Am J Transl Res 2026;18(5):4536-4546
www.ajtr.org /ISSN:1943-8141/AJTR0172013

Original Article

Kangfuxin liquid enema plus adalimumab for ulcerative colitis: a retrospective cohort study

Meimei Zhao, Tao Yu

Department of Spleen-Stomach Diseases I, Shaanxi Provincial Hospital of Traditional Chinese Medicine, Xi'an 710003, Shaanxi, China

Received February 10, 2026; Accepted March 27, 2026; Epub May 15, 2026; Published May 30, 2026

Abstract: Objectives: Ulcerative colitis (UC) is a chronic inflammatory bowel disease requiring effective treatment. This study aimed to evaluate the efficacy and safety of Kangfuxin liquid enema combined with adalimumab compared to adalimumab monotherapy in patients with UC. Methods: This retrospective cohort study included 240 UC patients treated between June 2022 and January 2024. Patients were divided into a combination therapy group (CT, adalimumab + Kangfuxin enema, n = 123) and a monotherapy group (MT, adalimumab alone, n = 117). We assessed clinical efficacy, adverse reactions, quality of life, serum inflammatory cytokines (interleukin-1 beta [IL-1β], interleukin-8 [IL-8], tumor necrosis factor-alpha [TNF-α]), endoscopic scores (Mayo, Baron), histologic score (Geboes), oxidative stress indicators (superoxide dismutase [SOD], malondialdehyde [MDA]), and intestinal barrier indicators (diamine oxidase [DAO], D-lactate) before and after 8 weeks of treatment. Results: Overall response rate observed in the CT cohort (88.62%) significantly exceeded that of the MT cohort (73.50%, P = 0.003). Mucosal healing rates were 56.10% vs. 32.48% (P < 0.001). Endoscopic remission rates were 65.04% vs. 47.01% (P = 0.005). Post-treatment inflammatory factor levels were decreased in the CT group (all P < 0.001). Oxidative stress and intestinal barrier markers also improved more in the CT group (all P < 0.001). Moreover, patient-reported quality of life (assessed by IBDQ-32) improved significantly more in the CT group (P < 0.001). Adverse reaction incidence (8.94% vs. 23.94%, P = 0.002) was decreased in the CT group. Conclusion: Combining Kangfuxin liquid enema and adalimumab was more effective and safer than adalimumab alone in the treatment of ulcerative colitis.

Keywords: Kangfuxin liquid, adalimumab, ulcerative colitis, combination therapy

Introduction

Ulcerative colitis (UC) is a chronic, relapsing inflammatory bowel disease. It primarily affects the colonic mucosa, causing symptoms such as persistent diarrhea, rectal bleeding, and abdominal pain. The disease course is often unpredictable, with alternating periods of remission and flare-up. This pattern imposes a substantial burden on patients' quality of life and poses a long-term risk for complications, including colorectal cancer [1-3].

UC pathogenesis involves complex interplay among genetic predisposition, environmental influences, gut microbiota, and a dysregulated immune response [4]. A key feature is excessive activation of the mucosal immune system. This leads to the overproduction of pro-inflammatory cytokines. Cytokines such as tumor necrosis factor-alpha (TNF-α), interleukin-1 beta (IL-1β), and interleukin-8 (IL-8) play central roles [5, 6]. They drive and sustain the inflammatory cascade, resulting in tissue damage and impaired intestinal barrier function [7].

Current management strategies aim to induce and maintain clinical remission. Biologic agents that target specific inflammatory pathways represent a major advancement [8, 9]. Adalimumab, a fully human monoclonal antibody, is one such therapy. It works by binding to and neutralizing TNF-α. This action effectively reduces inflammation and promotes mucosal healing in a significant proportion of patients with moderate-to-severe UC [10, 11]. However, clinical experience shows that not all patients achieve an adequate response to anti-TNF therapy [12]. Some experience a loss of response over time, and others face adverse effects. This highlights the need for therapeutic strategies that can improve outcome.

https://doi.org/10.62347/QHVY7929

In parallel, traditional Chinese medicine offers complementary approaches. Kangfuxin liquid, derived from Periplaneta americana extract, has been used for various gastrointestinal disorders [13]. Experimental and clinical studies suggest it possesses multiple beneficial properties. These include anti-inflammatory effects, the promotion of tissue regeneration and ulcer repair, and modulation of immune responses [14]. When administered as an enema, Kangfuxin liquid acts directly on the colonic mucosa. This localized delivery may enhance healing at the site of inflammation. This demonstrates the potential of traditional Chinese medicine in treating ulcerative colitis, a notion supported by a meta-analysis comparing a traditional Chinese herbal formula with routine antiulcer drugs [15]. Thus, integrating TCM into UC management may offer additional therapeutic benefit.

The theoretical rationale for combining these two modalities is strong. Adalimumab provides systemic, targeted suppression of a key inflammatory cytokine [16]. Kangfuxin liquid enema may offer local mucosal protection, repair, and additional immunomodulation [17]. Their mechanisms of action are distinct yet potentially synergistic. A combined regimen could therefore address multiple aspects of UC pathophysiology more comprehensively than either agent alone. This approach aligns with the growing interest in integrative treatment models for complex chronic diseases.

Despite the promising rationale, high-quality clinical evidence, particularly from comparative studies with adequate sample sizes, is still scarce. Existing reports on Kangfuxin enema are often limited to small case series or focus on combination with aminosalicylates, leaving its specific additive value when combined with biologics like adalimumab largely unexplored. Therefore, this study aimed to assess clinical effectiveness and safety of Kangfuxin liquid enema combined with adalimumab, compared to adalimumab monotherapy, in patients with ulcerative colitis.

Patients and methods

Research design and cohort selection

This study was carried out strictly adhering to the Declaration of Helsinki and received approval from the Ethics Committee of Shaanxi Provincial Hospital of Traditional Chinese Medicine. All research data were sourced from medical information systems. This study is a retrospective cohort study. Given that this study only utilized existing, de-identified medical records without direct patient contact and posed no additional risks or burdens to patients, the Shaanxi Provincial Hospital of Traditional Chinese Medicine Ethics Committee approved a waiver of the informed consent requirement.

The study population consisted of 240 patients diagnosed with ulcerative colitis and treated at Shaanxi Provincial Hospital of Traditional Chinese Medicine between June 2022 and January 2024. Patients diagnosed with ulcerative colitis according to the diagnostic criteria listed in Diseases of the Colon (Key Points) with complete clinical data required for treatment and age between 18 and 75 years were included. Patients experiencing allergic reactions of any degree post-medication, individuals with cognitive impairment hindering study cooperation, those with severe liver or kidney dysfunction, immune disorders, or other severe digestive system ailments, and patients presenting severe organic lesions, malignant tumors, or malignant diseases were excluded.

Treatments

Based on the actual treatment regimens received during the treatment period, patients were retrospectively divided into a combination therapy group (adalimumab combined with Kangfuxin liquid enema, n = 123) or a monotherapy group (adalimumab alone, n = 117).

The MT group received adalimumab alone (manufactured by Shanghai Henlius Biopharmaceuticals Co., Ltd., approval number: S20-200026) by subcutaneous injection. The induction regimen was 160 mg at week 0, 80 mg at week 2, followed by a maintenance regimen of 40 mg every other week. The CT group received the same adalimumab regimen as the MT group, plus Kangfuxin liquid enema. Kangfuxin liquid enema (manufactured by Sichuan Haoyisheng Panxi Pharmaceutical Co., Ltd., approval number: Z51021834) was administered once daily by rectal infusion. Prior to rectal infusion, 50 mL of Kangfuxin liquid enema was diluted with 150 mL of 0.9% sodium chlo-

ride solution and heated to 37°C. The infusion was retained in the intestines for at least 30 minutes. Both groups were observed for treatment effects after 8 weeks of therapy. Clinical and assessment data before and after treatment were collected from the patients.

Data collection and outcome measures

Baseline characteristics: Demographic and clinical data including age, gender, disease extent (Montreal classification: E1/E2/E3), disease duration, smoking/alcohol history, past operation history, and prior medication history (aminosalicylates, corticosteroids, immunomodulators) were collected. Patients were classified according to the Montreal Classification, which proposes three subtypes of ulcerative colitis: E1, E2, and E3. E1 refers to ulcerative proctitis, with lesions limited to the rectum and inflammation not extending beyond the rectosigmoid junction. E2 represents left-sided ulcerative colitis (distal UC), with lesions extending beyond the rectosigmoid junction but not reaching the splenic flexure. E3 indicates extensive ulcerative colitis (pancolitis), with lesions extending up to the splenic flexure or involving the entire colon.

Clinical efficacy: Assessed according to a composite criterion integrating symptom improvement and biomarker normalization, and categorized into three levels: Markedly effective: After treatment completion, IL-1, IL-8, TNF-α levels return to normal, mucous bloody stools, diarrhea, and other symptoms completely disappear; Effective: After treatment completion, IL-1, IL-8, TNF-α levels gradually approach normal, mucous bloody stools, diarrhea, and other symptoms significantly improve, and the disease does not worsen; Ineffective: After treatment completion, IL-1, IL-8, TNF-α levels do not change significantly; mucus containing or bloody stools, diarrhea, and other symptoms persist, and the condition gradually worsens. The overall response rate of treatment = (Markedly Effective + Effective) cases/Total cases × 100%.

Endoscopic and histological scoring systems: Mayo score: The Mayo scoring system was utilized, comprising four components, each rated on a scale from 0 to 3. For Stool Frequency, a score of 0 indicates normal frequency, while a score of 3 indicates more than five times daily above baseline. Rectal Bleeding is scored as 0 for no bleeding and 3 for the passage of pure blood. Endoscopic Findings are graded from 0 for normal mucosa to 3 for severe inflammation with spontaneous bleeding. Physician's Global Assessment ranges from 0 for normal conditions to 3 for severe disease activity. The cumulative score ranges from 0 to 12. Mucosal healing was defined as an endoscopic subscore of 0 or 1 on the Mayo scale. Endoscopic remission was identified by a Mayo endoscopic subscore of 0.

Baron endoscopic score: Mucosal appearance was graded during colonoscopy as: 0 = normal mucosa; 1 = mild inflammation (erythema, decreased vascular pattern); 2 = moderate inflammation (marked erythema, absent vascular pattern, friability, no erosions); 3 = severe inflammation (spontaneous bleeding, ulceration).

Geboes histological score: For histologic remission assessment, colonic biopsy samples obtained during endoscopy were evaluated by two experienced pathologists blinded to the clinical data. The Geboes scoring system was used, which grades architectural changes, chronic inflammatory infiltrate, lamina propria neutrophils and eosinophils, neutrophils in the epithelium, crypt destruction, and erosions/ulcerations. A score of < 3.0 was defined as histologic remission.

Laboratory and biomarker assays: Fasting peripheral blood samples were collected in the morning at baseline and after 8 weeks of treatment. Serum was separated by centrifugation (3,000 rpm for 15 min) and stored at -80°C until batch analysis.

Inflammatory cytokines: Serum levels of Interleukin-1 beta (IL-1β), Interleukin-8 (IL-8), and Tumor Necrosis Factor-alpha (TNF-α) were quantified using specific commercial sandwich Enzyme-Linked Immunosorbent Assay (ELISA) kits (Human IL-1β/IL-8/TNF-α Quantikine ELISA Kit, R&D Systems, USA). Absorbance was read on a microplate reader (Multiskan GO, Thermo Fisher Scientific, USA).

Oxidative stress markers: Serum Superoxide Dismutase (SOD) activity was measured using the WST-8 method with a commercial kit (SOD Assay Kit-WST, Dojindo Laboratories, Japan).

Serum Malondialdehyde (MDA) concentration, reflecting lipid peroxidation, was determined by the thiobarbituric acid reactive substances (TBARS) assay using a commercial kit (MDA Assay Kit, Nanjing Jiancheng Bioengineering Institute, China). Absorbance was measured on a spectrophotometer (UV-1800, Shimadzu Corporation, Japan).

Intestinal barrier function markers: Serum Diamine Oxidase (DAO) activity was measured using a spectrophotometric method based on the oxidation of cadaverine (DAO Activity Assay Kit, Cloud-Clone Corp., China). Serum D-lactate concentration was determined with a specific enzymatic colorimetric assay kit (D-Lactate Colorimetric Assay Kit, Sigma-Aldrich, St. Louis, USA). Analyses were performed on a fully automated biochemical analyzer (AU5800, Beckman Coulter, USA).

Adverse reactions: Adverse reactions, including nausea, constipation, and dizziness, were evaluated with the total incidence rate calculated as follows: (number of cases with nausea + constipation + dizziness)/total cases × 100%.

Quality of life assessment: To comprehensively assess treatment effects, patient quality of life was evaluated using Chinese version of the Inflammatory Bowel Disease Questionnaire-32 (IBDQ-32) [18]. The scale comprises 32 items across four areas: bowel symptoms (10 questions), systemic symptoms (5 questions), emotional function (12 questions), and social function (5 questions). Responses are recorded on a 7-point Likert scale for each item. The cumulative score can range from 32 to 224, with higher scores indicative of a better quality of life.

Statistical analysis

Data were processed using SPSS 25.0 (IBM Corp., Armonk, NY, USA). Normally distributed continuous data were presented as mean ± standard deviation (SD), and independent sample t-tests were utilized for comparisons between groups. Counted data were reported as frequencies (n) and percentages (%), with comparisons conducted using the chi-square test. A two-tailed *P* value of less than 0.05 was considered significant.

Results

Baseline characteristics

The CT group comprised 123 patients, with 77 males and 46 females, and an average age of 42.73±9.04 years. Disease extent according to the Montreal classification was as follows: E1 in 85 patients (69.11%), E2 in 30 patients (24.39%), and E3 in 8 patients (6.50%). The MT group comprised 117 patients, with 71 males and 46 females, and an average age of 41.82±8.61 years. Disease extent distribution was: E1 in 78 patients (66.67%), E2 in 31 patients (26.50%), and E3 in 8 patients (6.83%). No notable variations were found between the two groups regarding age, gender, disease extent, smoking history, alcohol use, operation history, disease duration, or prior medication history (P > 0.05) (**Table 1**).

Clinical efficacy comparison

Overall response rate in the CT group (88.62%) significantly exceeded that of the MT group (73.50%) (P = 0.003). In the CT group, treatment in 54.47% of patients was considered markedly effective and in 34.15% it was considered effective, whereas in the MT group, the corresponding proportions were 38.46% and 35.04%, respectively (**Table 2**).

Mucosal and histologic results comparison

Mucosal healing (Mayo endoscopic subscore 0 or 1) was attained by 56.10% of CT group, whereas it was reached by 32.48% in MT group (P < 0.001). Endoscopic remission (Mayo endoscopic subscore 0) was observed in 65.04% of CT group patients versus 47.01% in the MT group (P = 0.005). Histologic remission (Geboes score < 3.0) was also significantly higher in the CT group (53.66%) than in the MT group (38.46%) (P = 0.018) (**Table 3**).

Mayo score components comparison

Before treatment, there were no significant differences in any Mayo score components between the two groups (P > 0.05). After treatment, all components - stool frequency, rectal bleeding, endoscopic findings, and physician's global assessment - demonstrated markedly better improvement in the CT group relative to the MT group (P < 0.001 for all) (**Table 4**).

Table 1. Comparison of baseline data between the CT group and the MT group

Factor	MT group (n = 117)	CT group (n = 123)	t/χ^2	P
Gender, n (%)			0.093	0.760
Female	46 (39.32%)	46 (37.40%)		
Male	71 (60.68%)	77 (62.60%)		
Age	41.82±8.61	42.73±9.04	0.796	0.427
Disease extent (Montreal), n (%)			0.167	0.920
E1	78 (66.67%)	85 (69.11%)		
E2	31 (26.50%)	30 (24.39%)		
E3	8 (6.83%)	8 (6.50%)		
Smoking history, n (%)	43 (36.75%)	50 (40.65%)	0.384	0.536
Alcohol use, n (%)	62 (52.99%)	60 (48.78%)	0.425	0.514
Operation history, n (%)	32 (27.35%)	41 (33.33%)	1.014	0.314
Disease duration (years)	5.32±1.89	5.15±1.76	0.745	0.457
Medication history, n (%)				
Aminosalicylic acid	35 (29.91%)	40 (32.52%)	0.190	0.663
Corticosteroids	25 (21.37%)	30 (24.39%)	0.310	0.578
Immunomodulators	15 (12.82%)	14 (11.38%)	0.117	0.733

Table 2. Comparison of clinical efficacy between the MT group and the CT group after treatment

Effect Outcome	MT group (n = 117)	CT group (n = 123)	t/χ^2	P
Markedly effective, n (%)	45 (38.46%)	67 (54.47%)		
Effective, n (%)	41 (35.04%)	42 (34.15%)		
Ineffective, n (%)	31 (26.50%)	14 (11.38%)		
Overall response rate, n (%)	86 (73.50%)	109 (88.62%)	8.991	0.003

Table 3. Comparison of mucosal and histologic results between the MT group and the CT group after treatment

Factor	MT group (n = 117)	CT group (n = 123)	t/χ^2	P
Mucosal healing, n (%)	38 (32.48%)	69 (56.10%)	13.539	< 0.001
Endoscopic remission, n (%)	55 (47.01%)	80 (65.04%)	7.923	0.005
Histologic remission, n (%)	45 (38.46%)	66 (53.66%)	5.571	0.018

Table 4. Comparison of Mayo scores between the MT group and CT group after treatment

Factor	Time	MT group (n = 117)	CT group (n = 123)	t	P
Stool frequency	Pre-treatment	2.40±0.40	2.44±0.41	0.302	0.763
	Post-treatment	1.52±0.35	1.32±0.31	4.560	< 0.001
Rectal bleeding	Pre-treatment	2.34±0.42	2.41±0.48	1.180	0.239
	Post-treatment	1.12±0.31	0.95±0.26	4.539	< 0.001
Endoscopic findings	Pre-treatment	2.36±0.38	2.37±0.37	0.049	0.961
	Post-treatment	1.65±0.34	1.42±0.36	4.878	< 0.001
Physician's global assessment	Pre-treatment	2.36±0.38	2.39±0.37	0.470	0.639
	Post-treatment	1.74±0.35	1.57±0.31	3.966	< 0.001

Baron endoscopic scores comparison

The Baron endoscopic score did not differ significantly between groups at baseline (P = 0.171). After treatment, the CT group exhibited a significantly lower score (0.86±0.28) compared to the MT group (1.37±0.32) (P < 0.001) (**Figure 1**).

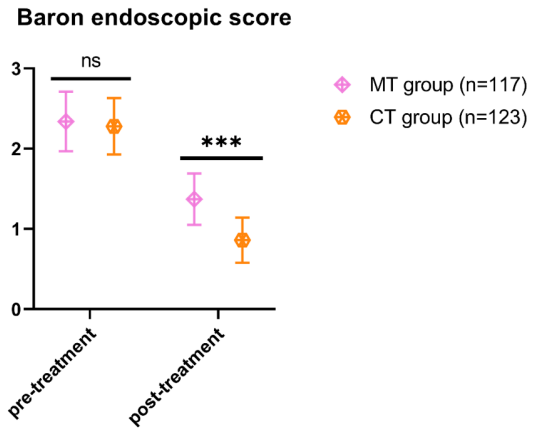

Figure 1. Comparison of Baron endoscopic score between MT group and CT group after treatment. ns, no statistically significant difference; ***, P < 0.001.

Inflammatory factor level comparison

Prior to treatment, inflammatory factor levels of IL-1β, IL-8, and TNF-α did not differ notably between the CT group and MT group (P > 0.05). After treatment, all three inflammatory factor levels in the CT group were markedly reduced compared to those in the MT group (P < 0.001) (**Table 5**).

Oxidative stress markers comparison

Baseline levels of SOD and MDA were similar between groups (P > 0.05). After treatment, SOD activity was markedly elevated and MDA concentration was lower in the CT group than the MT group (P < 0.001) (**Figure 2**).

Intestinal barrier function marker comparison

No notable variations were found in DAO activity or D-lactate concentration at baseline (P > 0.05) (**Table 6**). Post-treatment, both markers were reduced in the CT group compared to the MT group (P < 0.001).

Adverse reaction incidence rate comparison

Overall incidence of adverse reactions was notably reduced in the CT group (8.94%) than in the MT group (23.94%) (P = 0.002). Individual adverse events (nausea, constipation, dizziness) also showed lower frequencies in the CT group (**Table 7**).

Patients' quality of life comparison

No statistically significant differences were observed in the IBDQ-32 total score or any subscores between the two groups at baseline (P > 0.05 for all). After treatment, the CT group achieved significantly higher scores compared to the MT group across all measures (P < 0.001 for all) (**Table 8**).

Discussion

The findings of this retrospective analysis indicated that the combination of Kangfuxin liquid enema with adalimumab offers a more favorable therapeutic profile for patients with ulcerative colitis compared to adalimumab monotherapy. This integrated approach was associated with superior clinical outcomes across multiple dimensions, including symptom control, endoscopic and histological remission, modulation of systemic inflammation and immune markers, improvement in oxidative stress and intestinal barrier integrity, and a more favorable safety profile.

Firstly, the combination therapy led to a higher overall clinical response rate. A larger percentage of patients in combination group attained both marked and effective outcomes based on composite criteria integrating symptomatic relief and biomarker improvement. This enhanced clinical efficacy suggests a synergistic interaction between the two treatments. Adalimumab exerts its effect by systemically neutralizing TNF-α, a pivotal cytokine in the inflammatory cascade of UC [19]. Kangfuxin liquid, when administered locally by enema, may provide complementary benefits directly at the mucosal level. Its documented properties in promoting tissue regeneration, epithelial repair, and local immunomodulation likely contribute to faster and more complete symptom resolution, explaining the observed clinical advantage over monotherapy [20, 21]. This aligns with previous studies suggesting that adjunctive local therapies can improve symptom scores in distal colitis [22].

Secondly, objective assessments of mucosal health strongly favored the combination regimen. Rates of mucosal healing, endoscopic remission, and histologic remission were all higher in the combination group. Endoscopic scores, including both the Mayo endoscopic subscore and the Baron score, showed greater improvement. This indicates that the combination therapy is more effective in reversing the visible and microscopic signs of intestinal

Table 5. Comparison of inflammatory factor levels in the MT group and the CT group

Factor	Time	MT group (n = 117)	CT group (n = 123)	t	P
IL-1β (pg/mL)	Pre-treatment	24.35±4.85	24.21±4.95	0.222	0.824
	Post-treatment	10.24±2.38	6.67±2.42	11.515	< 0.001
IL-8 (pg/mL)	Pre-treatment	282.21±28.23	281.95±28.12	0.073	0.942
	Post-treatment	192.61±18.14	160.55±16.73	14.245	< 0.001
TNF-α (pg/mL)	Pre-treatment	66.08±6.61	65.64±6.56	0.523	0.602
	Post-treatment	30.60±6.12	18.56±3.77	18.245	< 0.001

IL-1β: Interleukin-1 beta; IL-8: Interleukin-8; TNF-α: Tumor Necrosis Factor-alpha.

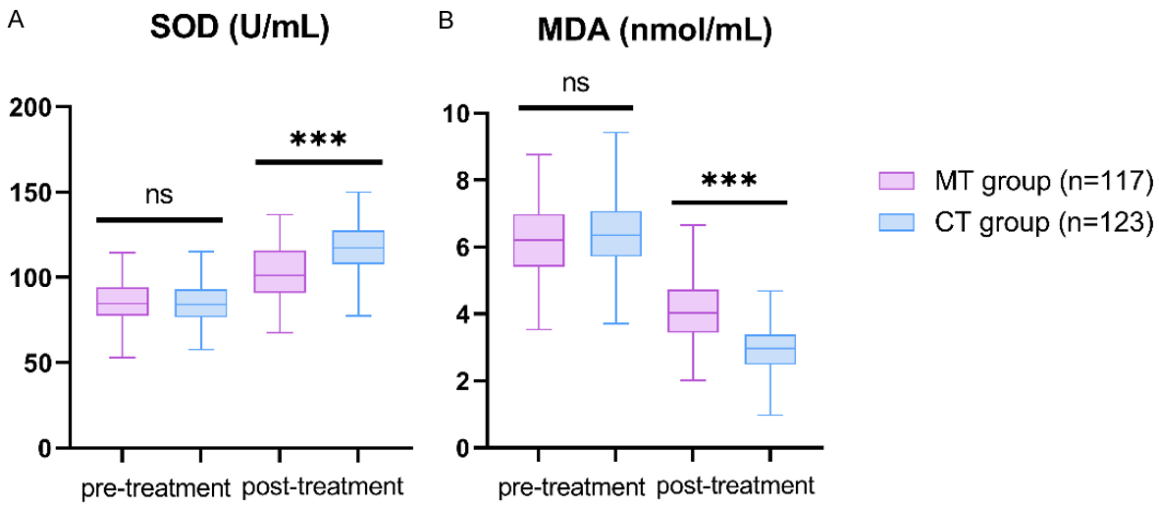

Figure 2. Comparison of oxidative stress indicators levels between MT group and CT group. A: SOD (U/mL); B: MDA (nmol/mL); SOD: Superoxide Dismutase; MDA: Malondialdehyde. ns, no statistically significant difference; ***, P < 0.001.

Table 6. Comparison of intestinal barrier function between the MT group and CT group

Factor	Time	MT group (n = 117)	CT group (n = 123)	t	P
DAO (IU/mL)	Pre-treatment	15.28±3.05	15.47±3.11	0.461	0.645
	Post-treatment	10.52±2.31	7.83±2.04	9.555	< 0.001
D-lactate (μmol/L)	Pre-treatment	18.45±3.61	18.67±3.74	0.471	0.638
	Post-treatment	12.76±2.65	9.53±2.54	9.634	< 0.001

DAO: Diamine oxidase.

Table 7. Comparison of the incidence rate of adverse reactions in the MT group and the CT group

Factor	MT group (n = 117)	CT group (n = 123)	t/χ^2	P
Overall, n (%)	28 (23.94%)	11 (8.94%)	9.898	0.002
Nausea, n (%)	8 (6.84%)	4 (3.25%)		
Constipation, n (%)	8 (6.84%)	2 (1.63%)		
Dizziness, n (%)	12 (10.26%)	5 (4.06%)		

inflammation. The rectal administration route used for Kangfuxin liquid in this study is a well-established method for delivering herbal therapies directly to the colonic mucosa. A systematic review of Da-Cheng-Qi decoction, another traditional Chinese herbal formula, demonstrated that rectal administration significantly improved clinical outcomes in patients with

Table 8. Comparison of IBDQ-32 scores between the MT group and the CT group

Factor	Time	MT group (n = 117)	CT group (n = 123)	t	P
IBDQ total score	Pre-treatment	128.47±21.36	127.82±20.18	0.240	0.810
	Post-treatment	160.75±19.04	175.63±17.25	6.347	< 0.001
Bowel symptoms subscore	Pre-treatment	31.25±7.12	30.88±6.94	0.408	0.684
	Post-treatment	45.16±6.33	52.47±5.87	9.285	< 0.001
Systemic symptoms subscore	Pre-treatment	16.84±4.52	16.57±4.31	0.482	0.630
	post-treatment	25.93±2.96	29.24±2.11	9.922	< 0.001
Emotional function subscore	Pre-treatment	54.12±10.88	53.76±10.24	0.262	0.793
	Post-treatment	68.41±5.07	72.15±5.16	5.670	< 0.001
Social function subscore	Pre-treatment	27.26±3.23	27.05±3.12	0.515	0.607
	Post-treatment	31.22±1.08	32.52±1.14	9.034	< 0.001

IBDQ-32: Inflammatory Bowel Disease Questionnaire-32.

intestinal obstruction, with a pooled risk ratio of 1.32 (95% CI 1.24 to 1.39) compared to conservative therapy alone [23]. This supports the rationale that locally delivered herbal therapies can exert direct therapeutic effects on the intestinal mucosa. The pathogenesis of UC involves sustained mucosal injury [24]. While adalimumab effectively suppresses the driving inflammatory signal [25], Kangfuxin's active components, such as polypeptides and mucopolysaccharides, are known to stimulate epithelial cell proliferation and granulation tissue formation. The direct topical application of Kangfuxin likely accelerates the repair of the damaged epithelial lining, facilitating the structural normalization observed as mucosal and histologic healing [26, 27]. This finding is consistent with research demonstrating the wound-healing and mucosa-protective effects of Kangfuxin in other gastrointestinal ulcer models [28].

Thirdly, combination therapy led to a more substantial reduction in systemic inflammatory burden. Post-treatment serum levels of key pro-inflammatory cytokines, namely IL-1β, IL-8, and TNF-α, were reduced in the combination group compared to the monotherapy group. This suggests that the local anti-inflammatory and immunomodulatory actions of Kangfuxin enema contribute to a broader systemic dampening of inflammation [29]. Chronic inflammation in UC is fueled by a network of cytokines. Adalimumab targets TNF-α specifically, but other pathways may remain active [30]. Kangfuxin has been shown in experimental studies to inhibit pathways like NF-κB, which regulates the expression of multiple cytokines, including IL-1β and IL-8 [31]. Therefore, the combination may disrupt the inflammatory network at more than one node, leading to a more comprehensive suppression of cytokine production, as reflected by the biomarker levels.

Furthermore, the combination therapy demonstrated a positive impact on oxidative stress markers and markers of intestinal barrier function. The activity of the antioxidant enzyme SOD was higher, while the level of the lipid peroxidation product MDA was lower in the combination group. Oxidative stress is a critical mediator of tissue damage in UC. The improvement in these markers suggests that the combination regimen better ameliorates the redox imbalance in the intestinal environment. This may be attributed to the known antioxidant properties of Kangfuxin liquid, which may complement the anti-inflammatory action of adalimumab to reduce overall oxidative insult [25, 32]. Concurrently, serum levels of DAO and D-lactate, which inversely correlate with intestinal mucosal integrity, were lower in the combination group. This indicates better preservation or restoration of the intestinal epithelial barrier. A leaky gut barrier allows bacterial translocation and perpetuates inflammation. By promoting mucosal healing and reducing inflammation, the combination therapy appears more effective in restoring this critical physical and functional barrier, which is a key therapeutic goal in UC management [33, 34].

An important practical finding is the lower overall occurrence of adverse reactions in combination group. This suggests that integrative approach may not only be more efficacious but

also well-tolerated. The localized action of Kangfuxin enema may allow for a synergistic therapeutic effect without amplifying systemic side effects commonly associated with biologic therapies. Alternatively, by potentially enhancing mucosal healing and reducing overall disease activity, the combination might mitigate some gastrointestinal discomfort. This improved safety profile is a significant consideration for long-term treatment strategies in a chronic condition like UC [16, 35, 36].

Finally, this combination therapy led to a superior improvement in patient-reported quality of life. The significant and consistent gains across all domains of the IBDQ-32 in the combination group - ranging from core bowel symptoms to emotional and social function - provide direct evidence that the clinical and endoscopic benefits translate into meaningful gains from the patient's perspective. This holistic improvement underscores the value of an integrative approach that not only targets mucosal healing but also addresses the broader well-being of patients living with a chronic disease like UC. The correlation between enhanced objective outcomes (mucosal healing, reduced inflammation) and superior subjective quality of life further strengthens the rationale for this combined regimen.

The observed benefits of this combination find support in the growing body of literature on integrative gastroenterology. While adalimumab is a cornerstone biologic therapy with well-established efficacy, research continues to seek strategies to improve response rates and durability [37]. Studies on other locally acting agents, like mesalamine enema, combined with systemic biologics have shown promise. Our findings extend this concept to a traditional herbal extract with documented reparative properties. The mechanisms - systemic cytokine blockade paired with local mucosal protection, repair, and broad-spectrum immunomodulation - provide a plausible framework for the superior outcomes [38].

Limitations

Several limitations are acknowledged in this study. The retrospective design introduced inherent risks of selection bias and unmeasured confounders, despite balanced baseline characteristics. The sample size, while larger than many preliminary reports, may still limit the generalizability of the findings. The single-center nature of the study means the results may have been influenced by local patient demographics and treatment protocols. The follow-up period was focused on short-term outcomes at 8 weeks; therefore, the long-term durability of the combined effect on clinical remission, quality of life, maintenance of remission, and impact on hospitalization or surgery rates requires investigation. Additionally, the specific immunological and molecular mechanisms underlying the observed synergy were not explored in depth and warrant further basic research.

Future prospective, randomized controlled trials with larger, multi-center cohorts and longer follow-up durations are essential to confirm these findings and evaluate the sustained benefits. Such studies should employ standardized outcome measures and consider exploring predictive biomarkers to identify patients most likely to benefit from this combination strategy. Investigations into the optimal dosing and duration of the Kangfuxin enema component within the combined regimen would also be valuable for clinical practice.

Conclusion

A combination of Kangfuxin liquid enema and adalimumab demonstrated a more comprehensive therapeutic effect in ulcerative colitis than adalimumab alone. This regimen was associated with enhanced clinical and endoscopic remission, greater suppression of systemic inflammation, improved oxidative stress and gut barrier markers, and a reduced burden of adverse events. These results support the potential of this integrative treatment model as a strategy for managing ulcerative colitis, meriting further rigorous clinical evaluation.

Acknowledgements

This study was supported by the Shaanxi Provincial Administration of Traditional Chinese Medicine (No. SXZYLP-2024005).

Disclosure of conflict of interest

None.

Address correspondence to: Tao Yu, Department of Spleen-Stomach Diseases I, Shaanxi Provincial

Hospital of Traditional Chinese Medicine, No. 4 Xihuamen, Lianhu District, Xi'an 710003, Shaanxi, China. E-mail: yutao202602@126.com

References

[1] Rubin DT, Ananthakrishnan AN, Siegel CA, Barnes EL and Long MD. ACG Clinical Guideline Update: ulcerative colitis in adults. Am J Gastroenterol 2025; 120: 1187-1224.

[2] Spence S and Zaghiyan K. Ulcerative colitis. Surg Clin North Am 2026; 106: 121-132.

[3] Voelker R. What is ulcerative colitis? JAMA 2024; 331: 716.

[4] Shimomori Y, Yokoyama Y, Kurumi H, Akita K, Kazama T, Hayashi Y, Mizukami K and Nakase H. Unraveling the complexity of ulcerative colitis: insights into cytokine dysregulation and targeted therapies. EXCLI J 2025; 24: 638-658.

[5] Kurumi H, Yokoyama Y, Hirano T, Akita K, Hayashi Y, Kazama T, Isomoto H and Nakase H. Cytokine profile in predicting the effectiveness of advanced therapy for ulcerative colitis: a narrative review. Biomedicines 2024; 12: 952.

[6] Świrkosz G, Szczygieł A, Logoń K, Wrześniewska M and Gomułka K. The role of the microbiome in the pathogenesis and treatment of ulcerative colitis-a literature review. Biomedicines 2023; 11: 3144.

[7] Marsool MDM, Vora N, Marsool ADM, Pati S, Narreddy M, Patel P, Gadam S and Prajjwal P. Ulcerative colitis: addressing the manifestations, the role of fecal microbiota transplantation as a novel treatment option and other therapeutic updates. Dis Mon 2023; 69: 101606.

[8] Ananthakrishnan AN, Murad MH, Scott FI, Agrawal M, Haydek JP, Limketkai BN, Loftus EV Jr and Singh S. Comparative efficacy of advanced therapies for management of moderate-to-severe ulcerative colitis: 2024 American Gastroenterological Association Evidence Synthesis. Gastroenterology 2024; 167: 1460-1482.

[9] Guo M and Wang X. Pathological mechanism and targeted drugs of ulcerative colitis: a review. Medicine (Baltimore) 2023; 102: e35020.

[10] Awan H, Fatima U, Eaw R, Knox N and Alrubaiy L. The efficacy of currently licensed biologics for treatment of ulcerative colitis: a literature review. Cureus 2023; 15: e37609.

[11] Kim SY, Shin SY, Saeed M, Ryu JE, Kim JS, Ahn J, Jung Y, Moon JM, Choi CH and Choi HK. Prediction of clinical remission with adalimumab therapy in patients with ulcerative colitis by fourier transform-infrared spectroscopy coupled with machine learning algorithms. Metabolites 2023; 14: 2.

[12] Tanida S, Ozeki K, Katano T, Tanaka M, Shimura T, Kubota E, Kataoka H, Takahama T, Sasoh S, Kubota Y, Ban T, Ando T, Nakamura M and Joh T. Induction therapy with a combination of weekly adalimumab plus intensive granulocyte and monocyte adsorptive apheresis in patients with ulcerative colitis and failure of conventional agents, biologics and janus kinase inhibitor. J Clin Med Res 2023; 15: 181-186.

[13] Wang T, Liu X, Zhang W, Wang J, Wang T, Yue W, Ming L, Cheng J and Sun J. Traditional Chinese medicine treats ulcerative colitis by regulating gut microbiota, signaling pathway and cytokine: future novel method option for pharmacotherapy. Heliyon 2024; 10: e27530.

[14] Tang M, Ni LL, Xu JL, Wang YJ, Zhang CG, Ali T, Wu XM, Liu H and He M. Kangfuxin liquid ameliorates dextran sulfate sodium (dss)-induced acute ulcerative colitis in mice by modulating immune response and suppressing inflammation. Med Sci Monit Basic Res 2021; 27: e930887.

[15] Yang B, Xu ZQ, Zhang H, Xu FY, Shi XY, Zou Z, Ling CQ and Tang L. The efficacy of Yunnan Baiyao on haemostasis and antiulcer: a systematic review and meta-analysis of randomized controlled trials. Int J Clin Exp Med 2014; 7: 461-482.

[16] Azadbakht S, Seighali M, Azadbakht S and Azadbakht M. Effectiveness of adalimumab in severe ulcerative colitis: a systematic review and a meta-analysis. Health Sci Rep 2024; 7: e2210.

[17] He M, Yu WX, Shen Y, Zhang JN, Ni LL, Li Y, Liu H, Zhao Y, Zhao HR and Zhang CG. Kangfuxin alleviates ulcerative colitis in rats by inhibiting NF-κB p65 activation and regulating T lymphocyte subsets. Iran J Basic Med Sci 2023; 26: 882-890.

[18] Zhang JJ, Lou DN, Ma H, Yu CH, Chen LH and Li YM. Development of a validated Chinese version of the inflammatory bowel disease disability index. J Dig Dis 2020; 21: 52-58.

[19] Salman A, Salman MA, Elewa A and Awwad AM. Efficacy and safety of infliximab versus adalimumab in adult subjects with moderate to severe ulcerative colitis: a systematic review and meta-analysis. Cureus 2024; 16: e61547.

[20] Zhao S, Zhang J, Qiu M, Hou Y, Li X, Zhong G, Gou K, Li J, Zhang C, Qu Y and Wang X. Mucoadhesive and thermosensitive Bletilla striata polysaccharide/chitosan hydrogel loaded nanoparticles for rectal drug delivery in ulcerative colitis. Int J Biol Macromol 2024; 254: 127761.

[21] Xue P, Wang L, Xu J, Liu J, Pan X, Zhao Y and Xu H. Temperature-sensitive hydrogel for rectal perfusion improved the therapeutic effect of Kangfuxin liquid on DSS-induced ulcerative colitis mice: the inflammation alleviation and the colonic mucosal barriers repair. Int J Pharm 2020; 589: 119846.
[22] Ge C, Shen Z, Lu Y, Liu X, Tong Y, Zhang M, Liu Y, Shen H and Zhu L. Propensity score analysis the clinical characteristics of active distal and extensive ulcerative colitis: a retrospective study. Front Physiol 2023; 14: 1136659.
[23] Yang B, Xu FY, Sun HJ, Zou Z, Shi XY, Ling CQ and Tang L. Da-cheng-qi decoction, a traditional Chinese herbal formula, for intestinal obstruction: systematic review and meta-analysis. Afr J Tradit Complement Altern Med 2014; 11: 101-119.
[24] Neurath MF and Travis SP. Mucosal healing in inflammatory bowel diseases: a systematic review. Gut 2012; 61: 1619-1635.
[25] Barreiro-de Acosta M, Lorenzo A and Dominguez-Muñoz JE. Adalimumab in ulcerative colitis: two cases of mucosal healing and clinical response at two years. World J Gastroenterol 2009; 15: 3814-3816.
[26] Li HB, Chen MY, Qiu ZW, Cai QQ, Li DT, Tang HM and Chen XL. Efficacy and safety of Kangfuxin liquid combined with aminosalicylic acid for the treatment of ulcerative colitis: a systematic review and meta-analysis. Medicine (Baltimore) 2018; 97: e10807.
[27] Lu S, Wu D, Sun G, Geng F, Shen Y, Tan J, Sun X and Luo Y. Gastroprotective effects of Kangfuxin against water-immersion and restraint stress-induced gastric ulcer in rats: roles of antioxidation, anti-inflammation, and pro-survival. Pharm Biol 2019; 57: 770-777.
[28] Tian M, Dong J, Wang Z, Lu S and Geng F. The effects and mechanism of Kangfuxin on improving healing quality and preventing recurrence of gastric ulcer. Biomed Pharmacother 2021; 138: 111513.
[29] Xie F, Zhang Y and Wang T. Effects of mesalazine suppository combined with Kangfuxin solution retention enema on inflammatory markers and adverse reactions in patients with active ulcerative colitis. Minerva Gastroenterol (Torino) 2024; [Epub ahead of print].
[30] Panés J, Colombel JF, D'Haens GR, Schreiber S, Panaccione R, Peyrin-Biroulet L, Loftus EV Jr, Danese S, Tanida S, Okuyama Y, Louis E, Armuzzi A, Ferrante M, Vogelsang H, Hibi T, Watanabe M, Lefebvre J, Finney-Hayward T, Sanchez Gonzalez Y, Doan TT, Mostafa NM, Ikeda K, Xie W, Huang B, Petersson J, Kalabic J, Robinson AM and Sandborn WJ. Higher vs standard adalimumab induction and maintenance dosing regimens for treatment of ulcerative colitis: SERENE UC trial results. Gastroenterology 2022; 162: 1891-1910.
[31] Shen L, Chen X and Zhang T. Assessment of the anti-inflammatory efficacy and symptom resolution time of kangfuxin liquid combined with metronidazole in recurrent oral ulcers. J Inflamm Res 2025; 18: 11925-11934.
[32] Zhang C, Hu Y, Yuan Y, Guo J, Li H, Li Q and Liu S. Liposome-embedded SOD attenuated DSS-induced ulcerative colitis in mice by ameliorating oxidative stress and intestinal barrier dysfunction. Food Funct 2023; 14: 4392-4405.
[33] Zhang Y, Jia D, Wu Y and Xu Y. Antipyretic and anti-inflammatory effects of inosine, an active component of Kangfuxin. Immunobiology 2024; 229: 152812.
[34] Sun YX, Yang GY, Karamacoska D, Wang X, Li YX, Hou WB, Zheng YY, Liu JP and Liu ZL. Chinese patent medicine as adjuvant for mild-to-moderate active ulcerative colitis: a network meta-analysis of randomized controlled trials. Evid Based Complement Alternat Med 2021; 2021: 1075886.
[35] Wu M, Ding H, Tang X, Chen J, Zhang M, Yang Z, Du Q and Wang J. Efficiency of a novel thermosensitive enema in situ hydrogel carrying Periplaneta americana extracts for the treatment of ulcerative colitis. Front Pharmacol 2023; 14: 1111267.
[36] Ren PW, Yang WJ, Wang DD, Shan JY, Kang DY, Hong Q, Wen S and Zhang RW. Kangfuxinye enema combined with mesalamine for ulcerative colitis: a systematic review and GRADE approach. Evid Based Complement Alternat Med 2017; 2017: 6019530.
[37] Zhang Z, Li D, Zheng S, Zheng C, Xu H and Wang X. Gene expression regulation and polyadenylation in ulcerative colitis via long-chain RNA sequencing. BMC Genomics 2025; 26: 147.
[38] Rafa H, Saoula H, Belkhelfa M, Medjeber O, Soufli I, Toumi R, de Launoit Y, Moralès O, Nakmouche M, Delhem N and Touil-Boukoffa C. IL-23/IL-17A axis correlates with the nitric oxide pathway in inflammatory bowel disease: immunomodulatory effect of retinoic acid. J Interferon Cytokine Res 2013; 33: 355-368.