRP levels and erythrocyte sedimentation rates can remain within normal ranges in patients with severe UC.²⁹ Furthermore, as an acute-phase reactant, CRP is not exclusively indicative of intestinal inflammation; it is also relevant in the context of systemic inflammatory diseases.³⁰ In the case of UC, CRP demonstrates a combined sensitivity of 0.49 and a specificity of 0.92.³¹

Colonoscopy is considered to be a fundamental method for the diagnosis of UC. However, the exclusive use of endoscopy to differentiate IBD from non-IBD colitis presents certain limitations, necessitating additional clinical and histological information to enhance the diagnostic accuracy. It is recommended that an ileocolonoscopy be conducted, with a minimum of two biopsies³² obtained from each inflamed region. In instances of severe disease, the risk of perforation during ileocolonoscopy is elevated; therefore, sigmoidoscopy accompanied by biopsy may suffice.³³ Navaneethan et al³⁴ evaluated perforation incidents among patients with IBD and reported 19 cases of perforation among 5295 colonoscopies. Their findings indicate a significant association between severe disease observed during endoscopy and the occurrence of intestinal perforation in patients with IBD.

Microscopic examination should be conducted by a pathologist with specialized knowledge in Gastroenterology.²¹ In UC, histological alterations are confined to the mucosal layer and typically exhibit a consistent pattern without discontinuities. Unlike infectious colitis, colonic tissue affected by UC demonstrates both acute and chronic inflammatory characteristics, including basal plasmacytosis, distortion of crypt architecture, Paneth cell metaplasia, pyloric gland metaplasia, and increased intralaminar cellularity.³⁴ The presence of a singular feature indicative of chronic inflammation is insufficient for the definitive diagnosis of UC; however, there are no established criteria delineating the requisite number of features necessary for such a diagnosis.³² Histiocytosis may represent the earliest histological change associated with UC, observed in approximately one-third of patients within two weeks of the onset of symptoms. In contrast, only 20% of the patients exhibited stable crypt distortion during the initial two weeks, complicating the differentiation between early UC and infectious colitis (See [Figure 2](#)).

Pathophysiology

The existing literature predominantly focuses on comparing the pathophysiological mechanisms of UC with those of Crohn's disease; however, significant distinctions between the two conditions remain. The morbidity mechanisms associated with UC are closely linked to defects in colonic epithelial cells, mucosal barrier, and epithelial barrier. Notably, the expression of peroxisome

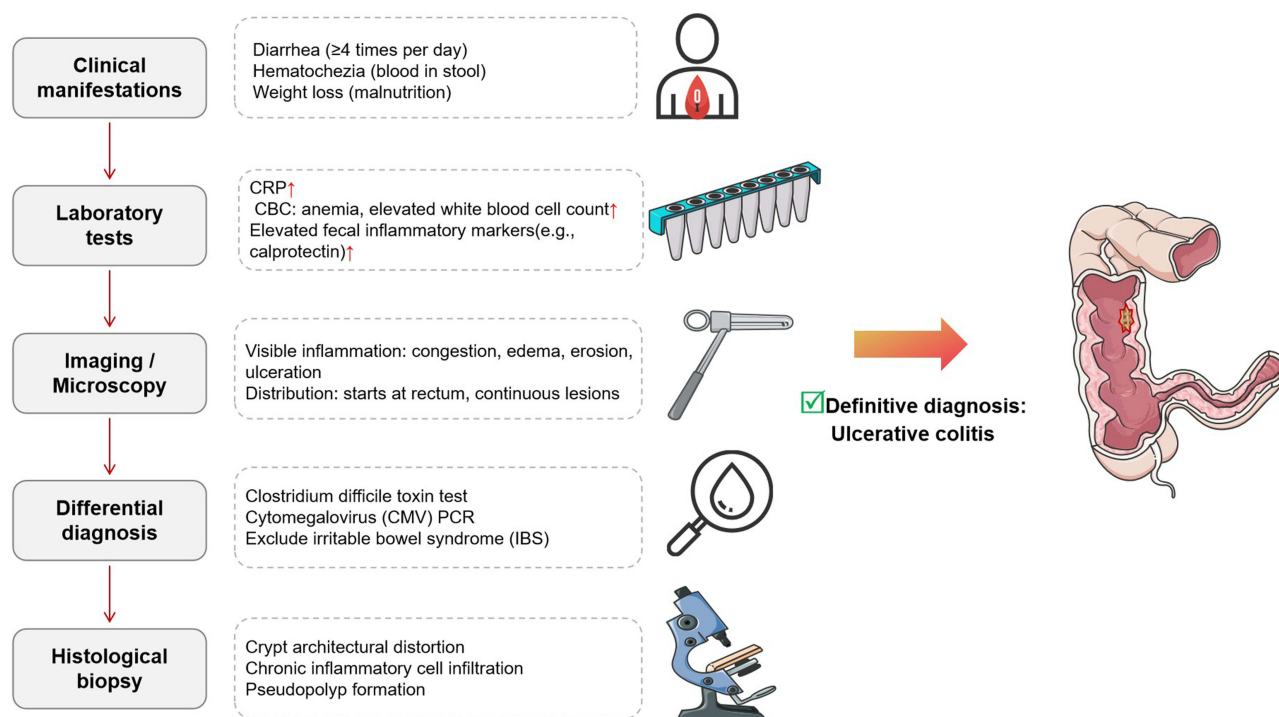


Figure 2 Diagnosis of UC.

proliferator-activated receptor gamma (PPAR- γ), which serves as a negative regulator of NF- κ B-dependent inflammation, is diminished in colonic cells derived from UC patients, indicating a potential causal relationship.^{35,36} In response to this, novel 5-aminosalicylic acid (5-ASA) analogs³⁷ are currently under development that exhibit enhanced PPAR- γ agonistic activity. Furthermore, an autoantibody targeting myosin associated with colon cells³⁸ has been identified in UC; however, there is insufficient conclusive evidence to categorize UC as an autoantibody-mediated disorder. Reports have also indicated defects in colon-associated XBPI expression³⁹ in patients with UC. Alterations in trefoil factors, a family of proteins derived from stellate cells that are produced in response to mucosal injury and play a role in maintaining mucosal barrier integrity, have been documented in individuals with ulcerative colitis.^{40,41} The hypothesis that impaired barrier function is a primary contributor to the disease is supported by observations of depleted colonic goblet cells and a compromised osmotic mucus barrier in patients with active ulcerative colitis.⁴² Additionally, dysbiosis has been observed in patients with ulcerative colitis, albeit to a lesser degree than in those with Crohn's.⁴³ Specifically, patients with ulcerative colitis exhibit reduced microbial biodiversity, a decrease in the proportion of Firmicutes, and an increase in the proportions of Gammaproteobacteria and Enterobacteriaceae.⁴⁴ Moreover, an increase in sulfite-reducing *Trigonoproteus*⁴⁵ has been noted in the colons of patients with UC. Nonetheless, the question of whether dysbiosis is a causative factor or consequence of mucosal inflammation remains unresolved.

Dysregulated innate and adaptive immune responses to microbial antigens in individuals with UC are well documented. Patients diagnosed with UC exhibit an increased accumulation of neutrophils and deployment of chromatin-based extracellular traps at sites of mucosal injury within the colon, which contribute to the persistence of inflammation by enhancing the production of tumor necrosis factor (TNF) and interleukin-1 β (IL-1 β).^{46,47} Dendritic cells, which function as antigen-presenting cells alongside macrophages, play a crucial role in mediating immune tolerance to external stimuli and guiding T cell differentiation to elicit adaptive immune responses. However, in the context of an inflamed colon, a specific subset of dendritic cells is redirected to produce pro-inflammatory cytokines, resulting in diminished tolerance and a reduced capacity to generate regulatory T cells.^{48–50}

Atypical responses of effector T helper (Th) cells and imbalances in T regulatory cells lead to the dysregulated production of several critical cytokines, thereby shifting the therapeutic focus of UC towards anti-cytokine agents. The cytokines involved include TNF, interferon-gamma, IL-5, IL-6, IL-13, IL-17, IL-21, and IL-22, all of which have been implicated in the

pathophysiology of UC through various mechanisms.⁵¹ Although the role of IL-22 in maintaining intestinal barrier integrity remains debatable, the presence of IL-22 regulatory transcripts in colonic biopsies from patients with UC has been associated with resistance to anti-p40 therapy, which targets the combined action of IL-12 and IL-23.⁵² Furthermore, IL-23, which regulates IL-22, has emerged as a specific target for a variety of clinically developed pharmacological agents, and its pathogenic role in UC and other immune-mediated disorders is becoming increasingly apparent.⁵³

Humoral immune responses remain relatively under-explored. A recent investigation into the molecular and phenotypic attributes of intestinal and circulating B cells identified significant disruptions, characterized by a reduction in both diversity and maturity.⁵⁴

The gastrointestinal microbiota has been associated with UC.⁵⁵ Investigations of surgical specimens analyzing the intestinal wall in relation to the microbiota have demonstrated a decrease in the symbiotic bacteria belonging to the Bacteroides and Proprietary phyla among patients diagnosed with UC.⁴⁴ Additionally, research has indicated a reduction in butyrate-producing species, specifically *Roseburia hominis* and *Faecalibacterium prausnitzii*, which are classified within the phylum Intrinsic.⁵⁶ The restoration of healthy microbiota through fecal microbiota transplantation has been shown to be advantageous and has been implemented with moderate success in the management of UC. Nonetheless, the observed response rates were comparable to those associated with existing treatment modalities.⁵⁷

The expression levels of Toll-like receptor 2 (TLR2) and TLR4 are elevated in the colonic cells and lamina propria of individuals with active UC; however, the relationship between mucosal inflammation and the increased expression of these receptors remains ambiguous, as it is uncertain whether inflammation is a causative factor or a resultant effect.^{58,59} Furthermore, activated neutrophils are more prevalent in both the bloodstream and colonic tissues of patients with active UC than in healthy controls.⁶⁰ Dendritic cells (DCs) derived from patients with UC exhibit increased expression of costimulatory molecules, suggesting that they may act as primary responders when the integrity of the mucosal barrier is compromised.⁴⁸

Innate lymphoid cells (ILCs) play a pivotal role in the pathophysiology of IBD.⁶¹ Furthermore, ILCs obtained from individuals with active UC exhibit elevated expression levels of key cytokines, transcription factors, and cytokine receptors associated with ILC3.⁶²

Elevated levels of immunoglobulin M (IgM), IgA, and nuclear IgG have been documented in individuals diagnosed with inflammatory bowel disease. However, a disproportionate increase in IgG1 antibodies has been observed specifically in patients with UC. The role of B cells in contributing to disease morbidity remains ambiguous, as it is uncertain whether they are active participants in pathogenesis or merely reactive to disruptions in the intestinal barrier. Preliminary findings indicate that UC may be characterized as a Th2 disorder, whereas Crohn's appears to be associated with Th1 responses. Analysis of colonic lamina propria cells from patients with UC revealed the presence of Th2-polarized T cells that produce IL-5.⁶³ Furthermore, the mRNA levels of IL-4 and IL-13 were significantly elevated in rectal biopsies from UC patients compared to those from control subjects.⁶⁴ IL-13, which is produced by nonclassical natural killer T cells, plays a critical role in mediating epithelial cytotoxicity and barrier dysfunction in UC.^{65,66}

One study reported a novel subset of CD4-positive Th cells that are influenced by transcription factor PU.1, which plays a role in the pathogenesis of UC.⁶⁷ This finding contributes to the existing Th1/Th2 paradigm associated with Crohn's and UC. In the presence of cytokines, such as transforming growth factor- β and IL-4, Th0 cells interact with MHC class II antigen complexes, leading to the differentiation of Th9 cells. IL-9 produced by Th9 cells inhibits cellular proliferation and tissue repair, thereby adversely affecting the integrity of the intestinal barrier. Furthermore, IL-9 has been observed to modestly and significantly elevate TNF- α levels.

Lastly, recent advances have highlighted the complex interplay between genetic susceptibility, environmental triggers, immune responses, and intestinal microbiota in the pathogenesis of UC. Genome-wide association studies have identified numerous UC-related loci, such as those involved in epithelial barrier integrity (eg, HNF4A, ECM1) and immune regulation (eg, IL23R, NOD2), which predispose individuals to dysregulated mucosal immunity.⁶⁸ Environmental factors, including diet, antibiotic exposure, and smoking status, can influence host immunity and gut microbial composition, further modulating disease risk.⁶⁹ The intestinal microbiota plays a particularly central role, not only by shaping immune tolerance but also by contributing to UC pathogenesis through mechanisms such as disruption of mucosal barrier function, production of pro-inflammatory or anti-inflammatory metabolites, and alteration of mucosal immune signaling.⁶⁹ Studies have shown that reduced microbial diversity, decreased abundance of SCFA-producing bacteria (eg, *Faecalibacterium prausnitzii*),⁷⁰ and

increased pro-inflammatory species (eg, *Escherichia coli*) are characteristic of UC patients.⁷¹ These microbial shifts can impair epithelial tight junctions, promote Th17 cell differentiation, and trigger abnormal immune responses. Thus, understanding these interconnected pathways offers a valuable framework for interpreting how Traditional Chinese Medicine may exert therapeutic effects by restoring microbiota-host-immune equilibrium.

Pathophysiological Mechanisms of TCM in the Treatment of UC

UC is classified within the framework of TCM as a form of “chronic dysentery” and is associated with the “intestine”. The pathophysiological mechanisms underlying UC are characterized by complex interactions across multiple systems and levels. According to TCM, the fundamental cause of this condition is attributed to deficiencies in the spleen and kidney, whereas the accumulation of dampness, heat, blood stasis, and toxins represents a more superficial manifestation. These factors are interrelated and contribute to a pathological cascade involving qi stagnation, blood stasis, and fluid retention.⁷² Recent advancements in research have yielded significant insights into the signaling pathways implicated in UC.

Research has demonstrated that the excessive activation of inflammatory cells and the aberrant release of inflammatory mediators are central to the pathogenesis of UC.⁷³ TLR4, a member of the Toll-like receptor family, plays a crucial role in the activation of the NF- κ B signaling pathway, which subsequently promotes the expression of inflammatory factors and triggers an inflammatory cascade via the MyD88-dependent pathway. In its inactive state, NF- κ B binds to the inhibitory protein, I κ B, in the cytoplasm. This binding leads to the phosphorylation and degradation of I κ B, facilitating the activation of NF- κ B and enhancing the production and release of proinflammatory factors. TLR4 can initiate an intracellular immune cascade by recognizing lipopolysaccharide (LPS) receptors, and therapeutic agents can ameliorate the inflammatory response in UC by inhibiting the TLR4/NF- κ B signaling pathway.⁷⁴ Deoxyschisandrin, an active component derived from *Schisandra chinensis*, has been shown to significantly alleviate the symptoms of colitis induced by dextran sulfate sodium (DSS) in murine models. This is achieved by downregulating the levels of TLR4, MyD88, NF- κ B, malondialdehyde (MDA), calpain I, and Bax, while upregulating the levels of superoxide dismutase (SOD), catalase (CAT), and Bcl-2 in colonic tissue. The underlying mechanism is associated with inhibition of the TLR4/NF- κ B signaling pathway, which reduces oxidative stress and mitigates the inflammatory response.⁷⁵ Total glucosides of paeony (TGP), an effective component of *Paeonia lactiflora* Pall., have been found in contemporary pharmacological studies to significantly downregulate the expression of TLR4 and NF- κ B in the colonic tissue of UC mice, while decreasing the levels of MDA and myeloperoxidase (MPO) in the colon.⁷⁶ Furthermore, Prakash et al⁷⁷ reported that varying doses of loganic acid, an active component of *Strychnos nux-vomica*, alleviated oxidative stress and diminished inflammatory cell infiltration in the affected areas of UC in rats by downregulating the expression of TLR4, NF- κ B, and inflammatory factors while upregulating the expression of heme oxygenase-1 (HO-1), thereby delaying the progression of UC.

The NLRP3 signaling pathway represents a significant intracellular signal transduction mechanism, comprising NLRP3, apoptosis-associated speck-like protein (ASC), and pro-caspase-1. Research has demonstrated a strong association between NLRP3 and UC onset and progression. This pathway exacerbates intestinal inflammation and damage by modulating the expression of proteins involved in inflammatory responses and apoptosis, thereby influencing the course of UC.⁷⁸ Apoptosis, a process of programmed cell death governed by inflammatory mediators, identifies caspase-1 as a critical effector.⁷⁹ The activation of NLRP3 leads to the downstream activation of caspase-1, facilitating the maturation of pro-inflammatory cytokines, such as IL-1 β and IL-18, and mediates apoptotic processes. Furthermore, NLRP3 can modulate the inflammatory response by activating the NF- κ B signaling pathway and upregulating inflammasome-associated proteins. Various monomers derived from traditional Chinese medicine have been shown to influence the expression of proteins related to the NLRP3 signaling pathway, thereby regulating inflammatory responses, inhibiting apoptosis, and retarding the progression of UC. Oxymatrine, an alkaloid isolated from *Sophora flavescens*, was reported by Sun et al⁸⁰ to downregulate the protein and mRNA levels of IL-1 β , IL-18, NLRP3, and caspase-1, inhibit activation of the NLRP3 signaling pathway, and slow the progression of UC. Additionally, matrine F has been observed to sustain intestinal homeostasis in UC mouse models by modulating the phosphorylation of NF- κ B p65 and the expression of NLRP3 in colonic tissues, while reducing the production of inflammatory factors and reactive oxygen species (ROS).⁸¹ Furthermore, studies have indicated that matrine F can enhance the expression of occludin and ZO-1 in the colon, thereby improving the integrity of the mucosal barrier and exerting anti-inflammatory effects.⁸¹

The JAK/STAT3 signaling pathway represents a critical intracellular transduction mechanism for JAK and STAT cytokines, which are essential for the regulation of gene transcription. This pathway plays a significant role in various biological processes, including immune regulation, inflammatory responses, cell proliferation, and apoptosis.^{82,83} Upon stimulation of T lymphocytes, the conformation of the corresponding receptors on the T cell surface undergo alterations, leading to the activation of intracellular protein tyrosine kinases. This activation facilitates the translocation of signals to the nucleus via STAT proteins, thereby initiating an immune response. As a well-established inflammatory pathway, aberrant activation of the JAK2/STAT3 pathway is closely associated with the progression of UC and other inflammatory diseases.⁸⁴ IL-6 levels have been positively correlated with the development of UC.⁸⁵ IL-6 interacts with its receptor to activate JAK2, which in turn promotes the phosphorylation of STAT3, mediates NF- κ B expression, and regulates the release of inflammatory mediators.⁸⁶ Furthermore, activation of the JAK-STAT5 signaling pathway can lead to the expression of the downstream target gene, Bal-2, which promotes T cell apoptosis and exacerbates intestinal inflammation.

Triptolide, the principal active compound derived from *Tripterygium wilfordii*, exhibits anti-inflammatory and immunosuppressive properties. ZT01, a novel derivative of triptolide, has been shown to mitigate the toxicity associated with triptolide while preserving its pharmacological efficacy.⁸⁷ Research indicates that ZT01 downregulates the expression of STAT1, STAT3, JAK1, and JAK2 in intestinal tissues by inhibiting JAK/STAT signaling, resulting in reduced inflammation and restoration of crypt structure in UC rat models.⁸⁸ Scutellaria polysaccharide, a major chemical constituent of *Scutellaria baicalensis* Georgi, has been pharmacologically demonstrated to modulate the IL-23/IL-17 inflammatory axis by downregulating JAK2 and STAT3 expression in the colonic tissues of UC mice, thereby diminishing the recruitment of inflammatory factors, such as IL-6, IL-17, and IL-23, and alleviating UC symptoms.⁸⁹ Atractylenolide III has also been shown to treat UC⁹⁰ by modulating the JAK2/STAT3 signaling pathway and reducing intestinal injury in murine models. Additionally, studies have indicated that curculigoside, the primary active component of *Curculigo orchioides*, can downregulate the expression of JAK1, JAK3, STAT3, TNF- α , IL-1 β , and IL-6, thereby inhibiting the inflammatory response mediated by the JAK/STAT signaling pathway and alleviating symptoms of DSS-induced UC in rat models.⁹¹

The PI3K/Akt signaling pathway primarily comprises phosphoinositide 3-kinase (PI3K) and Akt. Dysregulated activation of this pathway has been implicated in the pathophysiology of UC, contributing to inflammation, cellular proliferation, and apoptosis. PI3K activates Akt by generating phosphatidylinositol triphosphate (PIP3), which subsequently interacts with phosphoinositide-dependent protein kinase 1 (PDK1) and Akt. Akt serves as a pivotal component in cellular signaling, modulating processes such as inflammation, apoptosis, and proliferation^{92,93} by phosphorylating various downstream target proteins, including mTOR, FOXO transcription factors, glycogen synthase kinase 3 (GSK3), members of the Bcl-2 family, and NF- κ B. Furthermore, aberrant activation of the PI3K/Akt signaling pathway has been shown to augment the expression and secretion of pro-inflammatory cytokines, including TNF- α , IL-1 β , and IL-6.⁹⁴

Rhein, the principal bioactive compound derived from rhubarb, exhibits anti-inflammatory, antioxidant, and antifibrotic properties. Research conducted by Dong et al⁹⁵ demonstrated that rhein significantly inhibits the expression of PI3K, Akt, mTOR, TNF- α , IL-1 β , and IL-6 in colon tissue, both in vitro and in vivo, thereby suggesting that rhein alleviates symptoms and intestinal inflammation in UC models by inhibiting the PI3K/Akt/mTOR pathway.

Paeoniflorin,⁹⁶ the primary active constituent of *Paeonia lactiflora* Pall, possesses antitumor, anti-inflammatory, antioxidant, and immunomodulatory effects. Investigations have indicated that paeoniflorin can ameliorate pathological alterations in UC models by downregulating the expression of Akt1, Bcl-2, mTOR, PI3K, and inflammatory mediators, thereby inhibiting the PI3K/Akt/mTOR signaling pathway and exerting protective effects against UC.⁹⁷

Additionally, Astragalus polysaccharide, an active component of *Astragalus membranaceus*, has been shown by Zhao et al⁹⁸ to inhibit the PI3K/Akt signaling pathway, leading to the downregulation of PI3K and Akt expression, which contributes to its anti-UC effects.

The Notch signaling pathway, which encompasses DNA-binding proteins, Notch receptors, and Notch ligands, is integral to the regulation of intestinal stem cell differentiation and proliferation, maintenance of intestinal epithelial homeostasis, and preservation of antimicrobial function in intestinal epithelial cells.⁹⁹ The morbidity associated with UC is linked to dysfunction of the Notch signaling pathway and the inflammatory microenvironment. Upon activation of Notch, the intracellular domain of Notch (NICD) translocates to the nucleus, where it initiates transcriptional activation of the Notch target gene hair/division enhancer (Hes1). This process represses the expression of the transcription factors

Atoh1 and Math1, resulting in an increase in intestinal epithelial cell populations. Concurrently, Notch signaling inhibits the differentiation of stellate cells and the expression of mucin 2 (MUC2), which compromises the mucus barrier and disrupts the intestinal epithelial barrier, thereby exacerbating UC.¹⁰⁰ Furthermore, Notch serves as a critical upstream regulator of the non-classical NF- κ B activation pathway. Following macrophage activation, the expression of Notch-1 is upregulated, which facilitates the phosphorylation of the I κ B kinase α/β complex, promotes NF- κ B activation, and leads to the overproduction of pro-inflammatory cytokines.¹⁰¹

Aloesin A, an active compound derived from aloe, has been shown to protect the mucosal barrier by inhibiting the Notch signaling pathway, resulting in the decreased expression of Notch1, Hes1, TNF- α , IL-1 β , and IL-6 in murine models of UC, while simultaneously enhancing the expression of ATOH1, MUC2, IL-10, ZO-1, and Occludin. This modulation reduces inflammation and mitigates the progression of UC.¹⁰² Additionally, 6-shogaol, an alkylphenolic compound extracted from *Zingiber officinale*, regulates the Notch pathway and facilitates the repair of damaged colonic mucosa¹⁰³ by upregulating Math-1 protein expression and downregulating Notch-1 and Hes-1 protein levels. Sinomenine, derived from *Caulis Sinomenii*,¹⁰⁴ has also been demonstrated to reduce the expression of Notch1 and Hes1 in colon tissue, as well as inflammatory markers in serum, through the modulation of the Notch signaling axis, thereby offering potential therapeutic benefits for the prevention and treatment of UC (See Figure 3).

Cross-Talk and Coordination Among Signaling Pathways Regulated by TCM in UC

The signaling pathways involved in the pathogenesis of UC, including NF- κ B, JAK/STAT3, NLRP3, PI3K/Akt and Notch, have been shown to not function independently but instead form an interconnected regulatory network, which orchestrates key biological processes such as mucosal inflammation, epithelial barrier function, and immune regulation.¹⁰⁵ Among these, the NF- κ B and JAK/STAT3 pathways have been shown to be closely linked through IL-6-mediated positive feedback: activation of STAT3 enhances NF- κ B nuclear translocation, which further promotes IL-6 transcription, creating an amplification loop that perpetuates inflammation.¹⁰⁶ Similarly, the PI3K/Akt signaling can activate NF- κ B by phosphorylating I κ B kinase (IKK), and Akt can also regulate downstream mTOR and STAT3 pathways, thereby influencing both inflammation and epithelial repair.¹⁰⁷ The NLRP3 inflammasome, another key pro-inflammatory mediator, is activated downstream of NF- κ B and is modulated by inputs from PI3K/Akt and JAK/STAT3 signaling, illustrating the extent of cross-regulation within this network.¹⁰⁸

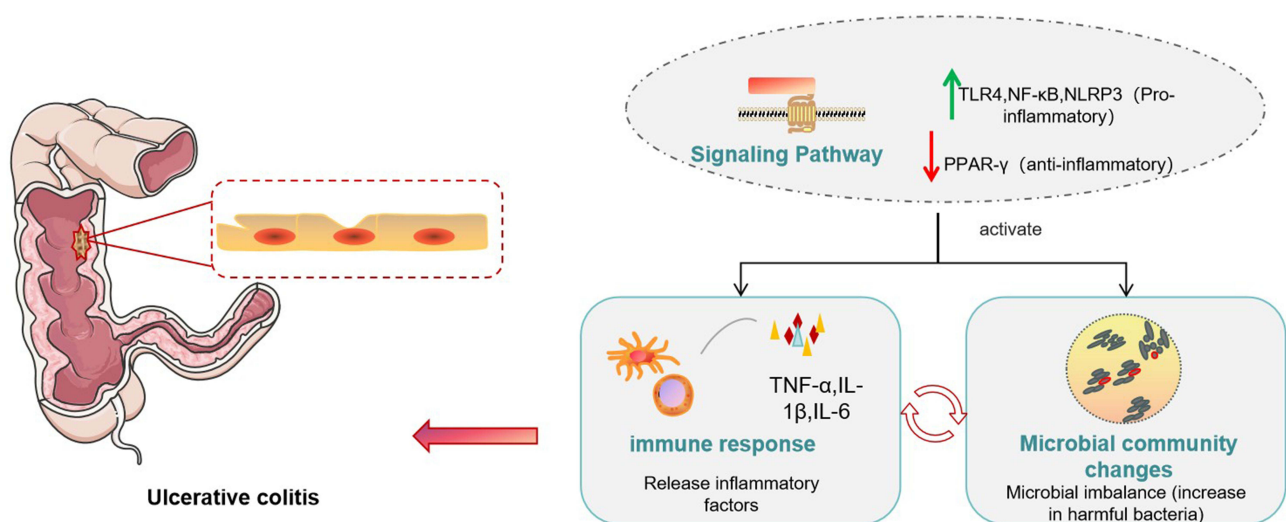


Figure 3 Pathophysiological mechanism of ulcerative colitis (UC). Green arrows indicate the activation or upregulation of pro-inflammatory pathways (TLR4, NF- κ B, NLRP3) and downstream cytokines (TNF- α , IL-1 β , IL-6). Red arrows represent the downregulation of the anti-inflammatory factor PPAR- γ . These changes lead to immune activation and gut microbiota dysbiosis, contributing to intestinal inflammation in UC.

Several TCM formulations may also exert coordinated effects on these interrelated pathways. For instance, Gegen Qinlian Decoction has been shown to simultaneously inhibit NF- κ B and JAK2/STAT3 signaling in DSS-induced colitis models, resulting in reduced expression of IL-6, TNF- α , and IL-1 β , as well as improved epithelial barrier integrity.¹⁰⁹ Similarly, Bawei Xileisan and Shenling Baizhu Powder downregulate NF- κ B and NLRP3 activation, while enhancing Treg differentiation through PI3K/Akt-mTOR modulation, highlighting their potential to restore immune balance.¹¹⁰

Collectively, these interconnected signaling pathways highlight the importance of examining TCM-based treatment for UC from a systems biology perspective. Future research should focus on elucidating the hierarchical organization and regulatory interactions among these pathways, and on determining how specific herbs or multi-component TCM prescriptions modulate this network to exert comprehensive and sustained therapeutic effects.

Treatment of UC with TCM

Gao et al¹¹¹ conducted a randomized controlled trial (RCT) to investigate the impact of the Kangyan Xiaozhong Pill on the intestinal mucosal barrier and intestinal microecology in patients diagnosed with UC of the large intestine damp-heat type. The study involved 92 participants who were randomly assigned to either a control group or a treatment group, with 46 individuals in each cohort. Both groups received standard symptomatic treatment. The control group was administered mesalazine enteric-coated tablets, while the treatment group received anti-inflammatory and swelling pills in addition to the control treatment. The duration of the intervention was six weeks. The researchers assessed and compared the efficacy, clinical signs and symptoms scores, intestinal mucosal barrier function, intestinal microecology, inflammatory markers, and adverse reactions between the two groups before and after the six-week treatment period. The findings indicated that Kangyan Xiaozhong Pill effectively reduced inflammation in UC patients with the large intestine damp-heat type and enhanced the intestinal mucosal barrier and microecology, subsequently leading to symptom improvement, increased efficacy, and a favorable safety profile.

Gao et al¹¹² conducted an RCT to evaluate the impact of the Anchang Jianpi Zhixie Decoction on endoscopic efficacy, inflammatory markers, and recurrence rates in patients with UC. The study involved 120 patients with UC who were randomly assigned to two equal groups. The control group received mesalazine, while the experimental group was administered a self-prepared Anchang Jianpi Zhixie Decoction in addition to mesalazine. Following a continuous treatment period of two months, various outcomes were assessed, including symptom efficacy, endoscopic efficacy, TCM syndrome scores, Mayo Endoscopy Score (MES), Ulcerative Colitis Endoscopy Severity Index (UCEIS), Ulcerative Colitis Luminal Inflammatory Load Severity Score (DUBLIN), levels of inflammatory markers (specifically TNF- α , IL-6, and CRP), recurrence rates, and adverse reactions. The findings indicated that the Anchang Jianpi Zhixie Decoction demonstrated a significant therapeutic effect in UC patients, as evidenced by a marked reduction in endoscopic scores, improvement in clinical signs and symptoms, a decrease in inflammatory marker levels, and an absence of notable adverse effects.

Cao et al¹¹³ conducted an RCT to evaluate the efficacy and underlying mechanisms of Shenling Baizhu Powder in the treatment of UC. The study involved 106 patients with UC exhibiting symptoms of spleen deficiency and dampness accumulation, who were randomly assigned to either a control group or an observation group, with 53 participants in each group. The control group received mesalazine enteric-coated tablets, whereas the observation group was administered Shenling Baizhu Powder in conjunction with mesalazine enteric-coated tablets. Both the groups underwent treatment for 12 weeks. The therapeutic outcomes were statistically analyzed, with assessments including TCM syndrome scores, modified Mayo scores, Geboes index, and quality of life metrics recorded before and after treatment. Additionally, serum inflammatory markers and Th17/Treg cell balance were evaluated before and after the intervention. These findings indicated that Shenling Baizhu Powder demonstrated significant efficacy in treating UC characterized by spleen deficiency and dampness accumulation syndrome. The proposed mechanism of action appears to involve the inhibition of pro-inflammatory cytokines such as IL-6, IL-17, and TNF- α , along with an increase in the release of anti-inflammatory cytokines IL-10 and TGF- β , thereby contributing to the regulation of the Th17/Treg cell balance (See [Figure 4](#)).

Although numerous clinical studies have investigated the therapeutic effects of TCM in UC, most are single-center and small-sample RCTs. While such studies provide important preliminary evidence, their limited sample sizes and lack of multicenter design may reduce generalizability and increase the risk of sampling bias. To date, high-quality, large-scale multicenter RCTs evaluating the efficacy and safety of TCM interventions in UC remain scarce. Furthermore,

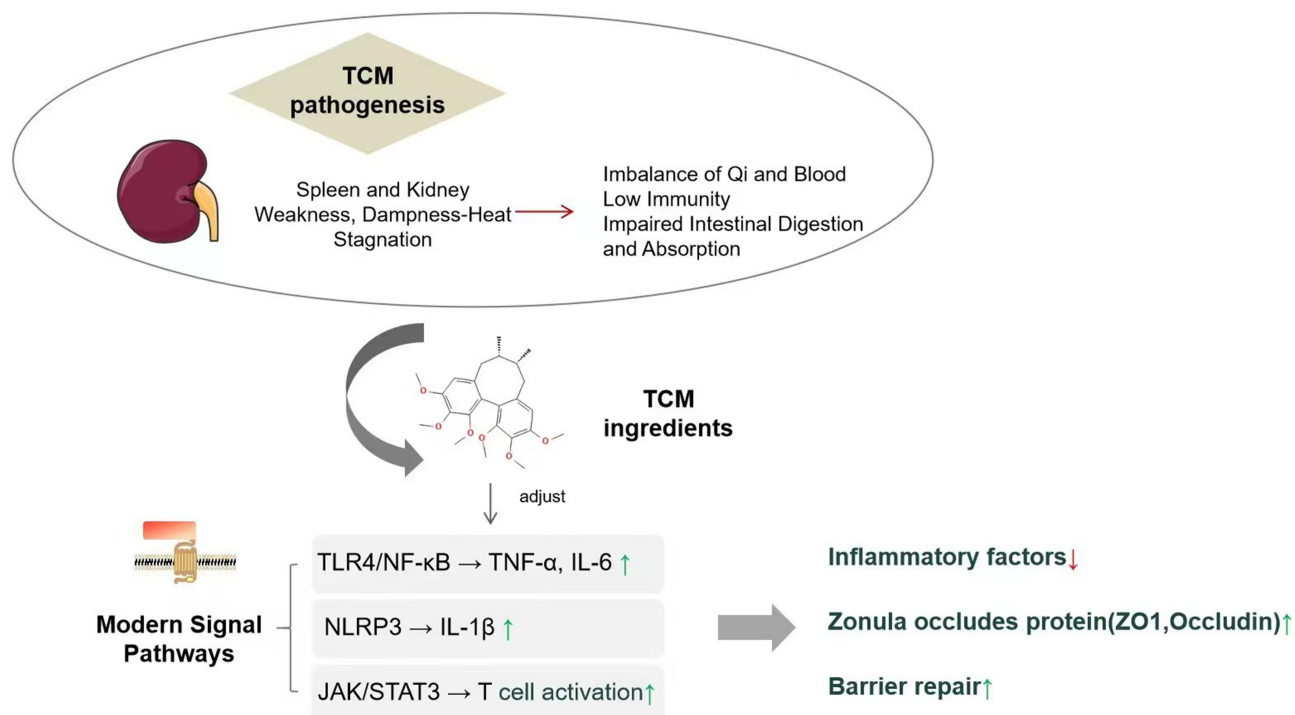


Figure 4 Mechanism of traditional Chinese medicine (TCM) in treating UC. Green arrows indicate TCM-induced upregulation of tight junction proteins (ZO-1, Occludin), T cell modulation, and barrier repair. Red arrows indicate downregulation of inflammatory cytokines (eg. TNF- α , IL-6, IL-1 β) via signaling pathway adjustment.

systematic reviews and meta-analyses integrating existing data are also limited. Therefore, future research should prioritize the design and implementation of rigorously conducted multicenter trials, along with comprehensive evidence synthesis approaches, to enhance the reliability and clinical applicability of TCM-based treatments for UC.

TCM Combined Therapy for UC

Chen et al¹¹⁴ conducted an RCT to evaluate the clinical efficacy of a modified version of the Gegen Qinlian Decoction in conjunction with acupuncture for patients diagnosed with UC exhibiting large intestine damp-heat syndrome. The study involved 120 participants who were randomly assigned to either a control group or an observation group, with 60 individuals in each cohort. The control group received treatment with Bifid Triple Viable Capsules and Mesalazine Sustained Release Granules, while the observation group was administered the modified Gegen Qinlian Decoction alongside acupuncture, building upon the treatment provided to the control group, over a duration of one month. Various outcomes were assessed, including clinical efficacy, symptom remission time, TCM syndrome scores, the Geboes index, lesion activity index, Baron score, inflammatory markers (IL-6, IL-8, TNF- α), immune function indicators (IgA, IgG, IgM), Inflammatory Bowel Disease Questionnaire (IBDQ) scores, and recurrence rates. The findings indicated that the combination of Jiawei Gegen Qinlian Decoction and acupuncture significantly enhanced the clinical manifestations and symptoms in UC patients with large intestine damp-heat syndrome, facilitated disease recovery, improved immune function and quality of life, and decreased recurrence rate.

Fan et al¹¹⁵ conducted an RCT to evaluate the efficacy of Zhuquan salt moxibustion in conjunction with Jianpi Yuchang Decoction for the treatment of UC characterized by spleen and stomach deficiency, as well as its impact on cytokine levels. The study involved 120 patients diagnosed with UC attributed to spleen-stomach deficiency who were randomly assigned to one of three groups, with 40 participants in each group. The control group received standard treatment; the Chinese medicine group received standard treatment along with Jianpi Yuchang Decoction; and the comprehensive treatment group received standard treatment, bamboo ring salt moxibustion, and Jianpi Yuchang Decoction. All groups underwent treatment for a duration of four weeks, after which clinical efficacy, TCM syndrome scores, and cytokine levels were compared. The results indicated that the total effective rate in the comprehensive treatment group surpassed that of both the Chinese medicine group and the control

group; the Chinese medicine group also demonstrated a higher effective rate than the control group ($P < 0.05$). Furthermore, post-treatment TCM syndrome scores were significantly lower across all groups than pre-treatment scores, with the comprehensive treatment group exhibiting the lowest scores, followed by the Chinese medicine group, and then the control group ($P < 0.05$). Additionally, the levels of TNF- α and IL-6 in all groups decreased after treatment compared to baseline levels, with the comprehensive treatment group showing lower levels than both the Chinese medicine and control groups, and the Chinese medicine group also exhibited lower levels than the control group ($P < 0.05$). Conversely, IL-10 levels increased in all groups post-treatment, with the comprehensive treatment group having higher levels than the Chinese medicine and control groups, and the Chinese medicine group also showed higher levels than the control group ($P < 0.05$). The findings of this study suggest that the combination of bamboo ring salt moxibustion and Jianpi Yuchang Decoction is an effective treatment for UC patients with spleen-stomach weakness, as it appears to modulate cytokine levels and enhance the clinical symptoms.

Ye et al¹¹⁶ conducted an RCT to investigate the clinical efficacy of external acupuncture utilizing the lifting and thrusting technique in conjunction with the oral administration of Tongxie Decoction for patients diagnosed with damp-heat UC. The study involved 81 participants with UC, who were randomly assigned to either a control group ($n = 40$) or an observation group ($n = 41$). The control group received oral mesalazine, while the observation group was treated with both the Tongxie Decoction and acupuncture. The treatment duration for both the groups was four weeks. The researchers compared the clinical efficacy, visual analog scale (VAS) scores, inflammatory bowel disease brief health scale (SHS) scores, ulcerative colitis Mayo scores (Mayo), intestinal mucosal barrier function indices, inflammatory markers, and adverse reactions before and after treatment between the two groups. The findings indicated that the combination of external acupuncture using the lifting and thrusting method and oral administration of Tongxie Decoction significantly benefited patients with UC characterized by damp-heat accumulation. This approach is associated with reduced pain, enhanced intestinal mucosal barrier function, and diminished inflammatory responses, demonstrating a favorable safety profile and considerable clinical applicability (Figure 5).

Practical Considerations for Clinical Integration of TCM Treatment

To facilitate the integration of TCM into clinical practice for UC, it is important to consider treatment strategies tailored to different disease stages and severities. In the active stage, where inflammation and symptoms such as abdominal pain, diarrhea, and hematochezia are prominent, TCM interventions often focus on resolving heat, dampness, and pathogenic factors. For example, modified Gegen Qinlian Decoction has been shown to reduce inflammatory cytokines such as IL-6, IL-8, and TNF- α in patients with large intestine damp-heat syndrome.¹¹⁷ Similarly, the combination of Tongxie Decoction with acupuncture was reported to alleviate active-stage symptoms and improve mucosal barrier function in patients with internal damp-heat accumulation.¹¹⁸ For patients with moderate to severe disease activity, integrated approaches such as Jianpi Yuchang Decoction combined with salt moxibustion demonstrated superior clinical efficacy in reducing inflammatory markers and improving symptom scores compared to oral TCM alone.¹¹⁹

In the remission stage, therapeutic goals shift toward stabilizing the disease, maintaining mucosal healing, and preventing relapse. Shenling Baizhu Powder has been used in this context, particularly for patients with spleen deficiency and dampness accumulation, by modulating the Th17/Treg balance and enhancing anti-inflammatory cytokine expression.¹²⁰ These findings suggest its potential as a maintenance therapy. However, most available studies are of short duration and lack stage-specific comparisons, limiting broader clinical translation.

Regarding disease severity, patients with mild to moderate UC generally respond well to oral TCM formulations, either as monotherapy or as adjuncts to standard treatments. In contrast, those with severe disease may require a combined regimen incorporating TCM and conventional agents such as mesalazine or immunosuppressants to achieve symptom control and mucosal repair.^{9,121} Despite promising results, there remains a lack of standardized treatment algorithms that stratify TCM usage by disease phase or severity. Therefore, future studies should aim to develop evidence-based, stage-specific protocols that integrate TCM syndrome differentiation with modern severity indices, such as the Mayo score and UCEIS, to improve individualized treatment planning.

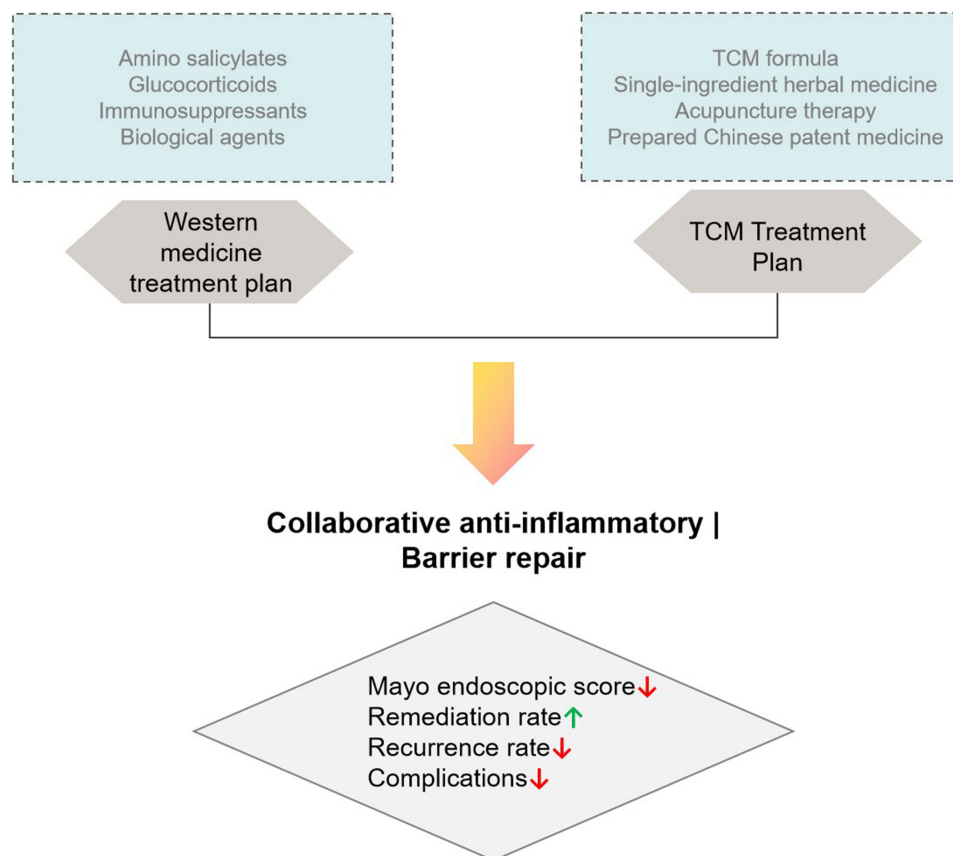


Figure 5 Comprehensive treatment strategy combining traditional Chinese medicine (TCM) and Western medicine. Green arrows indicate positive outcomes, such as an increased remediation rate. Red arrows indicate reductions in key clinical indicators, including Mayo endoscopic score, recurrence rate, and complications. This combined approach achieves synergistic anti-inflammatory effects and promotes intestinal barrier repair.

Innovative Mechanisms and Emerging Research Directions in TCM Treatment of Ulcerative Colitis

Recent advances in TCM research have identified various innovative mechanisms that offer new perspectives on UC treatment, complementing traditional theories with modern biomedical insights. One notable direction involves the regulation of ferroptosis, a form of iron-dependent programmed cell death characterized by lipid peroxidation. Studies have demonstrated that TCM monomers such as curculigoside can upregulate GPX4 expression, enhance intracellular glutathione synthesis, and reduce malondialdehyde (MDA) and reactive oxygen species (ROS) accumulation, thereby suppressing ferroptosis in DSS-induced colitis models.¹²² Similarly, curcumin, a bioactive compound from *Curcuma longa*, has been shown to inhibit ferroptosis and oxidative stress, leading to the attenuation of colonic injury.¹²² Classical herbal formulations also contribute to ferroptosis inhibition; for example, Shaoyao Gancao Tang decreases iron deposition and GSH consumption while reducing MDA levels, primarily through GPX4-mediated pathways.¹²³

In parallel, the gut microbiota and its metabolites have emerged as critical mediators of TCM's therapeutic effects in UC. Metabolomic profiling of TCM-treated models has revealed altered levels of uric acid and other key metabolites following administration of Shaoyao Decoction, with significant changes observed in both proximal and distal colonic tissues.¹²⁴ Additionally, several herbal prescriptions have been reported to normalize gut dysbiosis by reducing the Firmicutes/Bacteroidetes ratio and increasing beneficial taxa such as Lactobacillus, thereby enhancing short-chain fatty acid production, preserving epithelial integrity, and reducing inflammation.¹²⁵

Another emerging focus is the modulation of the gut-brain axis, wherein TCM interventions exert neuroimmune regulatory effects. Herbal treatments targeting serotonin (5-HT) signaling have shown promise in alleviating both gastrointestinal symptoms and mood disturbances associated with UC.¹²⁵ Moreover, acupuncture and moxibustion at specific acupoints,

including ST36 (“Zusanli”) and ST25 (“Tianshu”), have been shown to activate the cholinergic anti-inflammatory pathway and reduce intestinal cytokine production, indicating that neuromodulation contributes to their efficacy.

Beyond single mechanisms, TCM compounds are capable of regulating multiple types of programmed cell death (PCD), including apoptosis, autophagy, necroptosis, and pyroptosis. For instance, curcumin not only inhibits ferroptosis but also modulates autophagic processes by downregulating Atg12, Beclin-1, and LC3II expression in colonic epithelial cells,¹²⁶ thereby simultaneously influencing multiple PCD pathways for a broader and potentially more effective approach to disease control than conventional single-target drugs.

Importantly, the integration of artificial intelligence (AI) and network pharmacology is accelerating the identification of novel TCM targets in UC. Wu et al employed machine learning to construct a compound-target-pathway network based on metabolomic data of Shaoyao Decoction, identifying key molecular targets such as STAT3, IL-1B, IL-6, AKT1, and ICAM1, and confirming high-affinity interactions with active metabolites including quercetin, baicalin, kaempferol, and wogonin.¹²⁷ Furthermore, multi-omics integration, including genomics, proteomics, and spatial transcriptomics, is enabling comprehensive analyses of the biological effects of TCM compounds, offering unprecedented insights into their mechanisms of action.¹²⁸

Building on these advances, these advances reflect a broader trend in TCM research toward the integration of high-throughput technologies and data-driven methodologies, contributing to a more refined and scientifically grounded approach to UC management.

Conclusion

While current therapies for UC, including biologics and small-molecule inhibitors, have improved disease control, issues such as high cost, limited accessibility, and long-term safety concerns remain. In this regard, TCM, with its multi-target and multi-pathway regulatory properties, offers a potential complementary approach. Numerous experimental and clinical studies have shown that TCM can reduce inflammation, regulate immunity, and protect the intestinal barrier by modulating pathways such as NF- κ B, JAK/STAT3, PI3K/Akt, and NLRP3. However, the clinical translation of TCM is limited by the lack of direct comparisons with standard therapies and insufficient data on pharmacokinetics, toxicity, and long-term safety. Few studies have evaluated how TCM compares to biologics or small molecules in terms of efficacy, cost, and accessibility. Furthermore, most clinical trials remain small, single-center studies without standardized endpoints.

To strengthen the role of TCM in modern UC management, future research could adopt a more rigorous and translational framework, such as designing multicenter randomized controlled trials that directly compare TCM interventions with standard therapies such as biologics and small-molecule inhibitors. In addition to efficacy endpoints, future studies could incorporate dose-finding protocols, pharmacodynamic assessments, and long-term safety monitoring. The integration of biomarker-based patient stratification, such as inflammatory profiles, microbiota composition and genetic susceptibility, could improve the precision of TCM application. Furthermore, aligning TCM syndrome differentiation with internationally accepted disease classification systems may enhance its clinical relevance. To elucidate the molecular basis of TCM efficacy, network pharmacology, high-throughput screening, and multi-omics approaches could also be applied. Together, these strategies may provide a more comprehensive understanding of TCM mechanisms and support its safe and evidence-based inclusion in contemporary treatment strategies for UC.

Abbreviations

UC, Ulcerative colitis; TCM, Traditional Chinese Medicine; EIMs, extraintestinal manifestations; CRP, C-reactive protein; PPAR- γ , peroxisome proliferator-activated receptor gamma; 5-ASA, 5-aminosalicylic acid; TNF, tumor necrosis factor; IL-1 β , interleukin-1 β ; Th, T helper; TLR2, Toll-like receptor 2; DCs, dendritic cells; ILCs, innate lymphoid cells; IgM, immunoglobulin M; LPS, lipopolysaccharide; DSS, dextran sulfate sodium; MDA, malondialdehyde; SOD, superoxide dismutase; CAT, catalase; TGP, total glucosides of paeony; MPO, myeloperoxidase; HO-1, heme oxygenase-1; ASC, apoptosis-associated speck-like protein; ROS, reactive oxygen species; PIP3, phosphatidylinositol triphosphate; PDK1, phosphoinositide-dependent protein kinase 1; GSK3, glycogen synthase kinase 3; NICD, intracellular domain of Notch; Hes1, hair/division enhancer; mucin 2; RCT, randomized controlled trial; MES, Mayo Endoscopy Score; UCEIS,

the Ulcerative Colitis Endoscopy Severity Index; DUBLIN, Ulcerative Colitis Luminal Inflammatory Load Severity Score; VAS, visual analogue scale; SHS, inflammatory bowel disease brief health scale; Mayo, Mayo scores.

Acknowledgment

Zhuolin Ma is the co-first author of the study.

Funding

1. Research Project of Heilongjiang Administration of Traditional Chinese Medicine (ZHY2024-235); 2. Research Project on Popularization of Traditional Chinese Medicine Classics of Heilongjiang Administration of Traditional Chinese Medicine (ZYW2024-027).

Disclosure

The authors declare that they have no affiliation with, or involvement in, any organization or entity with any financial interest in the subject matter or materials discussed in this paper.

References

1. Høivik ML, Moum B, Solberg IC, et al. Work disability in inflammatory bowel disease patients 10 years after disease onset: results from the IBSEN study. *Gut*. 2013;62(3):368–375. doi:10.1136/gutjnl-2012-302311
2. Torres J, Billioud V, Sachar DB, et al. Ulcerative colitis as a progressive disease: the forgotten evidence. *Inflamm Bowel Dis*. 2012;18(7):1356–1363. doi:10.1002/ibd.22839
3. Peyrin-Biroulet L, Sandborn W, Sands BE, et al. Selecting therapeutic targets in inflammatory bowel disease (STRIDE): determining therapeutic goals for treat-to-target. *J Am College Gastroenterol*. 2015;110(9):1324–1338. doi:10.1038/ajg.2015.233
4. Magro F, Rodrigues A, Vieira AI, et al. Review of the disease course among adult ulcerative colitis population-based longitudinal cohorts. *Inflamm Bowel Dis*. 2012;18(3):573–583. doi:10.1002/ibd.21815
5. Burisch J, Zhao M, Odes S, et al. The cost of inflammatory bowel disease in high-income settings: a lancet gastroenterology & hepatology commission. *Lancet Gastroenterol Hepatol*. 2023;8(5):458–492. doi:10.1016/S2468-1253(23)00003-1
6. Cohen R, Yu A, Wu E, et al. Systematic review: the costs of ulcerative colitis in Western countries aliment. *Pharmacol Ther*. 2010;31(7):693–707. doi:10.1111/j.1365-2036.2010.04234.x
7. Wang T, Liu X, Zhang W, et al. Traditional Chinese medicine treats ulcerative colitis by regulating gut microbiota, signaling pathway and cytokine: future novel method option for pharmacotherapy. *Heliyon*. 2024;10(6):e27530. doi:10.1016/j.heliyon.2024.e27530
8. Teschke R, Wolff A, Frenzel C, et al. Herbal traditional Chinese medicine and its evidence base in gastrointestinal disorders. *World J Gastroenterol*. 2015;21(15):4466–4490. doi:10.3748/wjg.v21.i15.4466
9. Hao WR, Cheng CY, Cheng TH. Enhancing ulcerative colitis treatment with traditional Chinese medicine. *World J Clin Cases*. 2024;12(30):6358–6360. doi:10.12998/wjcc.v12.i30.6358
10. Ungaro R, Mehandru S, Allen P, et al. Colitis ulcerosa. *Lancet*. 2017;389(10080):1756–1770. doi:10.1016/S0140-6736(16)32126-2
11. Kleinman RE, Goulet O-J, Mieli-Vergani G, et al. *Walker's Pediatric Gastrointestinal Disease: Physiology, Diagnosis, Management*. PMPH USA, Ltd; 2018.
12. Magro F, Gionchetti P, Eliakim R, et al. Third European evidence-based consensus on diagnosis and management of ulcerative colitis. Part 1: definitions, diagnosis, extra-intestinal manifestations, pregnancy, cancer surveillance, surgery, and ileo-anal pouch disorders. *J Crohn's Colitis*. 2017;11(6):649–670. doi:10.1093/ecco-jcc/jjx008
13. Roussomoustakaki M, Satsangi J, Welsh K, et al. Genetic markers may predict disease behavior in patients with ulcerative colitis. *Gastroenterology-Orlando*. 1997;112(6):1845–1853. doi:10.1053/gast.1997.v112.pm9178675
14. Wyllie R, Hyams JS, Kay M. *Pediatric gastrointestinal and liver disease E-Book*. Elsevier Health Sciences. 2020.
15. Vavricka SR, Brun L, Ballabeni P, et al. Frequency and risk factors for extraintestinal manifestations in the Swiss inflammatory bowel disease cohort. *J Am College Gastroenterol*. 2011;106(1):110–119. doi:10.1038/ajg.2010.343
16. Hyams J, Markowitz J, Treem W, et al. Characterization of hepatic abnormalities in children with inflammatory bowel disease. *Inflamm Bowel Dis*. 1995;1(1):27–33. doi:10.1097/00054725-199503000-00003
17. Lindberg J, Stenling R, Palmqvist R, et al. Early onset of ulcerative colitis: long-term follow-up with special reference to colorectal cancer and primary sclerosing cholangitis. *J Pediatr Gastroenterol Nutr*. 2008;46(5):534–538. doi:10.1097/MPG.0b013e31815a98ef
18. Roth N, Biedermann L, Fournier N, et al. Occurrence of skin manifestations in patients of the Swiss inflammatory bowel disease cohort study. *PLoS One*. 2019;14(1):e0210436. doi:10.1371/journal.pone.0210436
19. Mir-Madjlessi SH, Taylor JS, Farmer RG. Clinical course and evolution of erythema nodosum and pyoderma gangrenosum in chronic ulcerative colitis: a study of 42 patients. *Am J Gastroenterol*. 1985;80(8):1.
20. Abreu MT, Harpaz N. Diagnosis of colitis: making the initial diagnosis. *Clin Gastroenterol Hepatol*. 2007;5(3):295–301. doi:10.1016/j.cgh.2006.12.032
21. Rubin DT, Ananthakrishnan AN, Siegel CA, et al. ACG clinical guideline: ulcerative colitis in adults. *J Am College Gastroenterol*. 2019;114(3):384–413. doi:10.14309/ajg.0000000000000152
22. Lawlor G, Moss AC. Cytomegalovirus in inflammatory bowel disease: pathogen or innocent bystander? *Inflamm Bowel Dis*. 2010;16(9):1620–1627. doi:10.1002/ibd.21275

23. Hendler SA, Barber GE, Okafor PN, et al. Cytomegalovirus infection is associated with worse outcomes in inflammatory bowel disease hospitalizations nationwide. *Int J Colorectal Dis.* 2020;35(5):897–903. doi:10.1007/s00384-020-03536-8
24. Lv Y-L, Han -F-F, Jia Y-J, et al. Is cytomegalovirus infection related to inflammatory bowel disease, especially steroid-resistant inflammatory bowel disease? A meta-analysis. *Infect Drug Resist.* 2017;10:511–519. doi:10.2147/IDR.S149784
25. Sager K, Alam S, Bond A, et al. cytomegalovirus and inflammatory bowel disease aliment. *Pharmacol Ther.* 2015;41(8):725–733. doi:10.1111/apt.13124
26. Domènech E, Vega R, Ojanguen I, et al. Cytomegalovirus infection in ulcerative colitis: a prospective, comparative study on prevalence and diagnostic strategy. *Inflamm Bowel Dis.* 2008;14(10):1373–1379. doi:10.1002/ibd.20498
27. Conrad K, Roggenbuck D, Laass MW. Diagnosis and classification of ulcerative colitis. *Autoimmunity Rev.* 2014;13(4–5):463–466. doi:10.1016/j.autrev.2014.01.028
28. Khan N, Patel D, Shah Y, et al. Albumin as a prognostic marker for ulcerative colitis. *World J Gastroenterol.* 2017;23(45):8008. doi:10.3748/wjg.v23.i45.8008
29. Solem CA, Loftus JR EV, Tremaine WJ, et al. Correlation of C-reactive protein with clinical, endoscopic, histologic, and radiographic activity in inflammatory bowel disease. *Inflamm Bowel Dis.* 2005;11(8):707–712. doi:10.1097/01.MIB.0000173271.18319.53
30. Nielsen OH, Vainer B, Madsen SM, et al. Clinical reviews: established and emerging biological activity markers of inflammatory bowel disease. *J Am College Gastroenterol.* 2000;95(2):359–367.
31. Mosli MH, Zou G, Garg SK, et al. C-reactive protein, fecal calprotectin, and stool lactoferrin for detection of endoscopic activity in symptomatic inflammatory bowel disease patients: a systematic review and meta-analysis. *J Am College Gastroenterol.* 2015;110(6):802–819. doi:10.1038/ajg.2015.120
32. Cohen SA, Gralnek IM, Ephraim H, et al. Capsule endoscopy may reclassify pediatric inflammatory bowel disease: a historical analysis. *J Pediatr Gastroenterol Nutr.* 2008;47(1):31–36. doi:10.1097/MPG.0b013e318160df85
33. Min SB, Le-Carlson M, Singh N, et al. Video capsule endoscopy impacts decision making in pediatric IBD: a single tertiary care center experience. *Inflammatory Bowel Dis.* 2013;19(10):2139–2145. doi:10.1097/MIB.0b013e31829a749c
34. Navaneethan U, Kochhar G, Phull H, et al. Severe disease on endoscopy and steroid use increase the risk for bowel perforation during colonoscopy in inflammatory bowel disease patients. *J Crohn's Colitis.* 2012;6(4):470–475. doi:10.1016/j.crohns.2011.10.005
35. Jiang C, Ting AT, Seed B. PPAR- γ agonists inhibit production of monocyte inflammatory cytokines. *Nature.* 1998;391(6662):82–86. doi:10.1038/34184
36. Dubuquoy L, Jansson EA, Deeb S, et al. Impaired expression of peroxisome proliferator-activated receptor γ in ulcerative colitis. *Gastroenterology.* 2003;124(5):1265–1276. doi:10.1016/S0016-5085(03)00271-3
37. Christel R, Bruno L, Laurent D, et al. Intestinal antiinflammatory effect of 5-aminosalicylic acid is dependent on peroxisome proliferator-activated receptor-gamma. *J Exp Med.* 2005;201(8):1205–15.
38. Geng X, Biancone L, Dai HH, et al. Tropomyosin isoforms in intestinal mucosa: production of autoantibodies to tropomyosin isoforms in ulcerative colitis. *Gastroenterology.* 1998;114(5):912–22.
39. Arthur K, Ann-Hwee L, Andre F, et al. XBP1 links ER stress to intestinal inflammation and confers genetic risk for human inflammatory bowel disease. *Cell.* 2008;134(5):743–56.
40. Mashimo H, Wu DC, Podolsky DK, Fishman MC. Impaired defense of intestinal mucosa in mice lacking intestinal trefoil factor. *Science.* 1996;274(5285):262–5.
41. Podolsky DK, Isselbacher KJ. Glycoprotein composition of colonic mucosa. Specific alterations in ulcerative colitis. *Gastroenterology.* 1984;87(5):991–8.
42. Malin EVJ, Jenny KG, Jessica H-L, et al. Bacteria penetrate the normally impenetrable inner colon mucus layer in both murine colitis models and patients with ulcerative colitis. *Gut.* 2013;63(2):281–91.
43. Akira A, Hirotsugu I, Tomoki A, et al. Comparison of the fecal microbiota profiles between ulcerative colitis and Crohn's disease using terminal restriction fragment length polymorphism analysis. *J Gastroenterol.* 2011;46(4):479–86.
44. Daniel NF, Allison LSA, Robert AF, et al. Molecular-phylogenetic characterization of microbial community imbalances in human inflammatory bowel diseases. *Proc Natl Acad Sci U S A.* 2007;104(34):13780–5.
45. Roediger WE, Moore J, Babidge W. Colonic sulfide in pathogenesis and treatment of ulcerative colitis. *Dig Dis Sci.* 1997;42(8):1571–1579.
46. Jennifer CB, Nancy AL, Charles AP. The role of polymorphonuclear leukocyte trafficking in the perpetuation of inflammation during inflammatory bowel disease. *Inflamm Bowel Dis.* 2013;19(7):1556–65.
47. Vincenzo D, Irene M, Davide DF, et al. Neutrophil extracellular traps sustain inflammatory signals in ulcerative colitis. *J Crohn's Colitis.* 2019;13(6):772–84.
48. Ailsa LH, Hafid Omar A-H, Rachael JR, et al. Characteristics of intestinal dendritic cells in inflammatory bowel diseases. *Gastroenterology.* 2005;129(1):50–65.
49. Hiroshi M, Hisako K, Junichi N, et al. CD103+ dendritic cell function is altered in the colons of patients with ulcerative colitis. *Inflamm Bowel Dis.* 2017;23(9):1524–34.
50. Elizabeth RM, David B, Siew CN, et al. Human gut dendritic cells drive aberrant gut-specific t-cell responses in ulcerative colitis, characterized by increased IL-4 production and loss of IL-22 and IFN γ . *Inflamm Bowel Dis.* 2014;20(12):2299–307.
51. Heitor SPDS, Claudio F. Immunopathogenesis of IBD: current state of the art. *Nat Rev Gastroenterol Hepatol.* 2015;13(1):13–27.
52. Polychronis P, Anastasia T, Eirini P, et al. Interleukin-22 regulates neutrophil recruitment in ulcerative colitis and is associated with resistance to ustekinumab therapy. *Nat Commun.* 2022;13(1):5820.
53. Tommaso Lorenzo P, Marietta I, Subrata G. Blockade of IL-23: What is in the pipeline? *J Crohn's Colitis.* 2022;16:ii64–72.
54. Uzzan M, Martin J, Mesin L, et al. Ulcerative colitis is characterized by a plasmablast-skewed humoral response associated with disease activity. *Nature Med.* 2022;28(4):766–779. doi:10.1038/s41591-022-01680-y
55. Paul BE, Elisabeth MB, Charles NB, et al. Diversity of the human intestinal microbial flora. *Science.* 2005;308:1635–8.
56. Julie S, Sumeet P, Melania C, et al. The short chain fatty acid butyrate imprints an antimicrobial program in macrophages. *Immunity.* 2019;50(2):432–45.
57. Magnus C, Kyaw M, Tahne V, et al. Fecal microbiota transplantation for chronic pouchitis: a systematic review and meta-analysis. *Microorganisms.* 2025;12(12):2430.

58. Hausmann M, Kiessling S, Mestermann S, et al. Toll-like receptors 2 and 4 are up-regulated during intestinal inflammation. *Gastroenterology*. 2002;122(7):1987–2000. doi:10.1053/gast.2002.33662
59. Çabuk B, Gökten DB, Solakoğlu T, et al. A single-center experience: enteropathic arthritis in inflammatory bowel diseases. *Egypt Rheumatol*. 2024;46(4):171–174. doi:10.1016/j.ejr.2024.07.001
60. Hiroyuki H, Ken T, Takayuki I, et al. Relationship between fecal calprotectin, intestinal inflammation, and peripheral blood neutrophils in patients with active ulcerative colitis. *Dig Dis Sci*. 2004;49(9):1438–43.
61. Buonocore S, Ahern P, Uhligh H, et al. Innate lymphoid cells drive interleukin-23-dependent innate intestinal pathology. *Nature*. 2010;464(7293):1371–1375. doi:10.1038/nature08949
62. Geremia A, Arancibia-Cárcamo C, Fleming M, et al. IL-23-responsive innate lymphoid cells are increased in inflammatory bowel disease. *J Exp Med*. 2011;208(6):1127–1133. doi:10.1084/jem.20101712
63. Fuss I, Neurath M, Boirivant M, et al. Disparate CD4⁺ lamina propria (LP) lymphokine secretion profiles in inflammatory bowel disease. Crohn's disease LP cells manifest increased secretion of IFN- γ , whereas ulcerative colitis LP cells manifest increased secretion of IL-5. *J Immunol*. 1996;157(3):1261–1270. doi:10.4049/jimmunol.157.3.1261
64. Inoue S, Matsumoto T, Iida M, et al. Characterization of cytokine expression in the rectal mucosa of ulcerative colitis: correlation with disease activity. *Am J Gastroenterol*. 1999;94(9):2441–2446. doi:10.1111/j.1572-0241.1999.01372.x
65. Fuss I, Heller F, Boirivant M, et al. Nonclassical CD1d-restricted NK T cells that produce IL-13 characterize an atypical Th2 response in ulcerative colitis. *J Clin Invest*. 2004;113(10):1490–1497. doi:10.1172/JCI19836
66. Heller F, Florian P, Bojarski C, et al. Interleukin-13 is the key effector Th2 cytokine in ulcerative colitis that affects epithelial tight junctions, apoptosis, and cell restitution. *Gastroenterology*. 2005;129(2):550–564. doi:10.1016/j.gastro.2005.05.002
67. Gerlach K, Hwang Y, Nikolaev A, et al. TH9 cells that express the transcription factor PU.1 drive T cell-mediated colitis via IL-9 receptor signaling in intestinal epithelial cells. *Nat Immunol*. 2014;15(7):676–686. doi:10.1038/ni.2920
68. Prager M, Buettner J, Buening C. Genes involved in the regulation of intestinal permeability and their role in ulcerative colitis. *J Dig Dis*. 2015;16(12):713–722. doi:10.1111/1751-2980.12296
69. Kobayashi T, Siegmund B, Berre LE, et al. Ulcerative colitis. *Nature Reviews Disease Primers*. 2020;6(1):74. doi:10.1038/s41572-020-0205-x
70. Zhao H, Xu H, Chen S, et al. Systematic review and meta-analysis of the role of Faecalibacterium prausnitzii alteration in inflammatory bowel disease. *J Gastroenterol Hepatol*. 2021;36(2):320–328. doi:10.1111/jgh.15222
71. Wu X, Li Y, Li P, et al. Structural variations in ulcerative colitis-associated Escherichia coli reduce fructose utilization and aggravate inflammation under high-fructose diet. *Gastroenterology*. 2025;S0016-5085(25). Epub ahead of print.
72. Hongjuan Y, Yanlong L, Xudong T, et al. Research progress on signaling pathway of ulcerative colitis treated by traditional Chinese medicine. *New Drug Clin Pharmacol Tradition Chin Med*. 2025;36(02):299–306.
73. Daniele N, Riccardo M, Giulia R, et al. The IL23-IL17 immune axis in the treatment of ulcerative colitis: successes, defeats, and ongoing challenges. *Front Immunol*. 2021;12:611256.
74. Huimiao M, Mengjing Z, Wenbin D, et al. Anemoside B4 prevents acute ulcerative colitis through inhibiting of TLR4/NF- κ B/MAPK signaling pathway. *Int Immunopharmacol*. 2020;87:106794.
75. Yu S, Qian H. Deoxyschizandrin treats mice with ulcerative colitis possibly via the TLR4/NF- κ B signaling pathway. *Am J Transl Res*. 2021;13(4):3856–3863.
76. Xiang J, Hu R, Li Q, et al. Total glucosides of paeony attenuates ulcerative colitis via inhibiting TLR4/NF- κ B signaling pathway. *Tohoku J Exp Med*. 2022;258(3):225–236. doi:10.1620/tjem.2022.073
77. Prakash A, Prasad N, Puppala E, et al. Loganic acid protects against ulcerative colitis by inhibiting TLR4/NF- κ B mediated inflammation and activating the SIRT1/Nrf2 anti-oxidant responses in-vitro and in-vivo. *Int Immunopharmacol*. 2023;122:110585. doi:10.1016/j.intimp.2023.110585
78. Bilian C, Jinzhu C, Xiaohua Q, et al. Research progress of NLRP3 inflammasome and related pathways in ulcerative colitis. *Guangdong Med J*. 2024;45(09):1211–1215.
79. Chao L, Li Z, Zhou J, et al. Shen-Ling-Bai-Zhu-San improves dextran sodium sulfate-induced colitis by inhibiting Caspase-1/Caspase-11-mediated pyroptosis. *Front Pharmacol*. 2020;11:814. doi:10.3389/fphar.2020.00814
80. Sun J, Wang S, Zhao Z, et al. Oxymatrine attenuates ulcerative colitis through inhibiting pyroptosis mediated by the NLRP3 inflammasome. *Molecules*. 2024;29(12):2897.
81. Xudong H, Chengzhu S, Haoyu N, et al. Study on the mechanism of matrine F regulating intestinal flora and improving immune response in mice with ulcerative colitis. *China Pharm*. 2024;35(17):2088–2095.
82. Elhefnawy E, Zaki H, Maraghy NEL, et al. Genistein and/or sulfasalazine ameliorate acetic acid-induced ulcerative colitis in rats via modulating INF- γ /JAK1/STAT1/IRF-1, TLR-4/NF- κ B/IL-6, and JAK2/STAT3/COX-2 crosstalk. *Biochem Pharmacol*. 2023;214:115673. doi:10.1016/j.bcp.2023.115673
83. Moon S, Kim K, Yoo J, et al. Phytochemicals targeting JAK-STAT pathways in inflammatory bowel disease: insights from animal models. *Molecules*. 2021;26(9):2824. doi:10.3390/molecules26092824
84. Aimei C, Defang F, Yan R, et al. Matrine protects colon mucosal epithelial cells against inflammation and apoptosis via the Janus kinase 2 / signal transducer and activator of transcription 3 pathway. *Bioengineered*. 2022;13(3):6490–9.
85. Yanrong L, Yujie J, Tingfang C, et al. IL-6/STAT3 signaling pathway regulates the proliferation and damage of intestinal epithelial cells in patients with ulcerative colitis via H3K27ac. *Exp Ther Med*. 2021;22(2):890.
86. Wei Q, Han L, Liu Y, et al. Rubia cordifolia L. ameliorates DSS-induced ulcerative colitis in mice through dual inhibition of NLRP3 inflammasome and IL-6/JAK2/STAT3 pathways. *Heliyon*. 2022;8(8):1.
87. Yingda Z, Fangfang L, Junmin F, et al. Novel nitric oxide-releasing derivatives of triptolide as antitumor and anti-inflammatory agents: design, synthesis, biological evaluation, and nitric oxide release studies. *Eur J Med Chem*. 2020;190:112079.
88. Junmin F, Yingda Z, Yu Z, et al. Exploring a novel triptolide derivative possess anti-colitis effect via regulating T cell differentiation. *Int Immunopharmacol*. 2021;94:107472.
89. Jie M, Yunzhi C, Lei T. Scutellaria polysaccharide improves inflammation in DSS-induced UC mice by regulating JAK2/STAT3 pathway and IL-23/IL-17 inflammatory axis. *J Sun Yat-Sen Univ*. 2023;44(03):423–429.

90. Huidong L, Yanmei L. Atractylenolide III attenuates intestinal injury in mice with ulcerative colitis by regulating JAK2/STAT3 signaling pathway. *Chinese J Pathophysiol.* 2023;39(01):142–149.
91. Hua X, Hongmei Y, Tuo C. Effect of curculigoside on JAK/STAT/NF- κ B signaling pathway in rats with ulcerative colitis. *China Pharm.* 2022;25(03):406–413.
92. Jinyan C, Chenyue Y, Lin Z, et al. JianPiTongLuo (JPTL) Recipe regulates anti-apoptosis and cell proliferation in colorectal cancer through the PI3K/AKT signaling pathway. *Heliyon.* 2024;10(15):1.
93. Linlin L, Shujing L, Jie K, et al. Inhibition of ABI2 ubiquitination-dependent degradation suppresses TNBC cell growth via down-regulating PI3K/Akt signaling pathway. *Cancer Cell Int.* 2024;24(1):222.
94. Min-Yao L, Hui-Juan L, Xue W, et al. Anti-inflammatory effects of huangqin decoction on dextran sulfate sodium-induced ulcerative colitis in mice through regulation of the gut microbiota and suppression of the Ras-PI3K-Akt-HIF-1 α and NF- κ B pathways. *Front Pharmacol.* 2020;10:1552.
95. Lingling D, Hongling D, Minyue Z, et al. Anti-inflammatory effect of Rhein on ulcerative colitis via inhibiting PI3K/Akt/mTOR signaling pathway and regulating gut microbiota. *Phytother Res.* 2022;36(5):2081–94.
96. Ailing Z, Zeng S, Xiangjuan K. Paeoniflorin alleviates H(2)O(2)-induced oxidative injury through down-regulation of MicroRNA-135a in HT-22 cells. *Neurochem Res.* 2019;44(12):2821–31.
97. Qifang L, Shuyue Z, Kai N, et al. Paeoniflorin improves ulcerative colitis via regulation of PI3K-AKT based on network pharmacology analysis. *Exp Ther Med.* 2024;27(4):125.
98. Haimei Z, Minfang H, Duanyong L, et al. Regulation of astragalus polysaccharide on PI3K/Akt signaling in colonic mucosa of rats with acute ulcerative colitis. *Chin Patent Med.* 2015;37(09):2029–2031.
99. Jiang YY, Yang S. Intestinal epithelial development homeostasis and its regulatory signals. *J Nanjing Med Univ.* 2024;44(01):89–104.
100. Hang N, Jiemin L, Jiaqian T, et al. The role of the Notch signalling pathway in the pathogenesis of ulcerative colitis: from the perspective of intestinal mucosal barrier. *Front Med.* 2024;10:1333531.
101. Peitao Z, Qianqin L, Shuwen S, et al. Interleukin 37 suppresses M1 macrophage polarization through inhibition of the notch1 and nuclear factor kappa B pathways. *Front Cell Dev Biol.* 2020;8:56.
102. Hui J, Gao-Feng S, Yu-Xi F, et al. Aloin A prevents ulcerative colitis in mice by enhancing the intestinal barrier function via suppressing the Notch signaling pathway. *Phytomedicine.* 2022;106:154403.
103. Hui Y, Shuguang Y, Qian W, et al. Effect of 6-shogaol on Notch signaling pathway in colonic epithelial cells of mice with ulcerative colitis. *Chin J Appl Physiol.* 2020;36(1):90–4+7–8. doi:10.12047/j.cjap.5889.2020.020
104. Linxia X. Study on the molecular mechanism of sinomenine-mediated Notch signaling pathway in the treatment of ulcerative colitis in mice. 2022.
105. Li L, An G, Li F, et al. Shared genes and pathways in ulcerative colitis and ankylosing spondylitis: functional validation and implications for diagnosis. *J Inflamm Res.* 2025;18:1657–1678. doi:10.2147/JIR.S497201
106. Long D, Mao C, Zhang W, et al. Natural products for the treatment of ulcerative colitis: focus on the JAK/STAT pathway. *Front Immunol.* 2025;16:1538302. doi:10.3389/fimmu.2025.1538302
107. Ye Z, Li Y, She Y, et al. Renshen Baidu powder protects ulcerative colitis via inhibiting the PI3K/Akt/NF- κ B signaling pathway. *Front Pharmacol.* 2022;13:880589. doi:10.3389/fphar.2022.880589
108. Ali F, Ibrahim IM, Ghogar OM, et al. Therapeutic interventions target the NLRP3 inflammasome in ulcerative colitis: comprehensive study. *World J Gastroenterol.* 2023;29(6):1026–1053. doi:10.3748/wjg.v29.i6.1026
109. Wang Y, Zhang J, Zhang B, et al. Modified Gegen Qinlian decoction ameliorated ulcerative colitis by attenuating inflammation and oxidative stress and enhancing intestinal barrier function in vivo and in vitro. *J Ethnopharmacol.* 2023;313:116538. doi:10.1016/j.jep.2023.116538
110. Sun YX, Liao X, Wang X, et al. An evidence mapping of systematic reviews and meta-analysis on traditional Chinese medicine for ulcerative colitis. *BMC Complement Med Therap.* 2021;21(1):228. doi:10.1186/s12906-021-03387-y
111. Zongyue GAO, Xiaoli ZHOU. Application of Kangyan Xiaozhong Pill in patients with ulcerative colitis of large intestine damp-heat type. *Jilin Traditional Chin Med.* 2025;45(02):186–190.
112. Yang G, Jianguo L, Lin L, et al. Effect of self-made Anchang Jianpi Zhixie Decoction on endoscopic efficacy, inflammatory factors and recurrence rate of ulcerative colitis. *Liaoning J Tradit Chin Med.* 2025;52(07):84–87.
113. Xia CAO, Rong QIU, Yunping TAO, et al. Study on the efficacy and mechanism of Shenling Baizhu Powder in the treatment of ulcerative colitis based on the regulation of Th17/Treg balance. *J Chinese Med Mater.* 2025;1:237–241.
114. Tian C, Zehui W, Yunhua P, et al. Clinical effect of modified Gegen Qinlian decoction combined with acupuncture on ulcerative colitis of large intestine damp-heat type. *Chin Patent Med.* 2025;47(02):453–457.
115. Xiaolin F, Jianhuan X, Huang L, et al. Curative effect of Zhuquan salt moxibustion combined with Jianpi Yuchang Decoction on ulcerative colitis with spleen and stomach weakness and its effect on cytokines. *J Jiangxi Univ Tradit Chin Med.* 2025;37(01):66–8+72.
116. Daobing Y, Huiju Y, Zongyue G. Effect analysis of external acupuncture with lifting and thrusting method combined with oral administration of Tongxie Decoction on ulcerative colitis with syndrome of internal accumulation of damp-heat. *J Clin Chin Med.* 2025;37(01):176–180.
117. Lu JZ, Ye D, Ma BL. Constituents, pharmacokinetics, and pharmacology of Gegen-Qinlian decoction. *Front Pharmacol.* 2021;12:668418. doi:10.3389/fphar.2021.668418
118. Yan J, Miao ZW, Lu J, et al. Acupuncture plus Chinese herbal medicine for irritable bowel syndrome with diarrhea: a systematic review and meta-analysis. *Evid Based Complement Alternat Med.* 2019;2019:7680963. doi:10.1155/2019/7680963
119. Liu ZX, Liu XY, Tan WW, et al. Clinical study of Jianpi Qingchang decoction in the treatment of ulcerative colitis patients with spleen deficiency and dampness-heat syndrome accompanied by fatigue: study protocol for a randomized controlled trial. *Contemp Clin Trials Commun.* 2024;42:101409. doi:10.1016/j.conctc.2024.101409
120. Chen J, Shen B, Jiang Z. Traditional Chinese medicine prescription Shenling BaiZhu powder to treat ulcerative colitis: clinical evidence and potential mechanisms. *Front Pharmacol.* 2022;13:978558. doi:10.3389/fphar.2022.978558
121. Yu YX, Wang S, Liu ZN, et al. Traditional Chinese medicine in the era of immune checkpoint inhibitor: theory, development, and future directions. *ChinMed.* 2023;18(1):59. doi:10.1186/s13020-023-00751-7
122. Wang Y, Hao Y, Yuan L, et al. Ferroptosis: a new mechanism of traditional Chinese medicine for treating ulcerative colitis. *Front Pharmacol.* 2024;15:1379058. doi:10.3389/fphar.2024.1379058

123. Li J, Tian X, Liu J, et al. Therapeutic material basis and underlying mechanisms of Shaoyao Decoction-exerted alleviation effects of colitis based on GPX4-regulated ferroptosis in epithelial cells. *ChinMed*. 2022;17(1):96. doi:10.1186/s13020-022-00652-1
124. Luo Y, Wu J, Liu Y, et al. Metabolomics study of Shaoyao plants decoction on the proximal and distal colon in mice with dextran sulfate sodium-induced colitis by UPLC-Q-TOF-MS. *Drug Des Devel Ther*. 2022;16:4343–4364. doi:10.2147/DDDT.S384607
125. Andrei C, Zanfrescu A, Ormeneanu VP, et al. Evaluating the efficacy of secondary metabolites in antibiotic-induced dysbiosis: a narrative review of preclinical studies. *Antibiotics*. 2025;14(2):138. doi:10.3390/antibiotics14020138
126. Cao Z, Tian K, Ran Y, et al. Beclin-1: a therapeutic target at the intersection of autophagy, immunotherapy, and cancer treatment. *Front Immunol*. 2024;15:1506426
127. Wu J, Luo Y, Shen Y, et al. Integrated metabolomics and network pharmacology to reveal the action mechanism effect of Shaoyao Decoction on ulcerative colitis. *Drug Des Devel Ther*. 2022;16:3739–3776. doi:10.2147/DDDT.S375281
128. Li Y, Liu X, Zhou J, et al. Artificial intelligence in traditional Chinese medicine: advances in multi-metabolite multi-target interaction modeling. *Front Pharmacol*. 2025;16:1541509. doi:10.3389/fphar.2025.1541509

International Journal of General Medicine

Publish your work in this journal

The International Journal of General Medicine is an international, peer-reviewed open-access journal that focuses on general and internal medicine, pathogenesis, epidemiology, diagnosis, monitoring and treatment protocols. The journal is characterized by the rapid reporting of reviews, original research and clinical studies across all disease areas. The manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use. Visit <http://www.dovepress.com/testimonials.php> to read real quotes from published authors.

Submit your manuscript here: <https://www.dovepress.com/international-journal-of-general-medicine-journal>

Dovepress
Taylor & Francis Group