Review

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Classical traditional Chinese medicine formulas for inflammatory bowel disease: Therapeutic evidence and mechanistic insights

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SUMMARY: Inflammatory bowel disease (IBD) is a digestive system disorder characterized by chronic recurrent inflammation, primarily including ulcerative colitis (UC) and Crohn's disease (CD). Although modern precision medicine therapies, represented by biologics and small-molecule drugs, have reshaped the IBD treatment landscape, clinical practice still faces challenges such as primary non-response, secondary loss of response, risks of severe opportunistic infections, and an increasingly heavy health-economic burden. Traditional Chinese Medicine (TCM), as a unique medical system with millennia of clinical experience and guided by its distinct theoretical framework of "holistic concept" and "treatment based on syndrome differentiation," shows great potential in IBD management. In recent years, advances in evidence-based medicine and modern biotechnology have propelled TCM research in IBD from empirical treatment toward precision medicine. TCM exerts its effects through multi-target and multi-pathway mechanisms, demonstrating unique advantages particularly in immunomodulation, intestinal barrier repair, and gut microbiota regulation. Furthermore, modern research, from holistic perspectives such as the "gut-lung axis" and "gut-brain axis," scientifically interprets the modern biological connotations of traditional TCM theories, providing new understanding for TCM's application in IBD. Concurrently, this article discusses the revolutionary progress of nanodrug delivery systems and multi-omics technologies in enhancing the bioavailability of TCM components, reducing toxicity, and elucidating complex mechanisms. It aims to construct a modern scientific framework for TCM in treating IBD through the dual macroscopic and microscopic perspectives of systems biology and translational medicine, offering insights for achieving precision therapy, whole-life-cycle management of IBD, and complementary integration of Chinese and Western medicine.

Keywords: Inflammatory bowel disease, traditional Chinese medicine, immunomodulation, intestinal barrier, gut microbiota

1. Introduction

Inflammatory bowel disease (IBD) is a chronic, relapsing inflammatory disorder of the gastrointestinal tract, driven by complex interactions between genetic susceptibility, immune dysregulation, environmental factors, and disturbances in gut microbiota that disrupt intestinal homeostasis (*1*). IBD primarily includes ulcerative colitis (UC) and Crohn's disease (CD). UC mainly involves the colon and rectum, presenting as continuous mucosal inflammation (*2*); whereas CD can affect the entire gastrointestinal tract, exhibiting skip lesions and transmural inflammation (*3*). IBD was long considered a disease specific to Western industrialized nations. However, accelerated globalization, profound dietary Westernization, antibiotic overuse, and environmental changes have led to its rapid spread in emerging economies across Asia, South America, and Africa, evolving it into a global epidemic (*4-7*) . This profound epidemiological shift further underscores the central role of complex gene-environment interactions in disease pathogenesis (*8*). According to the Global Burden of Disease (GBD) 2021 estimates, there are approximately 3.83 million cases of chronic inflammatory bowel disease worldwide, with 375,000 new cases and 42,000 deaths in 2021, resulting in more than 1.5 million disability-adjusted life years (DALYs) lost (*9*). IBD significantly impacts patients' quality of life, with long-term and severe symptoms contributing to substantial social, emotional, and economic burdens. Studies show that the prevalence of anxiety and depression among IBD patients is 35.1% and 21.6%, respectively (*10*). Furthermore, the long-term complications of IBD, including colorectal cancer (CRC) (with a 7% risk for patients with 30 years of disease duration) (*11*), intestinal strictures, fistula formation, and extra-intestinal manifestations (such as

arthritis and liver disease), increase the risk of disability and mortality. Among Crohn's disease (CD) patients, approximately 33% will develop intestinal strictures, with 7.8% having multiple strictures; 10.6% will develop fistulas, with perianal fistulas being the most common. Long-term follow-up studies indicate that around 50% of CD patients will experience strictures and/or fistulas within 20 years of diagnosis, significantly impacting quality of life and increasing clinical resource consumption (*12*).

Current therapeutic goals have evolved from mere clinical symptom remission to endoscopic mucosal healing and even deeper histological healing. Although modern medicine has achieved milestone progress in IBD treatment — from conventional 5-aminosalicylic acid (5-ASA), corticosteroids, and immunomodulators to biologics and small-molecule drugs — limitations remain in clinical practice. Some patients exhibit primary non-response to biologics or develop secondary loss of response due to anti-drug antibodies. Furthermore, the risks of infection and malignancy associated with long-term immunosuppressive therapy cannot be ignored (*13*). Although these treatments improve clinical outcomes, they do not provide a cure, and their side effects limit their long-term use. Additionally, the high cost of biologic treatments and their accessibility remain a critical issue, particularly in low-resource settings (*14*). Therefore, novel, safer, and more effective therapies are urgently needed to address the remaining gaps in the management of IBD.

Traditional Chinese Medicine (TCM), a treasure of Chinese civilization, has a rich theoretical foundation in the treatment of IBD. UC is often categorized as "chronic dysentery". Its pathogenesis is generally characterized by the intermingling of deficiency and excess, with damp-heat accumulation in the large intestine and qi stagnation regarded as major pathogenic factors (*15*). The pathogenesis of CD is more complex, often involving intermingled cold and heat, deficiency and excess, and is prone to forming intestinal strictures ("accumulation") as the disease progresses (*15,16*). Unlike modern medicine's focus on "antagonistic" therapy blocking single or specific inflammatory pathways, TCM emphasizes "harmonization," restoring the body's immune homeostasis, microecological balance, and barrier integrity through the synergistic action of multiple components, targets, and levels. Recently, with the rigorous introduction of evidence-based medicine methodologies and rapid development of modern biotechnology, TCM research in IBD has successfully transcended the boundaries of empirical medicine, entering a new stage of mechanistic elucidation and precision translation. This is not only due to numerous high-quality randomized controlled trials (RCTs) confirming the efficacy of Chinese herbs in inducing and maintaining remission but also because basic research has deeply revealed their fine regulatory mechanisms at the molecular and cellular levels (*17,18*). Furthermore, research and application of nanodrug delivery systems can significantly enhance the solubility and bioavailability of TCM components, reduce side effects through targeted delivery, opening new prospects for the modernization and internationalization of TCM.

This article will review and summarize the application and research progress of TCM formulas in IBD treatment, focusing on their mechanisms of action in regulating the immune microenvironment, intestinal barrier function, and gut microbiota balance. It aims to provide theoretical support for the evidence-based application of TCM in IBD treatment and offer a scientific basis for future precision therapy. A comprehensive literature search was conducted across multiple databases, including PubMed, Web of Science, MEDLINE, EMBASE, Springer LINK, Wanfang Database, China Biomedical Literature Database, and China National Knowledge Infrastructure (CNKI). The keywords used for the search were "inflammatory bowel disease" (including "ulcerative colitis" or "Crohn's disease") and "Traditional Chinese Medicine". All selected articles were published between 2016 and 2026.

2. New evidence for clinical efficacy and application strategies of classical TCM formulas

TCM formulas are the core vehicle of TCM treatment, designed according to the rigorous compatibility principle of "sovereign, minister, assistant, and envoy" ("Jun Chen Zuo Shi"), embodying the essence of systematic TCM therapy. TCM formulas holds unique advantages in treating IBD, manifested through synergistic regulation of multiple targets and pathways (Figure 1). Its application strategies are flexible and diverse, serving as independent therapy for mild-to-moderate patients or as adjuvant therapy for severe or refractory cases to enhance Western drug efficacy and reduce side effects (Table 1). Its clinical value has been validated through long-term practice, and recent evidence from evidence-based medicine has further solidified its therapeutic efficacy.

2.1. Shenling Baizhu San

Shenling Baizhu San, originating from the Taiping Huimin Heji Ju Fang in the Song Dynasty, consists of ginseng, Atractylodes, Poria, Chinese yam, lotus seed, hyacinth bean, coix seed, Amomum, Platycodon, and licorice. It is a classic formula for treating "Spleen Deficiency and Dampness Stagnation," commonly used in the clinical practice of IBD, particularly during the remission phase or for mild to moderate active IBD. It is effective in improving symptoms such as diarrhea, fatigue, and poor appetite (*19,20*). In the context of IBD, especially UC, this formula is explicitly recommended as the first choice for treating the spleen deficiency

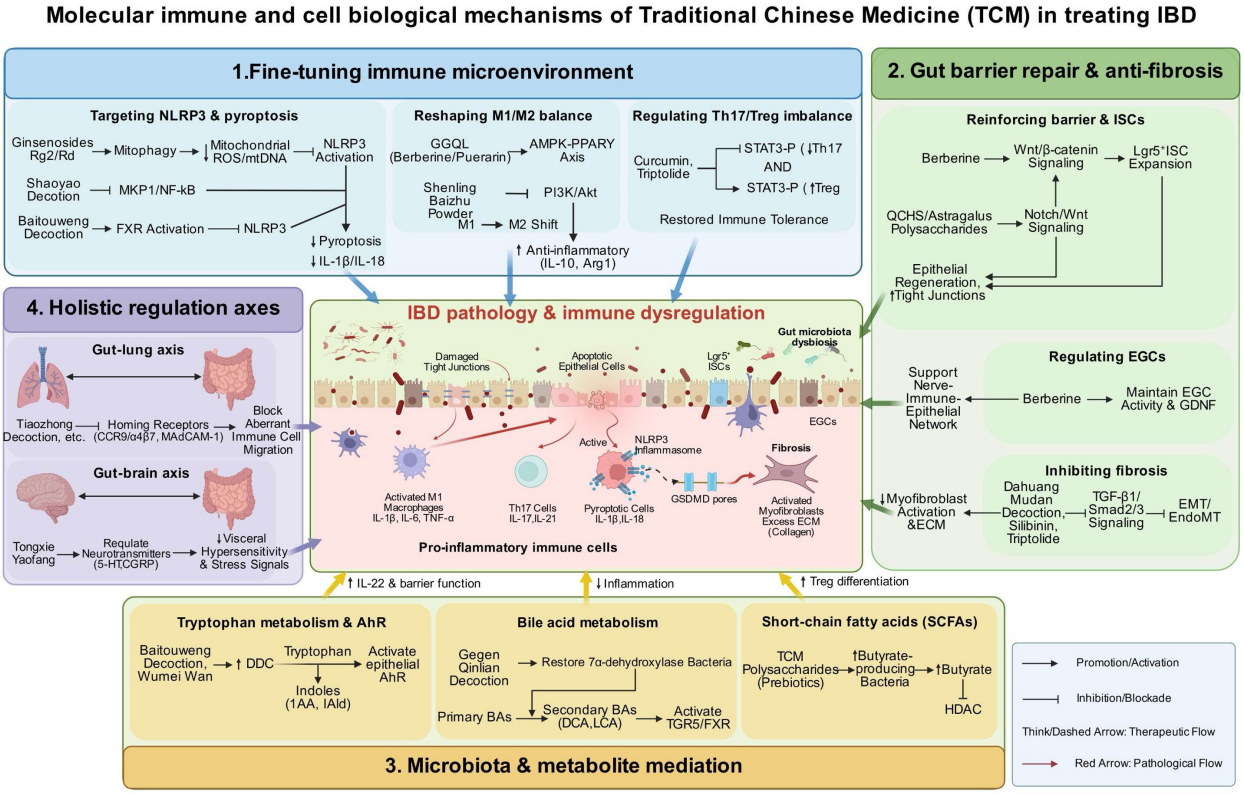

Figure 1. Molecular immune and cell biological mechanisms of traditional Chinese medicine (TCM) in treating inflammatory bowel disease (IBD). This figure depicts the multifaceted therapeutic actions of TCM in IBD, organized into four core modules: 1. Immune microenvironment fine-tuning: TCM modulates NLRP3 inflammasome/pyroptosis, M1/M2 macrophage balance, and Th17/Treg tolerance to suppress inflammation. 2. Gut barrier repair & anti-fibrosis: TCM promotes Lgr5+ ISC expansion and epithelial regeneration, sustains EGC activity, and inhibits myofibroblast activation/ECM deposition to mitigate fibrosis. 3. Microbiota & metabolite mediation: TCM regulates gut microbiota as well as the metabolism of tryptophan, bile acids, and short-chain fatty acids to enhance barrier function and reduce inflammation. 4. Holistic regulation: TCM suppresses aberrant immune cell trafficking by regulating homing receptors (CCR9/CCL25 and α4β7/MAdCAM-1) in the gut-lung axis, and modulates neurotransmitters (5-HT, CGRP) to attenuate visceral hypersensitivity in the gut-brain axis, exerting holistic therapeutic effects.

and dampness stagnation type according to diagnostic and therapeutic guidelines (*21,22*), and is suitable for mild to moderate active phase and remission phase UC, especially for managing chronic relapsing UC.

Recent evidence from evidence-based medicine has further confirmed the clinical efficacy and synergistic value of Shenling Baizhu San (*23*). For example, a meta-analysis published in China Pharmacy (including 14 RCTs with 1,177 UC patients) demonstrated that the combination of Shenling Baizhu San with 5-aminosalicylic acid (5-ASA) significantly improved the total response rate compared to 5-ASA alone, reducing the disease activity index (DAI) and lowering pro-inflammatory cytokines such as TNF-α and IL-17 (*24*). The 2023 Guidelines for the Integrated Diagnosis and Treatment of UC further consolidated the evidence, confirming the advantages of combining Shenling Baizhu San with Western medications in improving clinical efficacy, reducing DAI scores, and alleviating symptoms such as abdominal pain and diarrhea. Additionally, recent randomized controlled trials (RCTs) have further verified its efficacy. For instance, a domestic study involving 100 UC patients, a study including 62 pediatric and adolescent UC patients, and another on 70 elderly UC patients with bloody diarrhea all confirmed the positive role of Shenling Baizhu San in UC treatment (*25-27*). A more comprehensive prospective cohort study (48 patients) showed that 8 weeks of Shenling Baizhu San combined therapy not only significantly improved clinical symptoms and endoscopic mucosal healing but also verified its effects through 16S sequencing and metabolomics, showing close associations with gut microbiota remodeling and increased levels of tryptophan metabolites (such as IPA, IAA) (*28*). This finding clarifies the key mechanism of the "microbiota-tryptophan metabolic axis" in the synergistic effect of Shenling Baizhu San. Overall, Shenling Baizhu San demonstrates multiple clinical advantages in UC treatment, including symptom relief, disease activity reduction, mucosal healing, and providing a new treatment mechanism through gut microbiota and metabolic pathway regulation.

2.2. Shaoyao Tang

Shaoyao Tang, originating from the "Su Wen Bing

Table 1. Representative traditional Chinese medicine formulas for inflammatory bowel disease: corresponding TCM syndromes, core molecular mechanisms, and key clinical/experimental effects

Classical TCM formulas	Corresponding TCM syndrome	Major active components	Core molecular mechanisms	Key clinical/experimental effects	Ref
Shenling Baizhu San	Spleen deficiency with dampness retention	Ginsenosides, atractylenolides, Poria polysaccharides	Activation of the AhR–CYP1A1–NF-κB pathway; regulation of the SLC6A14/PI3K–AKT axis; improvement of the comorbidity network linking insulin resistance and intestinal inflammation	Enhancement of intestinal barrier integrity; significant reduction of inflammatory and metabolic indicators in patients with T2DM complicated by UC; regulation of Th17/Treg balance	(*19,20,28,67*)
Shaoyao Decoction	Damp-heat in the large intestine	Paeoniflorin, berberine	Blockade of the MKP1/NF-κB pathway; inhibition of NLRP3 inflammasome assembly and activation; suppression of ferroptosis in intestinal epithelial cells; improvement of hypercoagulable status	Significant reduction of serum TNF-α, IL-1β, and IL-6 levels; improvement of microcirculation; alleviation of DSS-induced colonic injury and bleeding	(*31,44*)
Baitouweng Decoction	"Heat-Toxin Excess" and "Damp-Heat Accumulation"	Pulsatilla saponins, berberine, fraxin	Upregulation of dopa decarboxylase (DDC), promoting tryptophan metabolism toward the indole pathway; increased IAA production and activation of the AhR/IL-22 axis; regulation of bile acid metabolism and activation of FXR	Promotion of deep mucosal healing; restoration of gut microbiota diversity; reduction of DAI scores; efficacy in refractory UC.	(*34-37,45,59*)
Tongxie Yaofang	Liver Qi stagnation and Spleen deficiency	Cimifugin glycoside, 5-O-methylvisamminol glycoside	Regulation of the brain–gut axis; reduction of visceral hypersensitivity; modulation of 5-HT, CGRP, and BDNF levels; inhibition of the RAGE signaling pathway	Alleviation of abdominal pain, diarrhea, and psychological symptoms; improvement of quality of life in patients with IBS-D and mild UC; regulation of stress-induced colitis	(*39,69,70*)
Gegen Qinlian Decoction	Damp-heat diarrhea	Puerarin, berberine, baicalin	Remodeling of the microbiota–bile acid axis; enrichment of 7α-dehydroxylase–producing bacteria; increased secondary bile acids (DCA, LCA); activation of TGR5/VDR receptors	Restoration of goblet cell function; promotion of mucin MUC2 secretion; improvement of intestinal inflammation associated with dysregulated glucose and lipid metabolism	(*40-42,61,82*)

Ji Qi Yi Bao Ming Ji", is based on the core functions of "clearing heat and drying dampness, regulating Qi and promoting blood circulation." It consists of nine herbs: white peony root, Chinese angelica root, Coptis root, areca nut, costus root, rhubarb root, Baikal skullcap root, cinnamon bark, and licorice root. This classic formula is used in the treatment of "Damp-Heat Accumulation in the Large Intestine" and has been strongly recommended in the 2023 Guidelines for the Integrated Diagnosis and Treatment of UC for mild to moderate active UC, especially those presenting with abdominal pain, tenesmus, and bloody diarrhea. It is also strongly recommended (Grade III evidence) as an adjunctive therapy in moderate to severe UC when used in combination with biologics (*21,29,30*).

Multiple evidence-based studies have confirmed its synergistic value. The latest meta-analysis (including 23 RCTs) demonstrated that Shaoyao Tang, whether used alone or in combination with Western medicines, significantly improved clinical efficacy, symptom efficacy, and quality of life (IBDQ scores), while also reducing recurrence rates and decreasing levels of pro-inflammatory cytokines such as TNF-α, IL-1β, and IL-6, and increasing the expression of anti-inflammatory cytokines such as IL-4 and IL-10 (*31*). The 2023 guidelines further summarize this evidence, confirming the combination of Shaoyao Tang with mesalazine in mild to moderate UC improves clinical remission rates, endoscopic response rates, and mucosal healing rates (*30*). RCTs of different disease stages further verify its efficacy: in mild to moderate UC (127 patients, RCT), Shaoyao Tang combined with mesalazine for 4 weeks showed a clinical remission rate of approximately 80%, significantly better than mesalazine alone, and significantly improved symptom scores for abdominal pain and diarrhea, as well as Baron endoscopic scores (*32*); in moderate to severe UC (68 patients, RCT), infliximab combined with Shaoyao Tang for 12 weeks showed superior clinical efficacy, Mayo scores, and endoscopic scores compared to infliximab alone (*33*). Moreover, Shaoyao Tang is considered to have good overall safety, with most RCTs reporting no significant adverse reactions. Meta-analysis results show that the incidence of adverse events in the combination therapy group was not higher than that in the monotherapy group, and some studies even suggested that combined therapy could significantly reduce adverse events, with no severe adverse events reported, though long-term safety still needs further verification.

2.3. Baitouweng Decoction

Baitouweng Decoction, originating from the Shang Han Lun, is based on the core functions of "clearing heat and detoxifying, cooling the blood, and stopping dysentery." It consists of four herbs: Pulsatilla root, Coptis root, Phellodendron bark, and Ash bark. This formula is a classic treatment for "Heat-Toxin Excess" and "Damp-Heat Accumulation" type UC. It is explicitly listed as a core formula for the active phase of UC in both the *Expert Consensus on the Diagnosis and Treatment of UC in Traditional Chinese Medicine (2017)* and the *Expert Consensus on the Diagnosis and Treatment of UC in Traditional Chinese Medicine (2023)*, particularly for patients with prominent symptoms of abdominal pain, diarrhea, and bloody stools, and is commonly administered orally or as a retention enema in combination with Western medications (*21*).

Multiple evidence-based studies have confirmed the significant efficacy of Baitouweng Decoction in UC treatment. A 2024 meta-analysis (including 24 RCTs with 2,131 patients) showed that Baitouweng Decoction, whether used alone or in combination with conventional Western medications, significantly improved clinical efficacy, reduced TCM syndrome scores and Baron endoscopic scores, and improved the inflammatory factor profile, with significant decreases in serum TNF-α and IL-8 levels, and an increase in anti-inflammatory IL-10 levels (*34*). Further clinical studies have verified its synergistic effect. A prospective cohort study (50 patients) demonstrated that Baitouweng Decoction combined with Western medicines for 30 days significantly improved clinical remission rates (69.2% *vs.* 37.5%) and total effective rates (84.6% *vs.* 58.3%) compared to Western medicines alone, with better reductions in ESR and fecal calprotectin levels and no significant adverse reactions (*35*); in another RCT (44 patients), Baitouweng Decoction combined with mesalazine for 30 days resulted in greater improvements in clinical efficacy and IBDQ quality of life scores compared to mesalazine alone, with significant increases in $CD4^+/CD8^+$ ratio and NK cell levels, and more significant reductions in TNF-α, IL-17, and IL-23 (*36*). A large sample RCT further confirmed that Baitouweng Decoction combined with mesalazine was superior in intestinal mucosal barrier repair, CRP, and mucin improvements, with a lower relapse rate compared to mesalazine alone (*37*). The overall safety of this formula is also good, with very few adverse events, mostly mild gastrointestinal discomfort such as nausea, and no severe adverse reactions reported. Meta-analysis results indicate no significant difference in adverse event rates between the combined therapy and monotherapy groups.

2.4. Tongxie Yaofang

Tongxie Yaofang, originating from Danxi Xinfa, consists of fried Atractylodes rhizome, fried white peony root, tangerine peel, and Saposhnikovia root. Its core functions include "soothing the liver, strengthening the spleen, dispelling dampness, and stopping diarrhea," making it a classic formula for treating "Liver Qi stagnation and Spleen deficiency" type ulcerative colitis (UC) in TCM. This formula is clearly recommended in relevant

guidelines and expert consensus, particularly for patients with mild to moderate active UC, especially those presenting with abdominal pain, diarrhea, and stress-related symptoms. It is commonly used in combination with mesalazine or other Western medications to enhance therapeutic efficacy (*21,30*).

In recent years, clinical studies based on randomized controlled trials (RCTs) have confirmed the clinical efficacy of Tongxie Yaofang. For example, a multicenter RCT including 40 UC patients with liver-spleen disharmony type in the active phase showed that after 12 weeks of combined treatment with mesalazine and Tongxie Yaofang, the experimental group significantly outperformed the control group (treated with mesalazine alone) in terms of the Sutherland index, Baron mucosal scores, and modified Mayo scores. Moreover, immune function markers (such as CD4+, CD4/CD8 ratio, and NK cell levels) and intestinal mucosal barrier function (with upregulation of tight junction proteins and downregulation of β-defensin) were significantly improved in the experimental group, demonstrating that Tongxie Yaofang enhances therapeutic outcomes through immune and mucosal barrier regulation (*38*). Additionally, several similar RCTs have reported that the combination therapy group showed significantly greater reductions in core symptoms such as abdominal pain, diarrhea, and bloody stools compared to the mesalazine-only group. This formula is also a representative remedy for regulating the "gut-brain axis." Research has confirmed its ability to reduce visceral hypersensitivity, regulate both central and peripheral serotonin (5-HT) levels, and modulate gut immune-epithelial communication through the IL-10RA/NF-κB pathway, alleviating stress-induced intestinal inflammation (*39*).

2.5. Gegen Qinlian Tang

Gegen Qinlian Tang is a classic TCM formula composed of Pueraria root, Baikal skullcap root, Coptis root, and roasted licorice root. Its core functions are "clearing heat, draining dampness, stopping diarrhea, and treating dysentery," and it is widely used to treat damp-heat type ulcerative colitis (UC). In clinical practice, Gegen Qinlian Tang is often used as an adjunctive therapy for UC patients with damp-heat syndrome, administered either orally or as a retention enema.

The clinical efficacy of Gegen Qinlian Tang has also been supported by relevant RCTs and meta-analysis evidence. An RCT including 60 patients showed that after 8–12 weeks of combined treatment with Gegen Qinlian Tang and mesalazine, the total effective rate was significantly higher than that of mesalazine alone (96.66% *vs.* 60.00%), with a reduction in the incidence of adverse effects. Additionally, combination therapy significantly lowered inflammatory markers such as IL-8, TNF-α, and CRP (*40*). Another RCT involving 120 patients with damp-heat type UC employed a modified version of Gegen Qinlian Tang combined with acupuncture and mesalazine/pefloxacin for 1 month. The total effective rate also increased significantly, and the combination group showed superior improvements in the Geboes index, Baron score, and IBDQ score, with a lower relapse rate at 6 months (*41*). The latest meta-analysis further confirmed that combination therapy improves the overall effective rate (RR = 1.22), reduces the adverse event rate (RR = 0.59), and significantly improves the modified Mayo score and Baron endoscopic score (*42*). The adverse effects of Gegen Qinlian Tang are mainly mild gastrointestinal discomfort, with no reports of serious adverse reactions, demonstrating good tolerance in treating damp-heat type UC. Therefore, it is commonly recommended by guidelines as an adjunctive therapy for damp-heat type UC (*30*).

3. Molecular immunology and cellular biology mechanisms of TCM in treating IBD

3.1. Fine-tuned regulation of the immune microenvironment

The immune microenvironment plays a pivotal role in the initiation and perpetuation of IBD. Immune dysregulation in IBD is mainly manifested by aberrant activation of immune cells, imbalanced cytokine secretion, and disruption of intestinal barrier integrity. Increasing evidence suggests that modulation of the immune microenvironment — particularly through key mechanisms such as NLRP3 inflammasome activation, macrophage polarization, and Th17/Treg imbalance — can provide novel theoretical support and therapeutic strategies for IBD management.

3.1.1. Targeting the NLRP3 inflammasome and pyroptosis

The NLRP3 inflammasome is a core sensor of the innate immune system. Its excessive activation leads to caspase-1–mediated cleavage of gasdermin D, thereby inducing pyroptosis and massive release of pro-inflammatory cytokines such as IL-1β and IL-18. The excessive production of these cytokines is considered one of the major driving forces of the inflammatory storm in IBD. Multiple active components derived from TCM have been shown to specifically inhibit NLRP3 inflammasome activation. For instance, ginsenosides Rg2 and Rd promote mitophagy, facilitating the clearance of damaged mitochondria and reducing the release of mitochondrial reactive oxygen species (ROS) and mitochondrial DNA (mtDNA), thereby blocking NLRP3 activation at its source (*43*). Shaoyao Decoction suppresses the upstream MKP1/NF-κB signaling pathway, resulting in reduced transcription of NLRP3 and pro-IL-1β (*44*). In contrast, Baitouweng Decoction modulates bile acid metabolism, activates the farnesoid X receptor (FXR), and interacts with NF-κB signaling to inhibit NLRP3 expression. This form of "metabolism–

immunity" crosstalk represents a novel perspective on TCM-based intervention, highlighting the potential of herbal medicine in regulating pyroptosis and immune-driven inflammation (*45*).

3.1.2. Remodeling macrophage polarization (M1/M2 balance)

Macrophages play a critical role in immune tolerance, and their plasticity determines the balance of the immune microenvironment. In IBD, macrophages are polarized toward the pro-inflammatory M1 phenotype, which secretes large amounts of pro-inflammatory factors and promotes disease progression. The therapeutic goal is to reprogram M1 macrophages into the anti-inflammatory and tissue-repairing M2 phenotype, thereby alleviating inflammation and promoting intestinal repair. The AMPK–PPARγ axis is a key pathway regulating M1/M2 macrophage polarization. The Gegen Qinlian (GGQL) nanoformulation contains components such as berberine and puerarin, which upregulate PPARγ expression through activation of AMPK phosphorylation. As a nuclear receptor, PPARγ can directly suppress the transcription of inflammatory genes and promote the expression of M2 markers (such as CD206, Arg1, and IL-10), thereby effectively enhancing immune tolerance and intestinal repair (*46*). Shenling Baizhu San has also been shown to reduce M1 polarization and increase the proportion of M2 macrophages by inhibiting the PI3K/Akt pathway, further promoting the repair of the intestinal mucosa. These TCM components exhibit significant effects in remodeling macrophage polarization, providing new insights into immunotherapy for IBD (*47*).

3.1.3. Regulation of Th17/Treg imbalance

Th17/Treg imbalance is a key event in the immunopathological process of IBD. Th17 cells drive intestinal mucosal inflammation by secreting pro-inflammatory cytokines such as IL-17 and IL-21, whereas Treg cells suppress excessive immune responses and maintain tolerance through IL-10 and TGF-β (*48*). The inflammatory microenvironment, STAT3/STAT5 signaling pathways, intestinal microbiota, and metabolic products jointly regulate the differentiation and function of Th17 and Treg cells. In IBD, the relative overexpression of pro-inflammatory Th17 cells and the reduction or functional impairment of suppressive Treg cells disrupt immune homeostasis, representing an important mechanism underlying persistent inflammation (*49*). Several TCM components, such as curcumin, triptolide, and Qingjie Fuzheng granules, have shown significant effects in restoring the Th17/Treg balance. These components inhibit Th17 differentiation by suppressing STAT3 phosphorylation while promoting Treg differentiation by enhancing STAT5 phosphorylation, thereby restoring immune tolerance. In this manner, curcumin and related compounds not only alleviate Th17-mediated pro-inflammatory responses but also enhance the immunosuppressive function of Treg cells, providing new immunomodulatory strategies for IBD treatment (*50*).

3.2. Repair and regeneration of the intestinal barrier

The homeostasis of the intestinal barrier is fundamental for maintaining the separation between the intestinal lumen and the internal environment of the host. Damage to the intestinal barrier is one of the key events in the pathogenesis of IBD. Repair of the intestinal barrier involves multiple aspects, including reinforcement of the mechanical barrier, regeneration of epithelial cells, neuroimmune interaction, and prevention of pathological fibrosis (*51*). Therefore, restoration of intestinal homeostasis and termination of chronic inflammation require a comprehensive repair of the intestinal barrier.

3.2.1. Reinforcement of the mechanical barrier and intestinal stem cells (ISCs)

The mechanical barrier is mainly composed of intestinal epithelial cells and their tight junction complexes (such as ZO-1 and occludin), which are usually severely disrupted during the active phase of IBD. Various TCM components can promote the expression of tight junction proteins and strengthen barrier function, thereby reducing inflammation caused by the translocation of pathogens and endotoxins (*51*). Intestinal stem cells (ISCs), located at the base of the crypts and characterized by the expression of the marker Lgr5, represent the fundamental driving force for epithelial renewal and repair. Recent studies have shown that certain Chinese patent medicines, such as berberine, not only exhibit anti-inflammatory effects but also regulate the microecological and signaling environments of ISCs, thereby promoting epithelial regeneration. Luo *et al.* found in a DSS-induced colitis model that berberine upregulated the expression of Wnt genes in resident stromal cells, enhanced the activity of the Wnt/β-catenin pathway, and promoted the activation and expansion of $Lgr5^+$ ISCs through this mechanism, thereby accelerating the repair of damaged intestinal mucosa. Blocking Wnt secretion significantly attenuated the reparative effects of berberine, indicating that Wnt/β-catenin signaling plays a critical role in this process (*52*). In addition, TCM formulas such as Qingchang Huashi Formula (QCHS) and Astragalus polysaccharides have been reported to promote the proliferation and differentiation of $Lgr5^+$ stem cells through the Notch and Wnt signaling pathways, enhancing the replenishment of multiple epithelial cell types, including goblet cells, and thereby accelerating the recovery of damaged regions (*85*). These mechanisms are consistent with findings from intestinal

organoid studies, which demonstrate the interactive roles of Wnt–Notch networks in cell fate determination, indicating that regulation of the stem cell niche is a key strategy for barrier repair (*53*).

3.2.2. Regulation of enteric glial cells (EGCs)

Enteric glial cells (EGCs), which are analogous to astrocytes in the central nervous system, constitute an important component of the intestinal microenvironment and maintain complex interaction networks with epithelial cells and the immune system. EGCs secrete regulatory factors such as neurotrophic factors (*e.g.*, GDNF), which promote epithelial cell maturation, enhance tight junction function, and strengthen antimicrobial defense, thereby supporting the integrity of the intestinal barrier (*54*). Studies have shown that in experimental colitis models, reduced expression or functional abnormalities of EGCs exacerbate barrier disruption; conversely, preservation or restoration of EGC function can alleviate inflammation and maintain barrier structure. In this context, the regulatory effects of alkaloids such as berberine on EGCs have gradually been revealed. Existing studies indicate that berberine can maintain the residence and activity of EGCs, regulate the interactions among EGCs, intestinal epithelial cells, and immune cells, and suppress the excessive release of pro-inflammatory gliotransmitters, thereby reducing epithelial injury and promoting barrier repair. The specific mechanisms may involve the modulation of inflammatory cytokines and neurotrophic factors, thereby stabilizing the immune environment and barrier function. These findings reflect the potential role of TCM in regulating the "neuro–immune–epithelial" network (*55*).

3.2.3. Inhibition of intestinal fibrosis

Intestinal fibrosis is a severe complication of IBD (especially Crohn's disease), characterized by excessive deposition of extracellular matrix (ECM) in the mucosa and intestinal wall, activation of myofibroblasts, and destruction of crypt architecture, leading to intestinal strictures and obstruction. This condition severely impairs patients' quality of life, and currently, no specific therapies are available. The TGF-β/Smad signaling pathway is the core mechanism driving fibrosis. TGF-β1 activates Smad2/3, which then forms a complex with Smad4 and translocates into the nucleus, promoting the differentiation of fibroblasts into myofibroblasts and enhancing the expression of ECM components, thereby facilitating fibrosis. Inhibition of this pathway is considered a key anti-fibrotic strategy (*56,57*).

With regard to TCM interventions, multiple formulas and monomeric compounds have demonstrated anti-fibrotic potential. Some compound formulas, such as Dahuang Mudan Decoction and Qingchang Tongluo Decoction, as well as monomeric compounds including silibinin and triptolide, have been confirmed *in vitro* and in animal experiments to significantly reduce TGF-β1–induced phosphorylation of Smad2/3, block the EMT/EndoMT process, and decrease the expression of fibrosis-related proteins (such as α-SMA and collagen), thereby inhibiting the transformation of intestinal fibroblasts into myofibroblasts and reducing ECM deposition (*58*). In addition, natural compounds (such as polyphenols and flavonoids) also exhibit anti-fibrotic effects by regulating the TGF-β/Smad, NF-κB, and ECM remodeling pathways, providing new directions for the treatment of intestinal fibrosis.

3.3. The key mediating role of gut microbiota and metabolites

The therapeutic effects of TCM *in vivo* are often exerted through its interactions with the gut microbiota. This "drug–microbiota–host" interplay constitutes an essential component of TCM efficacy. The gut microbiota not only influences drug absorption and metabolism but also regulates immune responses, intestinal barrier function, and systemic health through its metabolites, such as short-chain fatty acids, bile acids, and tryptophan-derived metabolites. Therefore, the roles of gut microbiota and metabolites in TCM-based treatment of IBD should not be overlooked.

3.3.1. Tryptophan metabolism and the aryl hydrocarbon receptor (AhR)

Tryptophan is an essential amino acid that can be metabolized by gut microbiota (such as *Lactobacillus* and *Clostridium* species) into indole derivatives, including indole-3-acetic acid (IAA) and indole-3-aldehyde (IAld). These metabolites serve as endogenous ligands for the aryl hydrocarbon receptor (AhR). AhR is a nuclear receptor that plays an important role in immune responses, mainly by regulating IL-22 secretion and intestinal barrier function, thereby contributing to the maintenance of intestinal immune homeostasis and barrier integrity. Activation of AhR promotes the repair of intestinal epithelial cells, enhances intestinal defense, and consequently suppresses intestinal inflammation. Studies have shown that TCM formulas such as Baitouweng Decoction and Wumei Pill can significantly upregulate the expression of dopa decarboxylase (DDC) in the intestine, thereby promoting the metabolism of tryptophan toward the indole pathway and increasing the production of AhR ligands. This mechanism contributes to intestinal barrier repair and alleviation of intestinal inflammatory responses (*59,60*). Through this pathway, TCM can modulate AhR signaling to exert anti-inflammatory and reparative effects, thereby facilitating the restoration of intestinal function.

3.3.2. Bile acid metabolism

Abnormal bile acid metabolism in the intestine is closely associated with the occurrence and progression of IBD. Patients with IBD often exhibit reduced levels of secondary bile acids, such as deoxycholic acid (DCA) and lithocholic acid (LCA), which leads to immune dysregulation and impairment of the intestinal barrier. Secondary bile acids exert anti-inflammatory effects by activating the TGR5 and FXR receptors, thereby promoting immune tolerance and barrier repair. Studies have found that Gegen Qinlian Decoction and its modified formulas can effectively reshape the gut microbiota structure and restore the abundance of bacteria with 7α-dehydroxylase activity, thereby promoting the conversion of primary bile acids into secondary bile acids. Through modulation of the FXR/NLRP3 signaling pathway, these formulas can suppress intestinal inflammatory responses (*61*). These findings indicate that TCM can exert anti-inflammatory effects and alleviate pathological responses in IBD patients by promoting bile acid metabolism and reshaping gut microbiota composition.

3.3.3. Short-chain fatty acids (SCFAs)

Short-chain fatty acids (SCFAs) are important metabolites produced by gut microbiota through the fermentation of dietary fiber, mainly including acetate, propionate, and butyrate. Among them, butyrate serves as a major energy source for intestinal epithelial cells and acts as a histone deacetylase (HDAC) inhibitor, regulating immune cell function at the epigenetic level, particularly in Treg cell differentiation. Polysaccharide components in TCM (such as Astragalus polysaccharides and Dendrobium polysaccharides) have been shown to possess prebiotic effects, promoting the growth of butyrate-producing bacteria (such as Faecalibacterium and Enterococcus) and increasing butyrate production. These butyrates not only provide energy for intestinal epithelial cells but also promote Treg cell differentiation through epigenetic regulation, thereby enhancing intestinal immune tolerance and modulating immune balance (*62*). Therefore, polysaccharide components in TCM exert immunomodulatory and intestinal-reparative effects by promoting the production of SCFAs.

3.4. New perspectives on holistic regulation: the "lung–gut axis" and the "brain–gut axis"

The core advantage of TCM in the treatment of IBD lies in its multidimensional regulation guided by the "holistic view." The gut-lung axis and gut-brain axis, as key inter-organ and inter-system communication networks, are essential mechanisms through which TCM achieves "local anti-inflammation and systemic homeostasis" (*63,64*). Both axes regulate the local inflammation in the gut in close association with systemic immunity, neurofunction, and gut microbiota balance, through pathways involving immune cell migration, neurotransmitter transmission, and microbiota-metabolite mediation. The precise modulation of these axes by TCM further highlights its "treating both the root and the branch" therapeutic characteristics.

3.4.1. The modern immunological basis of the theory that "the lung and the large intestine are interior–exteriorly related"

In TCM theory, the lung and the large intestine are considered to have an "interior–exterior" relationship. This concept has been reinterpreted in modern immunology, giving rise to the concept of the "gut–lung axis." This concept indicates that the lung and the intestine interact through the immune system, nervous system, and microbiota, thereby maintaining systemic immune homeostasis. The mucosal immune systems of the gut and the lung are interconnected through lymphocyte trafficking. Immune cells in the gut, under the guidance of specific chemokines, express receptors such as CCR9 and α4β7/MAdCAM-1, which bind to their corresponding ligands and thereby "home" to intestinal tissues. Similarly, immune cells in the lung also "home" to pulmonary tissues through these receptor-mediated mechanisms. Under pathological conditions, aberrant homing of immune cells may occur, leading to the migration of inflammatory cells from the lung to the intestine, thereby triggering or exacerbating enteritis, and vice versa (*65,66*). This phenomenon has been observed not only in IBD but also in other immune-related diseases.

TCM plays an important role in regulating the "gut–lung axis." Studies have shown that herbs such as Tiaozhong Decoction, Chebula (*Terminalia chebula*), and *Astragalus* polysaccharides can not only alleviate colitis but also reduce concomitant pulmonary inflammation. The underlying mechanisms may involve regulation of the expression of homing receptors such as CCR9/CCL25 and α4β7/MAdCAM-1, blocking cross-organ immune cell migration, and maintaining the balance of the microbiota in both the lung and the intestine (*68*). Related studies have demonstrated that these formulas exhibit significant immunomodulatory effects in both clinical and animal experiments, providing cellular and molecular evidence for the theory of "treating different diseases with the same method." This discovery offers new support for the use of TCM in treating diseases associated with lung–gut interactions.

3.4.2. The brain–gut axis and emotion-related pathogenesis

The brain–gut axis refers to the bidirectional communication network between the gut and the brain, involving multiple mechanisms, including neural, endocrine, and immune pathways. Recent studies have shown that patients with IBD often experience

psychological symptoms such as anxiety and depression, and psychological stress can in turn trigger disease activity. Psychological factors directly affect intestinal immune function and microbiota balance through the brain–gut axis, thereby exacerbating disease progression. Tongxie Yaofang, a classical formula for treating "liver stagnation and spleen deficiency" in TCM, has traditionally been used to regulate emotional disorders. Modern studies have confirmed that it can alleviate intestinal diseases by modulating the brain–gut axis. Tongxie Yaofang can regulate the levels of neurotransmitters such as 5-hydroxytryptamine (5-HT, serotonin) and calcitonin gene-related peptide (CGRP) in both the central and peripheral nervous systems, reduce visceral hypersensitivity, and alleviate abdominal pain, particularly in patients with IBS-D (diarrhea-predominant irritable bowel syndrome) and UC, thereby demonstrating the advantages of TCM in treating both the body and the mind (*69,70*). This therapeutic mechanism, which acts through modulation of the brain–gut axis, not only improves intestinal inflammatory responses but also helps relieve intestinal discomfort caused by psychological factors, highlighting the unique role of TCM in regulating the interaction among intestinal immunity, the nervous system, and emotional states. A detailed summary of the mechanism of action is provided in Figure 1.

4. The dual engines of the modernization of traditional Chinese medicine

Although classic TCM formulas have accumulated substantial clinical evidence for the treatment of IBD, and their multi-component and multi-target synergistic advantages have been scientifically elucidated through cellular and molecular mechanism studies, challenges remain in bridging traditional experience with modern precision medicine. On one hand, the complexity of formula components, poor water solubility of certain active ingredients, gastrointestinal degradation, and non-targeted tissue distribution lead to low bioavailability, limiting the maximal clinical efficacy (*71*). On the other hand, traditional research methods struggle to fully decipher the complex regulatory network of "multi-components—multi-targets—multi-pathways," hindering the precise identification of key active ingredients and their mechanisms of action (*72*). To overcome these challenges, two key technologies have become the "dual engines" driving the modernization of TCM formulas — nanomedicine through smart encapsulation and targeted regulation to address drug delivery issues, and multi-omics integration with network pharmacology to systematically clarify the core mechanisms. Together, they provide revolutionary solutions for the standardization, precision, and clinical translation of TCM formulas (Table 2).

4.1. Nanomedicine-based drug delivery systems

Nanomedicine, or nanodrug delivery systems (NDDS), is the core technology to solve drug delivery challenges in TCM. By precisely encapsulating and intelligently regulating active ingredients, NDDS can significantly enhance drug stability, targeting, and bioavailability while reducing systemic toxicity. In recent years, breakthrough advances have been made in the development of intestinal-targeted nanocarriers, especially in the areas of "environmentally responsive drug release" and "biological targeting modifications."

In the design of responsive carriers, pH-sensitive or reactive oxygen species (ROS)-responsive smart materials have become research hotspots due to the characteristics of the colonic inflammatory microenvironment. For example, low pH or high ROS-sensitive PLGA (Poly lactic-co-glycolic acid) nanoparticles enable selective drug release at the site of colonic inflammation, avoiding early degradation in the stomach and small intestine (*73*). Natural polysaccharides like hyaluronic acid and chitosan can specifically bind to the CD44 receptors overexpressed at the site of colonic inflammation, enhancing macrophage targeting (*74*). Additionally, by combining nanocarriers with microparticles or biomimetic coatings, multiple protective barriers can be constructed to further prevent enzymatic and acid-base degradation in the gastrointestinal tract, promoting efficient drug accumulation at the colonic site. In practical applications, the combination of nanotechnology and TCM ingredients with a "controlled release + targeted delivery" strategy effectively addresses the challenges of traditional formulations, significantly improving clinical applicability and safety. For example, berberine (berberine alkaloid) encapsulated in PLGA nanoparticles (BPL-NPs) can target and inhibit the IL-6/IL-6R signaling axis, reducing M1 macrophage infiltration in the colon, and significantly improving DSS-induced colitis (*75*). Similarly, composite nanoparticles prepared from the core components of Gegen Qinlian Decoction (berberine, puerarin, baicalin, and glycyrrhizic acid) activate the AMPK-PPARγ pathway to promote M2 macrophage polarization, enhancing drug accumulation at the ulcer site and balancing intestinal immunity (*46*). Additionally, nanotechnology can be used to encapsulate toxic TCM ingredients like triptolide, effectively reducing their accumulation in the kidneys and reproductive system, thereby minimizing side effects. For instance, silk fibroin nanoparticles (SFNP) of triptolide demonstrate enhanced anti-inflammatory and anti-tumor effects, significantly reducing liver and kidney toxicity in both cell and animal experiments (*76*). By loading triptolide and Atractylodes macrocephala into red blood cell membrane-coated liposomes (RBCm@Lip), immune cells can be "confused," prolonging the residence time of the drug in the blood and significantly reducing toxicity to normal tissues (*77*).

Overall, the synergistic effect of nanocarriers and TCM active ingredients significantly enhances

Table 2. Advanced technological strategies in traditional Chinese medicine–based IBD research: applications and key scientific/clinical problems addressed

Technological field	Specific technologies	Application examples in TCM-based IBD research	Key clinical problems addressed	Ref
Nanomedicine-based drug delivery systems	Plant-derived exosome-like nanovesicles (PELNs)	PELNs derived from grapes, ginger, and garlic for the treatment of colitis; loading with siRNA	Natural targeting: exploiting the intrinsic acid- and enzyme-resistant properties of plant vesicles to achieve colon-targeted delivery after oral administration; Safety: low immunogenicity, high biocompatibility, and absence of cytotoxicity; Therapeutic carrier–drug integration: the vesicles themselves exhibit intrinsic anti-inflammatory activity	(*84*)
	Smart stimulus-responsive nanocarriers	pH-responsive (targeting colonic pH), ROS-responsive (targeting the oxidative inflammatory microenvironment), and enzyme-responsive polymeric or liposomal encapsulation of triptolide and curcumin	Toxicity reduction and efficacy enhancement: drug release restricted to lesion sites (high ROS, specific pH), thereby markedly reducing the systemic toxicity of agents such as triptolide; Improved solubility and bioavailability of poorly soluble compounds (*e.g.*, curcumin)	(*73,76,77*)
	Colon-targeted microspheres/hydrogels	Chitosan-, pectin-, and alginate-based microspheres loaded with TCM formula extracts (*e.g.*, Baitouweng Decoction)	Prolonged retention: increased contact time and adhesion to the intestinal mucosa, enhanced local therapeutic effects, and reduced dosing frequency	(*74,83*)

drug delivery efficiency, bioavailability, and safety. Through chemical modification or biological coating of nanoparticles, characteristics can be conferred that respond to the intestinal environment (such as pH, ROS, and intestinal enzymes), further enabling targeted controlled release, maximizing the anti-inflammatory effect of TCM, and minimizing systemic exposure (*78*).

4.2. Multi-omics integration and network pharmacology

The integration of multi-omics and network pharmacology has provided a feasible path for systematically analyzing the "multi-component—multi-target—multi-pathway" mechanisms of TCM formulas (*72*). Multi-omics, based on high-throughput data, reveals the global coordination of TCM intervention on gene expression, metabolic networks, and gut microbiota ecology. Network pharmacology, through the construction of "drug—component—target—disease" association networks, identifies key active ingredients and core pathways, offering clear clues for experimental validation and translational research.

Several studies have demonstrated the value of this integrative approach: Wang *et al*. explored the mechanisms of Qing-Re-Hua-Shi Decoction (QRHSD) in treating UC, showing that QRHSD significantly modulates gut microbiota, increases beneficial Lactobacillus, inhibits pathogenic Morganella, and alters 507 metabolites, including bile acids and amino acid-related substances (*79*). Transcriptomic and network pharmacology analyses further revealed that QRHSD regulates gut homeostasis by downregulating key inflammatory signaling pathways such as PI3K/AKT, NF-κB, and MAPK. Additionally, correlation analysis demonstrated a close relationship between clinical indicators, microbiota changes, and metabolites, indicating that the formula restores gut homeostasis through a multi-layered mechanism. Another study used UPLC-QE-MS metabolomics and network pharmacology to analyze the mechanisms of Cynanchum wilfordii in treating UC, identifying 117 targets (such as JAK2, STAT3) and metabolic pathways related to inflammation through IL-17, HIF-1, and TNF signaling (*80*). Similarly, Wu *et al.* integrated metabolomics and network pharmacology to reveal the mechanism of Baicalin in experimental colitis, involving various metabolites and signaling pathways, including TNF, IL-6, and AKT1 (*81*). These studies have all employed the "multi-omics + network pharmacology" approach to systematically reveal the mechanisms of action of TCM formulas. They highlight the importance of multi-omics integration in uncovering the interactions between gut microbiota, metabolites, and signaling pathways, further deepening the understanding of TCM formulas' multi-target and multi-effect mechanisms.

Such studies underscore the core value of multi-omics integration in elucidating the interactions between gut microbiota, metabolites, and signaling pathways,

moving TCM mechanism research from "vague states" to "precise analysis." This provides scientific support for key ingredient selection, target validation, and new drug development, accelerating the modernization and clinical translation of TCM formulas.

5. Limitations

Several limitations of the current evidence base should be recognized. First, the currently available clinical evidence for classical TCM formulas in IBD is derived predominantly from ulcerative colitis rather than Crohn's disease, and many clinical studies are constrained by small sample sizes, single-center designs, geographically concentrated populations, and inadequate reporting of inclusion and exclusion criteria, thereby increasing the risk of selection bias and limiting the generalizability of the findings. Second, because IBD is a chronic relapsing disease, the relatively short follow-up period of many studies is insufficient to fully evaluate long-term efficacy, relapse prevention, and safety. Third, the compositional complexity and insufficient standardization of TCM formulas continue to hinder reproducibility and cross-study comparison. In addition, although TCM is characterized by multi-component and multi-target actions, many existing mechanistic studies remain focused on single pathways or targets, with limited validation of synergistic effects among different constituents. Furthermore, current animal models do not always align well with TCM syndrome differentiation, which may weaken the translational relevance of preclinical findings. Finally, the gut–brain axis, gut–lung axis, and nanodrug delivery systems discussed in this review should be regarded as promising but still emerging directions rather than clinically mature evidence. Future studies should emphasize better-designed multicenter trials, longer follow-up, improved standardization, and more integrative mechanistic validation.

6. Conclusion

IBD remains a major clinical challenge. Recent studies suggest that TCM is gradually moving from empirical use toward a more evidence-informed framework. Its core advantage lies in holistic and syndrome-oriented intervention strategies, which are inherently consistent with contemporary therapeutic goals, including mucosal healing, immune homeostasis, and microbial balance.

Mechanistic investigations have demonstrated that TCM does not merely exert general anti-inflammatory effects but regulates key pathological processes in IBD, including immune microenvironment remodeling, intestinal barrier repair, and microbiota–host metabolic interactions. These effects involve pathways such as NLRP3 inflammasome-mediated pyroptosis, macrophage polarization, Th17/Treg balance, and systemic regulatory axes such as the gut–lung and brain–gut axes. Meanwhile, emerging technologies, including nanomedicine-based delivery systems, multi-omics integration, and network pharmacology, are accelerating the modernization and mechanistic elucidation of TCM.

Future research should focus on precision-oriented and translational paradigms, integrating artificial intelligence, multi-omics data, and TCM syndrome classification to enable individualized therapy. Greater attention should also be given to long-term outcomes, safety evaluation, and integrative treatment strategies. Collectively, these efforts may establish TCM as a scientifically interpretable, mechanism-driven, and globally applicable therapeutic system for IBD.

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