Review Article

Systematic Evaluation of Randomized Clinical Trials of Huangqin Tang in Combination with Mesalazine for Ulcerative Colitis

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Objective. To systematically evaluate the efficacy and safety of Huangqin Tang (HQT) combined with mesalazine for the treatment of ulcerative colitis (UC).

Methods. The China Knowledge Network, Wanfang Data, VIP, PubMed, SinoMed, Embase, and Cochrane Library databases were searched for randomized controlled trials (RCTs) of UC with HQT in Chinese and English. The search time was from the establishment of the database to October 2021. The included literature was evaluated for data extraction and risk of bias, efficacy and safety were evaluated using the RevMan5.3 software, and the quality of evidence was evaluated using GRADE.

Results. Six studies with a total of 565 subjects were included, and a meta-analysis showed that HQT combined with mesalazine for UC significantly improved the cure rate (RR = 1.56, 95% CI [1.23, 1.98], P < 0.0003) and overall efficacy rate (RR = 1.24, 95% CI [1.14, 1.35], P < 0.0001), which significantly reduced the clinical symptom scores; however, all had high heterogeneity. HQT combined with mesalazine modulated the patients’ serum IL-6, IL-10, IgA, and IgG levels. HQT combined with mesalazine for UC tended to reduce adverse effects; however, the difference was not statistically significant. All GRADE ratings of the quality of evidence were of low quality.

Conclusions. HQT combined with mesalazine in the treatment of UC significantly improved the cure rate and overall treatment efficiency and regulated the expression levels of serum IL-6, IL-10, IgA, and IgG.

1. Introduction

Ulcerative colitis (UC) is a chronic nonspecific intestinal inflammatory disease characterized by continuous and diffuse inflammatory changes in the colorectal mucosa; however, its etiology has not been fully understood. The lesions are mainly limited to the colorectal mucosa and the submucosa [1]. Clinical manifestations include recurrent diarrhea with mucus and pus, hematochezia, abdominal pain, and tenesmus with varying degrees of severity. It can also be accompanied by anemia, skin, and mucosal damage (such as oral ulcers and erythema nodosa), joint damage (such as peripheral or spinal arthritis), eye lesions (such as iritis or uveitis), metabolic bone disease, hepatobiliary system lesions (such as primary biliary cirrhosis PSC), and other extra-intestinal manifestations. The “Consensus Opinions on the Diagnosis and Treatment of Ulcerative Colitis with Integrated Traditional Chinese and Western Medicine 2017” proposes that the main points of UC diagnosis are typical clinical manifestations, endoscopic changes, and pathological diagnosis [1]. In 2019, the ACG Clinical Guideline: Ulcerative Colitis in Adults [2] pointed out that the assessment of disease severity is mainly used to guide treatment, and the assessment should be mainly based on (1) professional scale assessment (bleeding volume and stool frequency); (2) inflammation assessment (endoscopic...
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by HQT combined with mesalazine. Earlier, our research

the evidence level of clinical studies on the treatment of UC

and there was no systematic evaluation and meta-analysis on

treatment of UC by HQT combined with sulphapyridine,

that there was only a small amount of meta-analysis on the

large number of research studies, our research group found

there is no evidence-based medical basis for the treatment of

enteritis, bacterial dysentery, and other diseases; however,

widely used in the clinical treatment of UC, acute gastro-

ASA is superior to topical corticosteroids in inducing re-

necrosis factor therapy. Bressler B [9] found that topical 5-

moderate UC lesions to a degree similar to that of antitumor

necrosis factor therapy. Bressler B [9] found that topical 5-

as a result of this study can provide a valuable reference for

future clinical experiments and clinical applications of HQT

in the treatment of UC.

2. Methods

2.1. Search Strategy and Study Selection. The CNKI, Wanfang Data, VIP, PubMed, SinoMed, Embase, and Cochrane Library databases were systematically searched from the establishment of each database to October 15, 2021. The Chinese database uses “Huangqin Tang” AND “ulcerative colitis” as the search mode, and supplementary search uses “Huangqin Tang,” “ulcerative colitis,” AND “inflammatory bowel disease” as the search terms and adopts the search mode of theme/keyword/abstract.

The English database search formula is (Huangqin Tang OR Huangqin Decoction OR Radix Scutellaria soup) AND (“nonspecific ulcerative colitis” OR “ulcerative Colitis” OR “ulcerative colitis” OR “ulcerous colitis” OR “colitis gravis”).

Subjects: we evaluated randomized controlled trials (RCTs) in which patients had a definitive diagnosis of ulcerative colitis; however, age, sex, and course of disease were not defined. There was no restriction on whether blinding was used in the study design. The intervention measures were HQT combined with mesalazine treatment and allowed for the addition of drugs in line with the requirements of the original prescription for the ShangHan Lun [6] based on the original prescription but excluding marked toxic drugs (refer to the 2020 edition of the People’s Republic of China Pharmacopoeia [10]). The control drug mesalazine was recommended as the first-line drug in the clinical guidelines for ulcerative colitis [11], and the dosage form was not limited.

The main outcome indicators were cure rate and total effective rate. The secondary outcome measures were clinical symptom score (abdominal pain, diarrhea, hematochezia, and tenesmus) and levels of serum inflammatory factors including interleukin 6 (IL-6), interleukin 10 (IL-10), tumor necrosis factor α (TNF-α), serum immunoglobulin A (IgA), immunoglobulin M (IgM), and immunoglobulin G (IgG), and safety.

2.2. Data Extraction. Two researchers independently completed the literature retrieval through the search formula or search terms, screened out and excluded the literature that did not meet the inclusion criteria, and finally confirmed the literature selections. The third researcher compared the screening results. Any disagreements were resolved through discussion or by a third researcher. Two researchers independently extracted the data from the included literature and established the data extraction table: basic information, the methodological characteristics, the research object,
intervention, outcome indicators, the results, and conclusions. Datasheets extracted by two researchers were compared, and a third researcher organized a discussion or resolution of different or divergent results.

2.3. Assessment of Methodological Quality. Referring to the Cochrane Handbook of Systematic Reviews [12], two researchers independently completed the quality assessment and bias risk assessment of the included studies using the risk of bias (ROB) tool in RevMan5.3, including the method of random sequence generation and hidden random-protocol allocation. They also noted if participants, people, and outcome assessments were blinded; if there was evidence of incomplete outcome data; and whether there was evidence of a risk of bias in the selective reporting of results. The evaluation results of the two researchers were compared, and a third researcher organized the discussion or resolution of the different or divergent results.

2.4. Statistical Analysis. The outcome index data of the included studies were entered into RevMan software (version 5.3). The relative risk (RR) meta-analysis was used for statistical analysis of the binary outcome index data, and the weighted mean difference (WMD) or standardized mean difference (SMD) meta-analysis was used for statistical analysis of the continuous outcome index data. The effect size was expressed with a 95% confidence interval (95% CI). The heterogeneity among the included studies was assessed. A fixed-effect model was adopted if the I2 between the results was less than 50%. If I2 was ≥50%, the random-effects model was adopted. Descriptive, systematic, or subgroup analyses were used if significant clinical heterogeneity existed between the included studies. The level of the meta-analysis was set at α = 0.05. The GRADE evidence quality grading system was used to evaluate the quality of evidence of the outcome indicators [13].

3. Results

3.1. Literature Search. A total of 411 original articles were retrieved from CNKI, Wanfang Data, VIP, PubMed, SinoMed, Embase, and the Cochrane Library. After preliminary screening, 225 articles were identified. In addition, 15 qualified articles were obtained through preliminary screening of literature titles and abstracts. After perusing the full text of the eligible literature, further screening was conducted according to the literature inclusion criteria. Finally, 6 studies were included, with a total of 565 patients.

3.2. Study Characteristics. A total of six studies were included [14–19], involving a total of 565 subjects with a definite diagnosis of UC, which were published in the last 5 years (2016–2021). The sample size of each study ranged from 68 to 126. The intervention was HQT plus mesalazine, and mesalazine was administered to the control group. The treatment course was 2 or 3 months, and the outcome indices included cure rate, effective rate, clinical symptom score, inflammatory factors, immunoglobulin levels, and adverse reactions. Further details are provided in Table 1.

3.3. Quality Assessment of the Included Studies. Among the six included studies, three used the random number table method to generate random sequences with a low risk of bias. The random sequence generation method of the remaining three studies was only described as “random” without specific explanation, indicating a high risk of bias. In blinding of outcome assessment, none of the six studies blinded the subjects, so the risk of bias could not be excluded. None of the six subjects dropped out; as a result, the risk of bias for incomplete outcomes was low. Moreover, none of the six studies mentioned whether the outcome evaluator was incomplete, and outcome bias was low. As it could not be determined whether the six study protocols were registered, the existence of reporting bias could not be ruled out (Figure 1).

3.4. Cure Rate and Total Efficiency Rate. Five studies that included cure rates [14–17, 19] were used to compare the difference in clinical cure rates between the HQT group and the control group—this included a total of 470 patients, with clinical heterogeneity I2 = 18%, <50%. Using the fixed-effect model, the meta-analysis results showed that the clinical cure rate of the HQT group was significantly higher than that of the control group (RR = 1.56, 95% CI (1.23, 1.98), P = 0.0003) (see Figure 2(a)).

Five studies that included total efficiency rates [14–16, 17] were used to compare the difference in clinical total efficiency rates between the HQT group and the control group. A total of 470 patients were included, with clinical heterogeneity I2 = 0%, <50%. Using the fixed-effect model, the meta-analysis results showed that the total clinical effective rate of the HQT group was significantly higher than that of the control group (RR = 1.24, 95% CI (1.14, 1.35), P = 0.00001) (see Figure 2(b)).

3.5. Clinical Symptom Score. In total, 242 patients were included in the clinical symptom score study [14, 15]. The differences in the symptom scores of abdominal pain, diarrhea, hematoma, and tenesmus were compared between the HQT and control groups. After careful reading of the literature scheme analysis, it was concluded that clinical heterogeneity I2 > 50% was caused by large differences in subjective scores. Using the random effect model, the meta-analysis results showed that the scores for diarrhea, hematoma, and tenesmus in the HQT group were significantly lower than those in the control group, and there was no statistically significant difference in the scores for abdominal pain (diarrhea: SWD = −3.2, 95% CI (−5.81, −0.58), P = 0.02; hematoma: SWD = −4.12, 95% CI (−6.17, −2.08), P = 0.00001; tenesmus: SWD = −3.14, 95% CI (−4.17, −2.12), P = 0.00001; and abdominal pain: SWD = −2.97, 95% CI (−6.27, 0.33), P = 0.08).
| Author, year | Sample size | Diagnostic criteria | Male % | Age (years) | Course of the disease | Treatment intervention | Control intervention | Period of treatment (months) | Outcome indicator |
|--------------|-------------|---------------------|--------|-------------|-----------------------|------------------------|----------------------|--------------------------|------------------|
| Hu et al., [14] | 116 | Clinical symptoms, colonoscopy, pathology | 51.7% | 42.37 ± 2.87 | 42.61 ± 2.82 | 8.71 ± 2.42 | 8.94 ± 2.4 | HQT\(^1\)+mesalazine\(^a\) | Mesalazine\(^a\) | 2 |
| Ding et al., [15] | 126 | Clinical symptoms, colonoscopy, pathology | 53.2% | 43.5 ± 9.6 | 42.4 ± 8.7 | 9.5 ± 3.2 | 9.2 ± 3.5 | HQT\(^2\)+mesalazine\(^a\) | Mesalazine\(^a\) | 2 |
| Yan [16] | 82 | Clinical symptoms, imaging | 54.9% | 36.68 ± 6.52 | 36.74 ± 6.58 | 6.52 ± 3.23 | 6.47 ± 3.18 | HQT\(^1\)+mesalazine\(^a\) | Mesalazine\(^a\) | 2 |
| Wang and Wang [17] | 78 | Clinical symptoms, colonoscopy | 57.7% | 35.36 ± 4.32 | 35.18 ± 4.29 | 3.91 ± 0.45 | 3.86 ± 0.41 | HQT\(^1\)+mesalazine | Mesalazine | 3 |
| Lu [18] | 95 | Clinical symptoms, colonoscopy, pathology | 51.6% | 36.57 ± 6.59 | 35.97 ± 6.29 | NA | NA | HQT\(^1\)+mesalazine\(^b\) | Mesalazine\(^b\) | 2 |
| Yang [19] | 68 | Clinical symptoms, colonoscopy, pathology, imaging | 48.5 | 42.6 ± 12.7 | 41.5 ± 12.5 | NA | NA | HQT\(^2\)+mesalazine\(^b\) | Mesalazine\(^b\) | 2 |

\(^1\) represents decoction of HQT; \(^2\) represents granule of HQT; \(^a\) represents mesalazine granules or sustained-release granules, and \(^b\) represents mesalazine enteric-coated tablets.
Inflammatory Factors. Three studies included information on serum IL-10 levels [15, 18, 19], involving 289 patients. These studies were used to compare the differences in serum IL-10 levels between the HQT and control groups. Clinical heterogeneity $I^2 = 24\%$, $<50\%$, fixed-effect model, and SMD meta-analysis results showed that HQT could significantly increase IL-10 content (SMD = 2.01, 95% CI (1.73, 2.30), $P = 0.00001$) (see Figure 3(a)).

Two studies included serum IL-6 levels [15, 19], involving 194 patients. We used them to compare the difference in serum IL-6 levels between the HQT and control groups. Clinical heterogeneity $I^2 = 0\%$, $<50\%$, fixed-effect model, and SMD meta-analysis results showed that HQT could significantly reduce IL-6 levels (SMD = −2.25, 95% CI (−2.61, −1.88), $P = 0.00001$) (see Figure 3(b)).

We analyzed three studies that included serum TNF-α levels [15, 18, 19], with a total of 289 patients, to compare the difference in serum TNF-α levels between the HQT and control groups. The clinical heterogeneity was $I^2 = 69\%$, $>50\%$. This may be because the TNF-α data units in Yang M’s experiment were different from those in the other two studies. The results of the meta-analysis using the random...
3.7. Immunoglobulin. Two studies included immunoglobulin IgA [16, 18], involving 177 patients, with clinical heterogeneity of $I^2 = 0\%$, <50%. The fixed-effect model was adopted, and the results of the meta-analysis of SMD showed that the expression of immunoglobulin IgA in the HQT group was significantly decreased (SMD = −0.65, 95% CI (−0.96, −0.35), $P = 0.00001$) (see Figure 4(a)).

Two studies included immunoglobulin IgM [16, 18], involving 177 patients, with clinical heterogeneity of $I^2 = 0\%$, <50%. The fixed-effect model was adopted, and the results of the meta-analysis of SMD showed that there was no significant difference in immunoglobulin IgM expression between the HQT and control groups (SMD = −0.09, 95% CI [−0.21, 0.38], $P = 0.56$) (see Figure 4(b)).

Two studies included immunoglobulin IgG [16, 18], involving 177 patients, with clinical heterogeneity of $I^2 = 0\%$, <50%. The fixed-effect model was adopted, and the results of the meta-analysis of SMD showed that the expression level of immunoglobulin IgG in the HQT group was significantly decreased (SMD = −3.20, 95% CI (−3.65, −2.75), $P = 0.00001$) (see Figure 4(c)).

3.8. Safety. Among the included studies, only one [17] reported safety. In the mesalazine group, eight patients showed adverse reactions, including 2 patients with nausea and vomiting, 3 patients with dizziness, and fatigue in 1 patient, and 2 patients with mild skin itching. In the HQT group, two patients showed adverse reactions, including one patient with nausea and vomiting and one patient with dizziness. We were able to contact the researchers of two studies [14, 15] by e-mail or telephone, and they replied that there were no adverse reactions. There was a trend of reduced adverse reactions in the adjuvant treatment of UC with HQT, but the difference was not statistically significant (RR = 0.25, 95% CI (0.06, 1.10), $P = 0.07$).

3.9. Evaluation of GRADE Evidence Quality. The 13 outcome indicators were evaluated for evidence quality using GRADE. The evaluation results indicated the low quality of evidence. Further details are provided in Table 2.

4. Discussion

At present, the pathogenesis of UC has not been fully elucidated, but it is generally accepted that many factors, such as genetics, environment, and microorganisms, increase susceptibility to this disease. The resulting mucosal barrier changes, intestinal microflora disorders, and immune system defects cause sustained inflammatory reactions. One of the main pathogenic factors of UC is abnormal immune regulation. Both IL-6 and IL-10 play an important regulatory role in the development, differentiation, and immune response of immune cells; they participate in the activation of some cells and are closely related to the occurrence, development, and outcome of UC [20]. Western medicine treats UC by inhibiting intestinal inflammation. Commonly prescribed drugs for this illness include aminosalicylic acid, glucocorticoids, immunosuppressants, and biological agents, among which mesalazine and sulfasalazine are first-line drugs [2, 11]. The basic principles of traditional Chinese medicine in the treatment of UC are as follows: clearing heat and removing dampness; regulating qi and blood; astringing ulcers and promoting muscle during the active phase; strengthening the spleen and nourishing qi in the remission phase; supplementing the kidney and strengthening the root; and supplementing with clearing heat and removing dampness [21]. The pharmacodynamics studies showed that the main bioactive ingredients of HQT include baicalin, wogonoside, baicalein, wogonin and oroxynil-A, paenoflorin, liquidity, and other herb components [22]. The main active ingredients of HQT for UC...
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Test for overall effect: \( Z = 13.91 \) (\( P < 0.00001 \))
Total (95% CI) 89 88 100.0 -3.20 [-3.65, -2.75]

YAN L 2019
LU LF 2017

Test for overall effect: \( Z = 0.59 \) (\( P = 0.56 \))
Total (95% CI) 89 88 100.0 0.09 [-0.21, 0.38]

YAN L 2019
LU LF 2017

Test for overall effect: \( Z = 4.20 \) (\( P < 0.0001 \))
Total (95% CI) 89 88 100.0 -0.65 [-0.95, -0.35]

LU LF 2017 1.25 0.63 48 1.67 0.77 47 54.2 -0.59 [-1.00, -0.18]
YAN L 2019 1.22 0.58 41 1.72 0.79 41 45.8 -0.79 [-1.16, -0.27]

YAN L 2019
LU LF 2017

(4) Meta-analysis of IgA (a) IgM (b) and IgG (c) content in the HQT group compared with the mesalazine group.

YAN L 2019
LU LF 2017

Heterogeneity: \( \chi^2 = 0.19, df = 1 (P = 0.67); I^2 = 0\%
Test for overall effect: \( Z = 3.91 \) (\( P < 0.0001 \))

Favours [experimental] Favours [control]

YAN L 2019
LU LF 2017

Favours [experimental] Favours [control]

YAN L 2019
LU LF 2017

Favours [experimental] Favours [control]

Figure 4: Meta-analysis of IgA (a) IgM (b) and IgG (c) content in the HQT group compared with the mesalazine group.

treatment are quercetin, kaempferol, baicalein, etc. [23–25]. The core targets are AKT1, JUN, IL6, VEGFA, STAT3, MYC, CASP3, EGFR, etc. [26]. The treatment of UC with HQT mainly acts on biological processes such as cancer pathway, MAPK signaling pathway, TNF signaling pathway, insulin resistance, JAK-STAT pathway, Th17 cell differentiation, NF-kB, and other signaling pathways, involving biological processes such as endotoxin response, regulation of apoptosis signaling pathway, regulation of small molecule metabolic process, reactive oxygen metabolic process, and negative regulation of cell proliferation [27]. Besides, some existing basic studies have shown that HQT may play a role in the treatment of UC through multiple targets and mechanisms; for example, by inhibiting the activation of IL-6, JAK, and STAT3 signaling pathways and the expression of HGBB-1, it can reduce the production of inflammatory cytokines and inflammatory responses, thus improving intestinal function and restoring intestinal structure [28]. The intestinal immune system is regulated by the expression of various cytokines, such as IL-6, IL1-β, and IL-10, to maintain homeostasis of the intestinal mucosal system [26]. By promoting the expression of the MHC II molecule and increasing ILC3 s cells, upregulating the expression of Treg cells and downregulating the expression of Th1 cells, inhibiting the secretion of a variety of proinflammatory factors, and then regulating the immune response of Th cells, DSS-induced mouse ulcerative colitis is alleviated [29].

Multicentre, large-sample RCTs have achieved the highest level of evidence-based medical evidence [30]. In recent years, the number of RCT studies on the treatment of UC by HQT has increased significantly. However, there is no systematic evaluation of the level of evidence in clinical studies of HQT combined with mesalazine for the treatment of UC. Six studies were included in this meta-analysis, and the results showed that HQT combined with mesalazine in the treatment of UC could significantly improve the cure rate and total effective rate, as well as the expression levels of IL-6, IL-10, IgA, and IgG in the serum of patients. However, there was no statistical difference in the expression of serum IgM. Clinical symptom scores have high heterogeneity, which may be caused by large differences in subjective scores. Heterogeneity was also high in the meta-analysis of the effects on TNF-α, which may be because the data unit of TNF-α in Yang’s experiment was different from that in the other two studies. Few reports provide data on adverse reactions; the effect of HQT on reducing the incidence of adverse reactions thus still needs to be verified by further studies. The limitations of this meta-analysis are as follows: (1) The sample size was small, and the experimental studies investigated were not rigorously designed. Among the included studies, only three described the random number table method for random sampling and none of them mentioned whether the blind method was adopted or whether allocation hiding was set, which has a high risk of bias. (2) Most of the articles only evaluated the efficacy rate, cure rate, and clinical symptoms; the clinical symptom score standard was not uniform and highly subjective, leading to high heterogeneity. (3) There was a lack of evaluation studies.
using objective indicators, such as the efficacy of colonoscopy and mucosal histology, and the data units of test indicators were inconsistent in some studies. (4) There was a lack of detailed reports on adverse reactions; furthermore, it was difficult to obtain contact details that could be accessed to obtain further information. (5) The course of HQT combined with mesalazine in the treatment of UC is not clear, and regular follow-up or follow-up results have not been reported.

Therefore, the results of this study suggest that the following aspects should be emphasized in later clinical trials of HQT for UC: (1) Expand the sample size, design a more scientific and rigorous randomized controlled trial, reduce risk bias as much as possible, improve the methodological quality, adopt standardized randomized methods, and allocate hidden and blind methods. (2) Strengthen the evaluation of clinical symptoms, colonoscopic efficacy, and mucosal histology and recommend the use of unified scoring criteria, such as the Modified Mayo Disease Activity Index and Original Geboes Score. (3) For the determination of serum or colon markers, high-quality immunokits should be used as far as possible, and strictly standardized operations should be performed. Possible detection indexes include serum IL-6, IL-1β, IL-10, TNF-α, COX2, routine blood examination, routine fecal examination, plasma protein, ESR, CRP, and fecal calprotectin. (4) Gather detailed data on adverse reactions and the safety of TCM compounds. (5) Gather data on the patients' quality of life, evaluate the patient's psychological and mental state, stage follow-up, and make detailed reports in the literature.

5. Conclusions

HQT combined with mesalazine in the treatment of UC significantly improved the cure rate and overall treatment efficiency and regulated the expression levels of serum IL-6, IL-10, IgA, and IgG.

Data Availability

The datasets presented in this study can be found in the online repositories. System evaluation registration: International Prospective System Evaluation Registration Platform (PROSPERO), CRD42021234614.

Disclosure

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations or those of the publisher, editors, and reviewers. Chengyu Pan and Mengru Liu are the co-first authors.

Conflicts of Interest

The authors declare no conflicts of interest.

Authors’ Contributions

Yaozhou Tian and Limei Gu conceived and designed the experiments. Chengyu Pan, Mengru Liu, Hui Li, Lanfu Wei, Pengcheng Wang, Kexuan Wu, and Xing Ji conducted the
database literature search and data extraction. Chengyu Pan and Mengru Liu conducted data analysis and coauthored the paper. Yaozhou Tian and Limei Gu helped analyze the data and provided constructive discussions. All authors read and agreed to the final version of the manuscript. Chengyu Pan and Mengru Liu contributed equally to this work.

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References
[1] Chinese Society of Integrated Traditional and Western Medicine Digestive Diseases Professional Committee, “Consensus opinion of Integrated Traditional and Western Medicine diagnosis and treatment of ulcerative colitis (2017),” Chinese Journal of Integrated Traditional and Western Medicine, vol. 26, no. 2, pp. 105–110, 2018.
[2] D. T. Rubin, A. N. Ananthakrishnan, and C. A. Siegel, “ACG clinical guideline: ulcerative colitis in Adults,” American Journal of Gastroenterology, vol. 114, no. 3, p. 384, 2019.
[3] R. Ungaro, S. Mehandru, P. B. Allen, L. Peyrin-Biroulet, and J. F. Colombel, “Ulcerative colitis,” The Lancet, vol. 389, no. 10080, pp. 1756–1770, 2017.
[4] W. Y. Mak, M. Zhao, S. C. Ng, and J. Burisch, “The epidemiology of inflammatory bowel disease: East meets West,” Journal of Gastroenterology and Hepatology, vol. 35, no. 3, pp. 380–389, 2019.
[5] L. Yang, F. Li, W. L. Liu, and Li. Fei, Experience in Treating Ulcerative Colitis with Zhongqing Zhili Recipe, Journal of Chengdu University of Chinese Medicine, vol. 37, no. 4, pp. 77–79, 2014.
[6] Z. Zhang, Treatise on Febrile Diseases, China Traditional Chinese Medicine Press, Beijing, China, 2011.
[7] Y. Fu and R. You, “Medical Prescription,” 2020, https://en.wikipedia.org/wiki/Medical_prescription.
[8] C. Le Berre, G. Roda, M. Nedeljkovic Protic, S. Danese, and L. Peyrin-Biroulet, “Modern use of 5-aminosalicylic acid compounds for ulcerative colitis,” Expert Opinion on Biological Therapy, vol. 20, no. 4, pp. 363–378, 2020.
[9] B. Bressler, J. K. Marshall, C. N. Bernstein et al., “Clinical practice guidelines for the medical management of nonhosptialized ulcerative colitis: the Toronto consensus,” Gastroenterology, vol. 148, no. 5, pp. 1035–1058.e3, 2015.
[10] Pharmacopoeia of the People’s Republic of China 2020 Edition, Chinese Pharmacopoeia, China Medical Science and Technology Press, Beijing, China, 2020.
[11] K. Wu, J. Liang, and Z. Ran, “Consensus opinions on the diagnosis and treatment of inflammatory bowel disease (2018-Beijing),” Chinese Journal of Practical Internal Medicine, vol. 38, no. 09, p. 796, 2018.
[12] J. Higgins, S. Green, and Cochrane Collaboration, Cochrane Handbook for Systematic Reviews of Interventions Version 5.1, John Wiley Sons Ltd and The Cochrane Collaboration, Chichester, UK, 2011.
[13] M. Kulig, M. Perleth, G. Langer et al., “[GRADE guidelines: 6. Rating the quality of evidence: imprecision],” Zeitschrift für Evidenz, Fortbildung und Qualität im Gesundheitswesen, vol. 106, no. 9, pp. 677–688, 2012.
[14] J. Hu, X. Guo, and D. Zhou, “Effects of Huangqin Tang combined with mesalazine on inflammatory factors in intestinal mucosal tissue in ulcerative colitis (active stage),” Chinese Archives of Traditional Chinese Medicine, vol. 39, no. 01, pp. 123–126, 2021.
[15] H. Ding, B. Wang, and Y. Yang, “The efficacy of Huangqin Tang granules combined with mesalazine in the treatment of ulcerative colitis and its effect on inflammatory factors,” Laboratory Medicine and Clinical, vol. 15, no. 06, pp. 806–809, 2018.
[16] L. Yan, “Clinical observation of modified Huangqin Tang combined with mesalazine in the treatment of ulcerative colitis,” Journal of Sichuan of Traditional Chinese Medicine, vol. 37, no. 05, pp. 101–103, 2019.
[17] H. Wang and X. Wang, “Treatment of 39 cases of ulcerative colitis with flavouring of Huangqin Tang and mesalazine,” Modern Traditional Chinese Medicine, vol. 39, no. 03, pp. 56–58, 2019.
[18] L. Lu, “Clinical study on the treatment of ulcerative colitis with Huangqin Baishao Tang,” Asia-Pacific Traditional Medicine, vol. 13, no. 12, pp. 118–119, 2017.
[19] M. Yang and D. Wu, “Clinical effect of Huangqin Tang granules combined with mesalazine on ulcerative colitis,” Chinese Journal of Integrated Traditional and Western Medicine on Digestion, vol. 24, no. 03, pp. 221–223, 2016.
[20] D. T. Forland, E. Johnson, L. Saetre, T. Lyberg, I. Lygren, and G. Hetland, “Effect of an extract based on the medicinal mushroom Agaricus blazei murill on expression of cytokines and calprotectin in patients with ulcerative Colitis and Crohn’s disease,” Scandinavian Journal of Immunology, vol. 73, no. 1, pp. 66–75, 2011.
[21] Spleen and Stomach Disease Branch of Chinese Association of Traditional Chinese Medicine, “Expert consensus on the diagnosis and treatment of ulcerative colitis in traditional Chinese medicine (2017),” Chinese Journal of Chinese Medicine (formerly Chinese Journal of Medicine), vol. 32, no. 8, pp. 3585–3589, 2017.
[22] F. Zuo, Z. M. Zhou, Q. Zhang et al., “Pharmacokinetic study on the multi-constituents of Huangqin-Tang decoction in rats,” Biological and Pharmaceutical Bulletin, vol. 26, no. 7, pp. 911–919, 2003.
[23] R. Sotnikova, V. Nosalova, and J. Navarova, “Efficacy of quercetin derivatives in prevention of ulcerative colitis in rats,” Interdisciplinary Toxicology, vol. 6, no. 1, pp. 9–12, 2013.
[24] M. Y. Park, G. E. Ji, and M. K. Sung, “Dietary kaempferol suppresses inflammation of dextran sulfate sodium-induced colitis in mice,” Digestive Diseases and Sciences, vol. 57, no. 2, pp. 355–363, 2012.
[25] S. Liang, X. Deng, L. Lei et al., “The comparative study of the therapeutic effects and mechanism of baicalin, baicalein, and their combination on ulcerative colitis rat,” Frontiers in Pharmacology, vol. 10, p. 1466, 2019.
[26] H. Song, X. Ma, and D. Wang, “Potential mechanism of Huangqin decoction for the treatment of ulcerative colitis based on network pharmacology,” Journal of Pharmacy, vol. 55, no. 02, pp. 247–255, 2020.
[27] X. Wen and H. Huang, “Molecular mechanism of Huangqin decoction on treatment of ulcerative colitis based on network pharmacology,” Traditional Chinese Drug Research & Clinical Pharmacology, vol. 31, no. 2, pp. 199–205, 2020.
[28] Ji Jia and Y. Chen, “Effects of Huangqin Decoction on IL-6, JAK-STAT3 signalling pathway and HMGB-1 expression in rats with ulcerative colitis,” *TCM Journal*, vol. 33, no. 07, pp. 1297–1301, 2018.

[29] C. Zhou, X. Zheng, X. Huang et al., “Huangqin Tang alleviates ulcerative colitis in mice by regulating ILC3s-Th cell response,” *Journal of Southern Medical University*, vol. 41, no. 02, pp. 256–263, 2021.

[30] H. Shen, “Review of TCM clinical research on ulcerative colitis,” *Jiangsu Journal of Traditional Chinese Medicine*, vol. 51, no. 10, p. 1, 2019.