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Research article

Clinical effect of wumei bolus on ulcerative colitis: A meta-analysis

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ABSTRACT

Wumei Bolus is a traditional Chinese medicine prescription, first appeared in Shennong Bencao Jing. Modern pharmacology believes that Wumei Bolus has antibacterial, antitussive, sedative, antiviral and anti-tumor effects, and plays a therapeutic role by acting on multi-target/multi-pathway. Moreover, it has great advantages in digestive system diseases, such as repairing the damaged gastrointestinal mucosa and improving the inflammatory environment.

Aim of the study: This review aimed to evaluate the efficacy and safety of prescriptions based on the Wumei Bolus treating ulcerative colitis (UC).

Materials and methods: In this meta-analysis, we searched CNKI, Wanfang Database, VIP, Pubmed, Web of Science (WOS) with language restrictions of Chinese and English for articles published from the establishment of the database to Dec 2022. This *meta*-analysis controlled randomized controlled trials (RCTs) assessing the efficacy and safety of Wumei Bolus against ulcerative colitis and using RevMan 5.4 and Stata 15.0to analyze information from the compliant studies.

Results: The search incorporated 3145 results (1617 cases assigned into Wumei Bolus group and 1528 cases assigned into control group), from which 37 studies fulfilled our inclusion criteria and were included. The outcomes of this meta-analysis showed that compared to the control group, the Experiment group was significantly more effective (RR = 1.24 , 95%CI [1.20 , 1.28])and lower adverse reactions (RR = 0.32, 95%CI [0.20, 0.53]). According to the subgroup analysis, The results showed that the RR = 1.23 and 95%CI [1.16, 1.30] in the group treated with Wumei Bolus alone and the group treated with Western medicine with RR = 1.25 and 95%CI [1.20, 1.30], indicating that the efficacy of Wumei Bolus in the treatment of UC was better and the difference was statistically significant (P < 0.00001). The results showed that compared with the control group, the experimental group had more advantages in reducing inflammatory factors whether TNF-α or IL-8 (TNF-α:SMD = −4.44, 95%CI [-5.75, −3.14]; IL-8: SMD = −3.02, 95%CI [-4.06, −1.97]) and improving TCM symptoms and reduced TCM syndrome points (SMD = −3.82, 95%CI

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[-4.30, −3.34]). There was significant association of the basic treatment of Wumei Bolus improving clinical efficacy, reducing serum pro-inflammatory factors, improving symptoms, and reducing adverse reactions in UC patients. These results were statistically significant ($P < 0.00001$).

Conclusions: The prescriptions based on the Wumei Bolus is greatly related to reducing serum pro-inflammatory factors, improving symptoms, improving clinical efficacy and reducing adverse reactions in the treatment of UC compared to conventional western medicine and improve the total clinical effective rate.

1. Introduction

Ulcerative colitis (UC), also known as chronic nonspecific ulcerative colitis, is mainly limited to colonic mucosa and submucosa. Clinical symptoms main include abdominal pain, diarrhea, mucus, pus, blood and stool, and tenesmus [1]. In recent years, with the development of social economy, the incidence of UC has been increasing. However, the cause of UC has not been clarified, and it is believed to be related to Ref. [2]genetics, region and environment, dietary habits, and intestinal flora [3]. At present, the clinical treatment of UC mostly relies on western drugs such as Sulfasalazine, corticosteroids, and Immunosuppressant, which have certain side effects on the treatment. Wumei Bolus, a Traditional Chinese medicine prescription, has the functions of moderating the liver, regulating spleen and stomach, clearing the upper, warming the lower, and is a common prescription for the treatment of chronic diarrhea. Traditional Chinese medicine believes that Mume Fructus has the effects of astringent and moisturizing, it is often used for long-term diarrhea, vomiting, abdominal pain. It can be used to treat symptoms of ulcerative colitis. Modern studies have confirmed that Wumei Bolus has significant clinical efficacy in the treatment of UC [4] and has the effects of anti-inflammatory, antibacterial, anti-tumor, immunosuppression, promoting ulcer healing, regulating gastrointestinal function and enhancing body immunity [5]. The objective of this study was to systematically review and conduct a meta-analysis to the efficacy and safety of Wumei Bolus in the

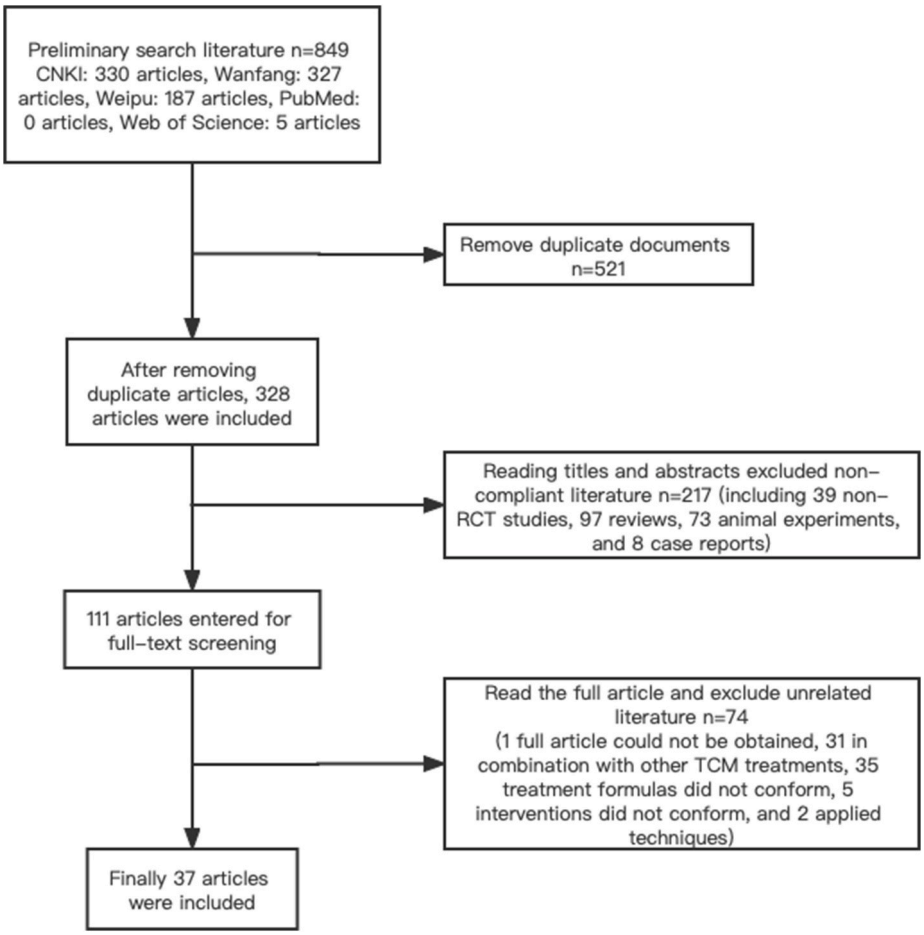

Fig. 1. Literature screening process of Wumei Bolus for ulcerative colitis.

Table 1
Basic information of the included studies.

Studies	Sample size		Sex ratio (M/W)		Age (years)		Course of disease		Course of treatment	Intervention	ORR			Adverse Reaction	
	T	C	T	C	T	C	T	C		T	C	T	C	T	C
Li KY 2022 [7]	47	47	31/16	28/19	N	N	N	N	4	WB +5-ASA	5-ASA	45/47	39/47	1	8
Yang J 2022 [8]	58	40	31/27	22/18	53.16 ± 5.63	53.62 ± 5.53	3.56 ± 1.41	3.63 ± 1.22	4	WB + SASP	SASP	54	31	7	12
Wang FY 2021 [9]	54	53	28/26	26/27	35.78 ± 3.99	36.25 ± 4.12	6.44 ± 2.67	6.14 ± 2.98	30 d	WB +5-ASA	5-ASA	51/54	38/53	/	/
Xing SH 2021 [10]	20	20	10/10	11/9	N	N	N	N	4w	WD + Prednisone	Prednisone	17/20	8/20	/	/
Li KY 2020 [11]	37	34	21/16	19/15	40.86 ± 6.57	42.17 ± 6.84	3.27 ± 0.46	3.15 ± 0.42	1 m	WB +5-ASA	5-ASA	36/37	28/34	/	/
Cui YH 2020 [12]	15	15	N	N	N	N	N	N	3w	WB (oral & enema)	5-ASA	13/15	10/15	/	/
Zhang WJ 2019 [13]	20	20	11/9	10/10	N	N	N	N	4w	WB +5-ASA	5-ASA	18/20	14/20	/	/
Zhang DY 2019 [14]	46	46	32/14	30/16	39.34 ± 6.53	40.34 ± 5.88	6.55 ± 2.62	6.48 ± 2.69	4w	WB +5-ASA	5-ASA	44/46	34/46	/	/
Sun MZ 2018 [15]	30	30	13/17	14/16	N	N	63.5 ± 21.4	66.3 ± 26.8	8w	WB +5-ASA	5-ASA	28/30	22/30	0	0
Hu WT 2018 [16]	30	30	21/9	20/10	36.3 ± 5.61	36.3 ± 7.01	13.0 ± 8.06	13.3 ± 7.65	30 d	WB +5-ASA	5-ASA	28/30	24/30	1	1
Li BJ 2018 [17]	24	24	13/11	12/12	46.3 ± 5.7	45.1 ± 4.9	7.3 ± 2.5	6.6 ± 2.1	3w	WD (enema)	5-ASA	23/24	22/24	1	6
Wang QY 2018 [18]	20	20	12/8	11/9	40.23 ± 11.13	42.82 ± 15.93	4.65 ± 3.96	3.12 ± 5.13	1w	WD (enema)	Nacl injection	17/20	9/20	/	/
Wei WX 2017 [19]	34	34	18/16	19/15	42.4 ± 2.5	45.9 ± 2.8	2.3 ± 0.5	3.1 ± 1.4	4w	WB + Prednisone	Prednisone	31/34	25/34	/	/
Tang JR 2017 [20]	35	34	16/19	17/17	41.5 ± 9.41	40.63 ± 9.13	N	N	12w	WB +5-ASA	5-ASA	34/35	28/34	/	/
Li LF 2017 [21]	33	22	N	N	N	N	N	N	15 d	WB	Norfloxacin	30/33	17/22	/	/
Wei H 2016 [22]	38	38	20/18	19/19	43.35 ± 4.36	43.38 ± 4.39	4.86 ± 1.22	4.88 ± 1.25	6w	WB +5-ASA	5-ASA	36/38	30/38	0	0
Jia N 2016 [23]	40	40	21/19	22/18	43.2 ± 11.5	42.6 ± 15.3	4.7 ± 1.5	4.6 ± 2.3	8w	WB +5-ASA	5-ASA	39/40	30/40	/	/
Wang JP 2016 [24]	49	47	20/29	19/28	31.0 ± 5.6	33.4 ± 4.2	23.1 ± 9.23	24.8 ± 8.5	30-60 d	WB	SASP	44/49	35/47	/	/
Wu XB 2015 [25]	35	35	23/12	24/11	37.5 ± 4.5	39.5 ± 5.5			8w	WB +5-ASA	5-ASA	33/35	26/35	/	/
Chen LS 2015 [26]	55	55	30/25	24/31	38.48 ± 4.82	37.52 ± 4.76	6.24 ± 3.08	6.31 ± 2.84	8w	WD	SASP	52/55	40/55	/	/
Wang JL 2014 [27]	62	60	33/29	31/29	45.2 ± 5.08	47.15 ± 6.23	4.91 ± 2.57	5.28 ± 2.91	4w	WB + SASP	SASP	59/62	45/60	/	/
Wu QP 2014 [28]	16	15	9/7	9/6	45.19 ± 11.461	45.80 ± 15.7	54.56 ± 29.052	52 ± 25.545	6 m	WB +5-ASA	5-ASA	15/16	11/15	/	/
Fan CX 2014 [29]	43	40	N	N	N	N	N	N	2 m	JWB + SASP	SASP	38/43	28/40	3	8
Xu BM 2014 [30]	61	61	35/26	39/22	40	42	N	N	4w	WB	SASP	55/61	43/61	0	5
Zhou Y 2013 [31]	20	20	12/8	11/9	32.0 ± 6.35	30.2 ± 6.17	21.18 ± 9.94	26.25 ± 6.92	60 d	WB + SASP	SASP	18/20	16/20	/	/

(*continued on next page*)

Table 1 (*continued*)

Studies	Sample size		Sex ratio (M/W)		Age (years)		Course of disease		Course of treatment	Intervention	ORR			Adverse Reaction	
	T	C	T	C	T	C	T	C		T	C	T	C	T	C
Yang JB 2013 [32]	50	50	N	N	N	N	N	N	4w	WD + SASP	SASP	46/50	34/50	/	/
Huang HT 2013 [33]	35	35	19/16	20/15	46	44	3.45	2.9	3w	WB	SASP	31/35	26/35	/	/
Li SJ 2012 [34]	35	35	17/18	20/15	45.47 ± 11.85	47.66 ± 12.21	5.8 ± 1.6	6.0 ± 1.5	8w	WB + Olsalazine	Olsalazine	32/35	25/35	5	6
Zhang H 2012 [35]	58	58	37/21	35/23	40	41	N	N	8w	WB (oral & enema)	SASP	54/58	48/58	0	1
Xin FB 2011 [36]	47	47	31/16	47/28	38	37.2	N	N	2w	WB + Amoxicillin + enema	Amoxicillin + enema	45/47	36/47	/	/
Yao MW 2010 [37]	29	27	N	N	N	N	N	N	2 m	WB	SASP	28/29	22/27	/	/
Zhang L 2009 [38]	60	26	42/18	18/8	N	N	N	N	40-60 d	WB	azathioprine	58/60	23/26	/	/
Yang YL 2008 [39]	63	57	27/36	25/32	35.5 ± 4.6	34.1 ± 4.2	6.3 ± 3.4	6.2 ± 3.8	2 m	WD	SASP	61/63	42/57	0	5
Guo HB 2007 [40]	44	44	20/24	23/21	35.4	33.6	1.42	1.12	6 m	WB	SASP	42/44	38/44	/	/
Shi DM 2005 [41]	200	198	114/86	102/96	41 ± 16	40 ± 14	3.62	3.44	10w	WB + SASP	SASP	182/200	151/198	/	/
Chen YB 2005 [42]	46	45	N	N	N	N	N	N	1 m	WB	SASP	37/46	24/45	/	/
Wang XP 2002 [43]	28	26	16/12	15/11	N	N	N	N	4w	WB (add drugs) +SASP	SASP	26/28	19/26	/	/

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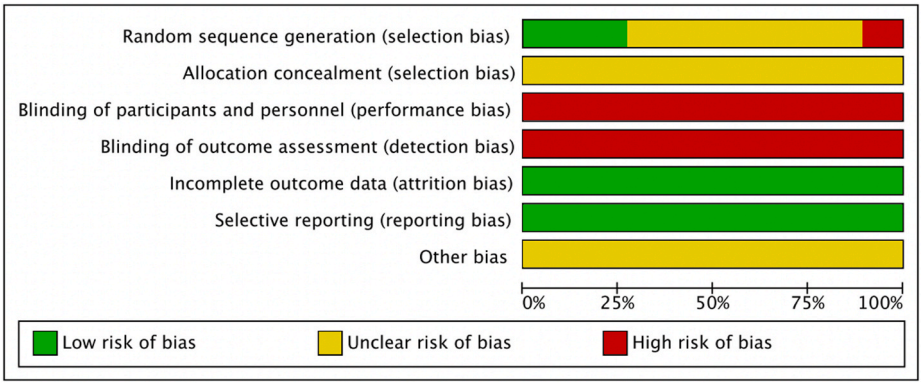

Fig. 2. Risk of bias graph.

treatment of UC with evidence-based medicine method to make contributions to clinical medication reference.

2. Methods

2.1. Selection of studies

Literature retrieval databases include CNKI, Wanfang Data database, VIP Full-text Database of Chinese Scientific and Technological Journals, Pubmed, Web of Science (WOS) and other databases. The collection of literature was from the date of database establishment to December 2022. The search words include: “Wu Mei” “fructus mume” “Ulcerative colitis”. The retrieval type is “Wu Mei” or “fructus mume” and “Ulcerative colitis".

2.2. Inclusion criteria

2.2.1. Study type

Included were Randomized Controlled Trials (RCT). Documents can be obtained in full or sufficient information can be obtained from abstract.

2.2.2. Study object

Patients diagnosed with ulcerative colitis according to relevant guideline criteria (e.g.: Patients have predominantly persistent or recurrent diarrhea. Other symptoms include abdominal pain, bloody mucus, weight loss, tenesmus, and vomiting), and patients with Crohn’s disease, other colitis, and inflammatory enteritis are excluded, regardless of age, gender, course of disease, region, etc.

2.2.3. Interventions

The experimental group was treated with Wumei Bolus or decoction alone or combined with Western medicine (the western medicine treatment should be the same as the control group); The control group was treated with western medicine.

2.2.4. Outcome indicators

The main indicator was clinical efficacy, refer to the standards formulated by the Inflammatory Bowel Disease Collaborative Group of the Gastroenterology Branch of the Chinese Medical Association [6]; other indicators included TCM symptom score, Inflammatory factors (TNF-α、IL-8) and adverse reactions, etc.

2.3. Exclusion criteria

(1) The experimental group combined with other TCM therapies; (2) non-RCT study; (3) Repeat passages; (4) Animal experiments; (5) No full-text articles, no outcome indicators, and no data extraction.

2.4. Data extraction

Two researchers independently conducted literature retrieval, collated literature, and extracted data according to the data extraction table, and then cross-checked. If there was any disagreement, it should be discussed or determined through negotiation with the third researcher. Data extraction includes basic information of the literature, research type and methodological characteristics of the literature, basic characteristics of the research object, sample size, intervention measures, outcome indicators, etc.

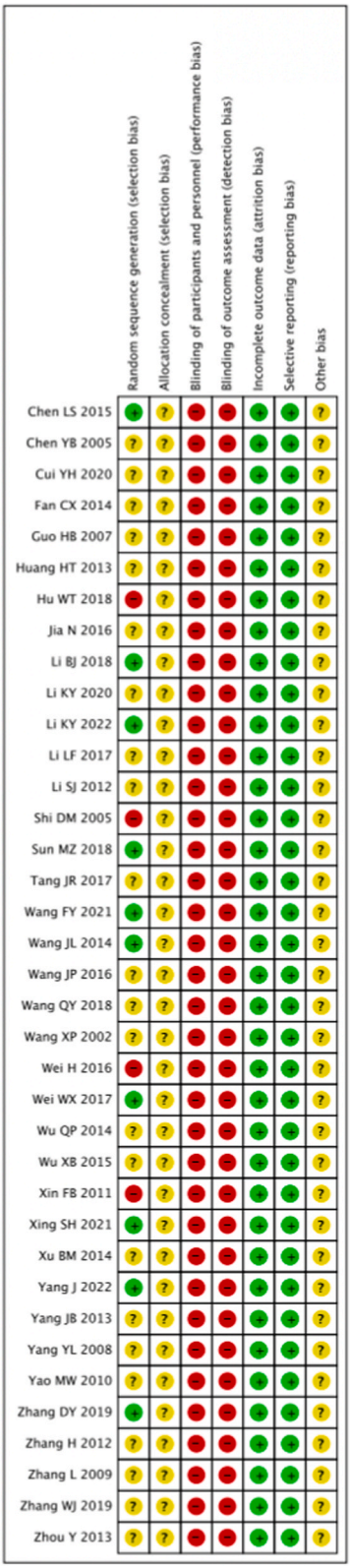

Fig. 3. Risk of bias summary.

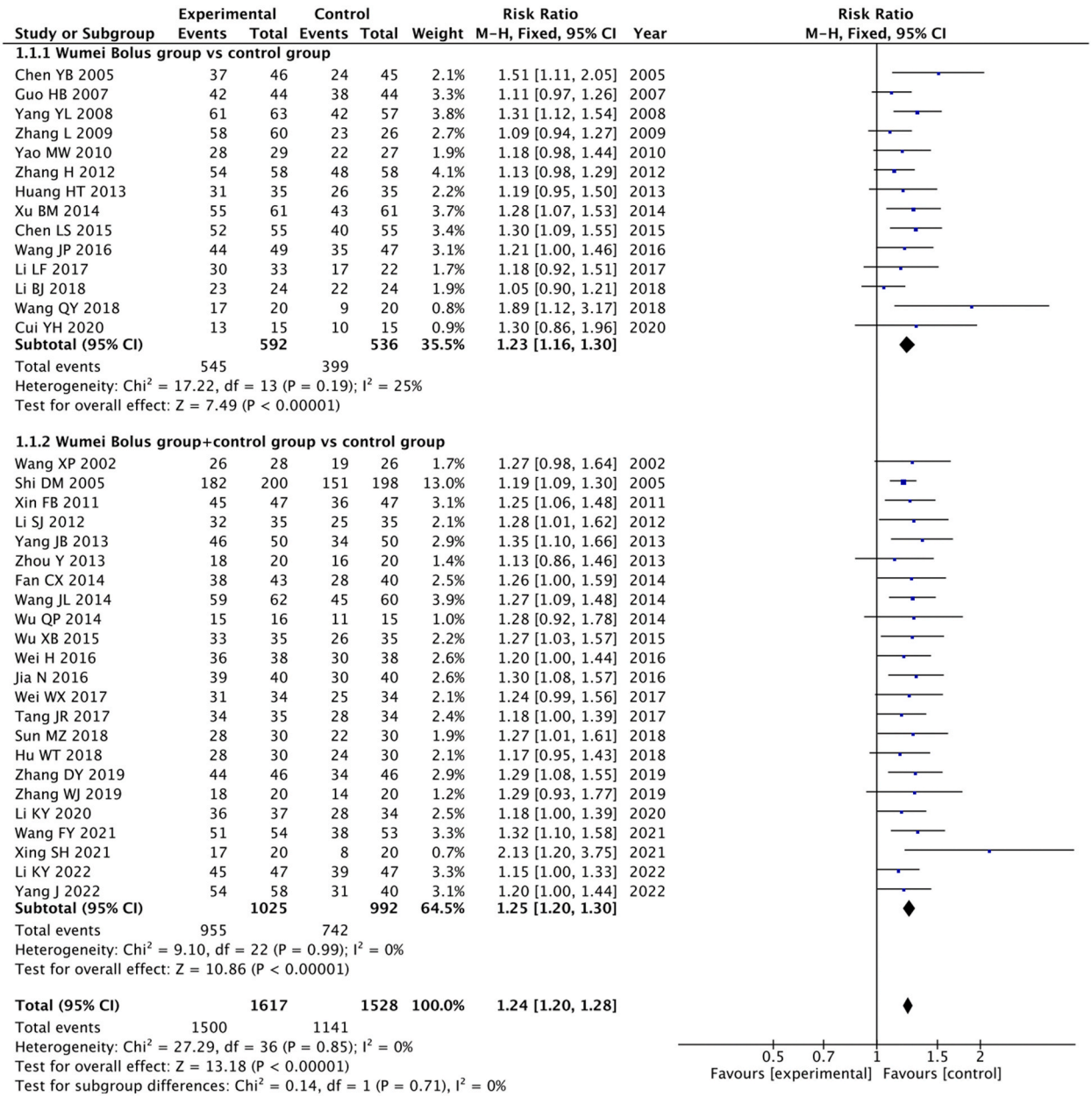

Fig. 4. Forest plot of ORR.

2.5. Quality evaluation

Quality assessment was carried out according to the bias risk assessment tool recommended by Cochrane system evaluator manual. The assessment items included: (1) Random sequence generation (selection bias); (2) Allocation concealment (selection bias); (3) Blinding of participants and personnel (performance bias); (4) Blinding of outcome assessment (detection bias); (5) Incomplete outcome data (attrition bias); (6) Selective reporting (reporting bias); (7) Other bias. Each item was evaluated as "unclear", "low risk" and "high risk" (low risk bias if satisfied, high risk bias if not satisfied; If not reported in the literature, it is evaluated as unclear).

2.6. Statistical analysis

Meta-analysis was performed using RevMan 5.4 and Stata 15.0 software. Odds ratio (*OR*) or relative risk (*RR*) were used as effect size to analyze dichotomous variable. The weighted mean difference (*WMD*) or standardized mean difference (*SMD*) were used as effect size to analyze continuous variable. And 95% confidence intervals (*CI*) were calculated for two kinds of variables. Heterogeneity

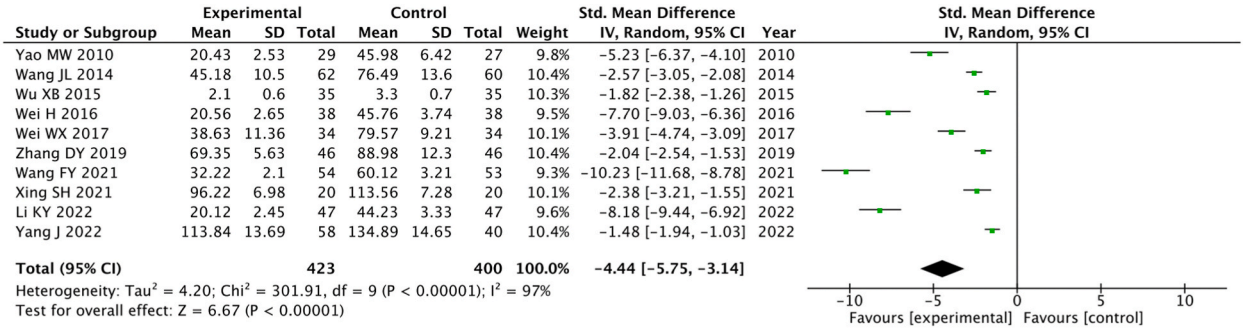

Fig. 5. Forest plot of inflammatory factor TNF-α.

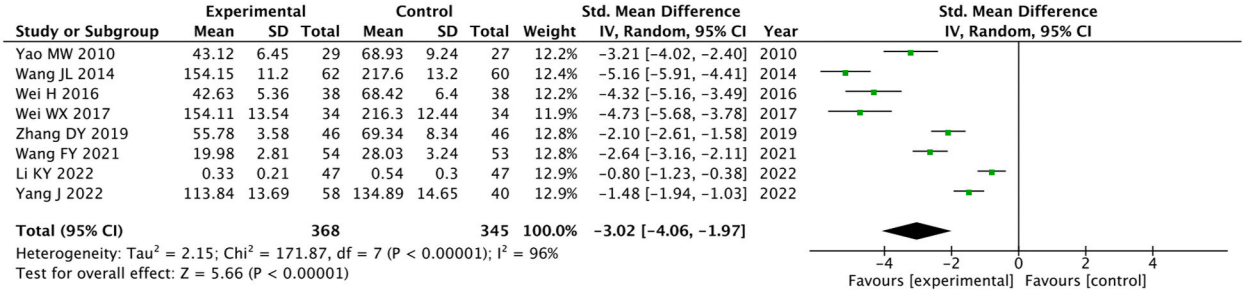

Fig. 6. Forest plot of inflammatory factor IL-8.

test was carried out according to I^2 value. If $P \geq 0.1$, $I^2 \leq 50\%$, fixed effect model was used. Otherwise, random effect model is used. Egger's test was used to examine the inclusion of studies for potential publication bias.

3. Results

3.1. Literature retrieval results

We initially retrieved 849 articles. After reading the title and abstract, a total of 111 literature were selected for full-text screening. After reading the full-text, 74 literatures were excluded again, and a total of 37 literature were finally included for analysis. (Fig. 1).

3.2. Basic features of the study

Among the 37 included RCT studies, the experimental group of 14 literature used Wumei Bolus or decoction, plus or minus to treat UC, and the experimental group of 23 literature combine western medicine to treat UC. There was a total of 3145 patients, including 1617 in the experimental group and 1528 in the control group (Table 1).

3.3. Risk assessment of literature bias

The included literature was evaluated according to the Cochrane Manual. The results showed that: (1) nine studies were assessed as 'low risk' by using random number table, one study used lottery and was rated as 'low risk', one study evaluated as 'high risk' based on

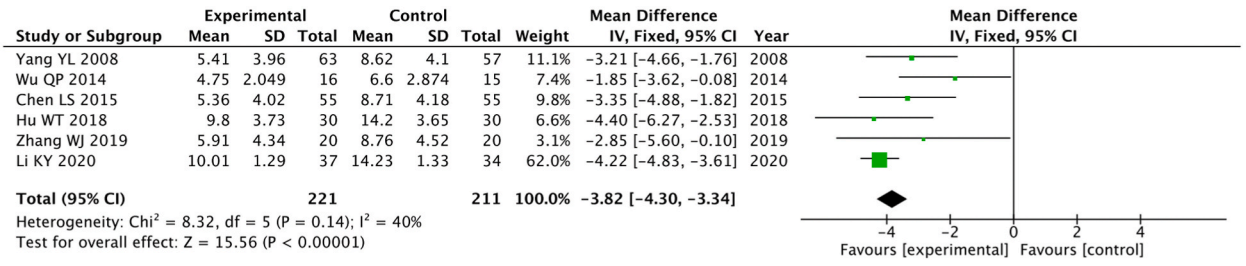

Fig. 7. Forest plot of Tcm syndrome points.

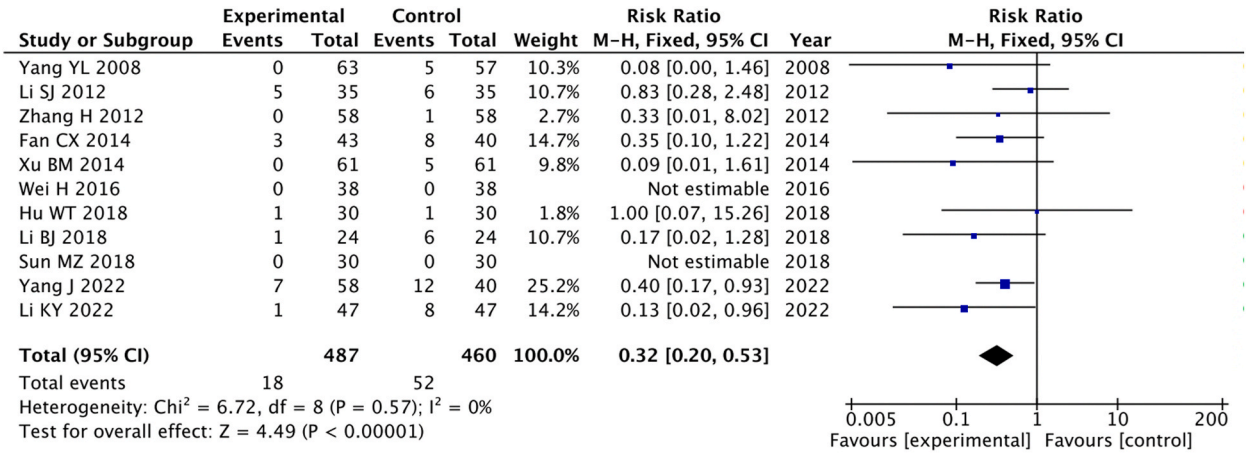

Fig. 8. Forest plot of safety evaluation.

treatment regimen, one study rated it as 'high risk' based on the patient's wishes, two studies were rated as 'high risk' based on the order of visit. The other literature did not describe the method of random grouping, which was evaluated as unclear. (2) All studies did not describe the allocation concealment, evaluation was 'unclear'; (3) None of the studies described the blinding to patients, researchers, and outcome evaluators, and the evaluation was 'high risk '; (4) All studies had complete outcomes and were evaluated as 'low risk'; (5) All studies were not selectively reported and were evaluated as 'low risk'; (6) All studies did not describe other biases and were evaluated as 'unclear'. Shown as 'Risk of bias graph' (Fig. 2) and 'Risk of bias summary'. (Fig. 3).

3.4. Results of meta-analysis

3.4.1. Evaluation of clinical overall response rate (ORR)

All the studies took the ORR as the outcome index. After heterogeneity test, the homogeneity of each study was good, and the fixed-effect model was adopted. The ORR was dichotomous variable, expressed by relative risk (*RR*) and 95%*CI*. (Fig. 4). The ORR was 1500/1617 (92.76%) in experimental group and 1141/1528 (74.67%) in control group. Combined effect size $RR = 1.24$, 95%*CI* [1.20, 1.28], $Z = 13.18$, $P < 0.00001$, the difference was statistically significant, indicating that the ORR of Wumei Bolus in the treatment of UC was higher than that of the control group, and the clinical efficacy was significant. According to the different intervention measures of the experimental group, subgroup analysis was conducted, and the results showed that compared with the western medicine group, the

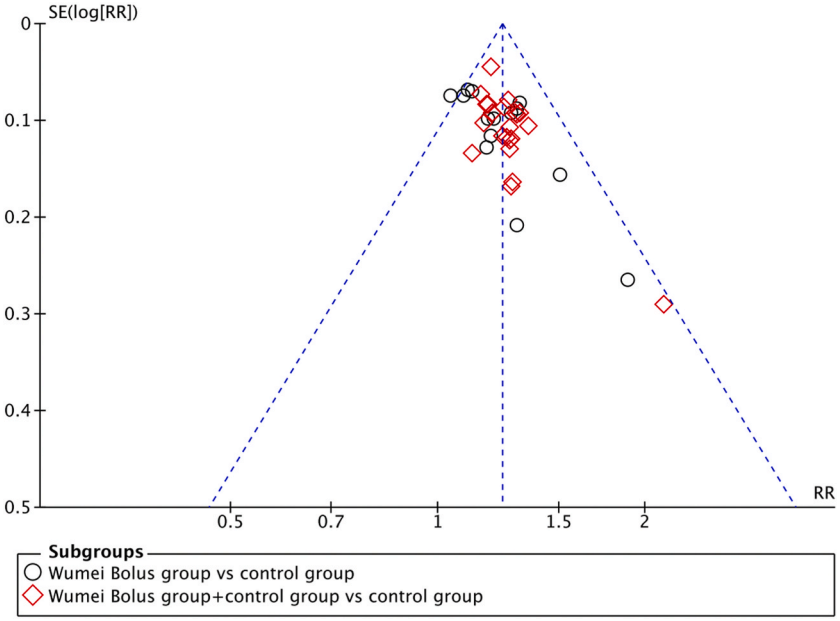

Fig. 9. Publish bias.

combined effect size ($RR = 1.23$, 95%CI [1.16, 1.30], $Z = 7.49$, $P < 0.00001$) in the group of Wumei Bolus was statistically significant, indicating that the ORR of Wumei Bolus in the treatment of UC was higher than that of the control group. Compared with the control group, the combined effect size ($RR = 1.25$, 95%CI [1.20, 1.30], $Z = 10.83$, $P < 0.00001$) in the group of Wumei Bolus combined with western medicine, the difference was statistically significant, indicating that the ORR of Wumei Bolus combined with western medicine was higher than that of the control group.

3.4.2. Evaluation of inflammatory factors TNF-α& IL-8

(1)A total of 10 studies described the results of the inflammatory factor TNF-α, and the heterogeneity test showed $P < 0.00001$, $I^2 = 97\%$, indicating that there was great heterogeneity between studies, and a random-effects model was used. TNF-α was a continuous variable but the scoring units were not uniform, and the Standardized Mean Difference (SMD) was used as the effect size analysis, the combined effect size $SMD = -4.44$, 95%CI was [−5.75, −3.14], $Z = 6.67$, $P < 0.00001$, the difference was statistically significant, indicating that the effect of Wumei Bolus in reducing the inflammatory factor TNF-α in UC patients was better than that of the control group (Fig. 5).

(2)8 studies reported the results of inflammatory factor IL-8, the results of heterogeneity test analysis $P < 0.00001$, $I^2 = 96\%$, heterogeneity, using random-effects model analysis, meta-analysis showed $SMD = -3.02$, 95%CI was [−4.06, −1.97], $Z = 5.66$, $P < 0.00001$, the difference was statistically significant, indicating that the effect of Wumei Bolus in reducing inflammatory factor IL-8 in UC patients was better than that of the control group (Fig. 6).

3.4.3. Evaluation of TCM syndrome points

Six studies in the included literature reported the results of TCM syndrome points, heterogeneity test analysis showed $P = 0.14$, $I^2 = 40\%$, because $I^2<50\%$, indicating that the homogeneity between studies was good, so a fixed-effect model was used, and the analysis results showed $SMD = -3.82$, 95%CI was [−4.30, −3.34], $Z = 15.56$, $P < 0.00001$, the difference was statistically significant, indicating that the effect of Wumei pills in alleviating symptoms in UC patients was better than that of the control group (Fig. 7).

3.5. Safety evaluation

Nine of the 37 studies described adverse effects. The results showed that, compared with the control group, the combined effect size ($RR = 0.32$, 95%CI [0.20, 0.53], $Z = 4.49$, $P < 0.00001$) was statistically significant, indicating that the incidence of adverse reactions in the treatment of UC in the experimental group was significantly lower than that in the control group (Fig. 8). Among the 11 studies, adverse reactions occurred in the experimental group in 6 of them, including nausea and vomiting in 9 patients and abdominal pain in 3 patients, which were analyzed as side effects of combined treatment with western drugs.

3.6. Publish bias assessments

With the total effective rate as the benchmark, RR value as the abscissa and logRR value as the ordinate to draw a funnel plot. The results show that although points are distributed in the inner part of 'the funnel', the distribution on both sides is not symmetrical, indicating the existence of publication bias (Fig. 9). Because too few studies included secondary indicators, the funnel chart lacked rigor, so further Egger's test showed that the P values of clinical efficacy, inflammatory factors, TCM syndrome scores and adverse reactions were 0.0001, 0.0001, 0.002, 0.127 and 0.14, respectively, among which the P values of TCM syndrome scores and adverse reactions >0.05, indicating no obvious publication bias. The P value of clinical efficacy and inflammatory factors <0.05, indicating significant publication bias.

3.7. Sensitivity analysis

The sensitivity analysis of the indicators of the results of the study results, the analysis of the included studies by the method of exclusion one by one, and the stability of the conclusions were evaluated, and the results showed that the combined results of the remaining studies did not show significant changes in the efficacy criteria after exclusion, indicating that the stability was good. (Fig. 10(A-E)).

4. Conclusions

As a refractory digestive tract disease, UC has a long and repeated course of disease, and some patients may even suffer from toxic megacolon, intestinal perforation, massive bleeding and canceration, which endangers people's health. Although there is no UC disease name in traditional Chinese medicine, it can be classified as "intestinal diarrhea", "diarrhea", "blood in the stool" and "long-term diarrhea" according to its clinical manifestations and combined with classical medical records, and modern medicine commonly uses plum pills to treat abdominal pain, diarrhea caused by spleen and stomach deficiency. Therefore, as a common prescription for the treatment of ulcerative colitis, Wumei Bolus has abundant clinical cases and experimental evidence. Wumei Bolus was first seen in 'Treatise on Cold Pathogenic and Miscellaneous Diseases'. It consists of *Prunus mume (Siebold) Siebold & Zucc, Asarum sieboldii Miq, Zingiber oj-jicinale Rosc, Coptis chinensis Franch, Phellodendron chinense Schneid, Angelica sinensis, Aconitum carmichaeli Debx, Zanthoxylum bungeanum Maxim, Cinnamomum cassia Presl and Panax ginseng C. A. Meyer* (The plant name has been checked with http://www.theplantlist.org)." Soak the plum with bitter wine (vinegar) overnight, remove the pit, steam it, and pound it into mud; More medicine

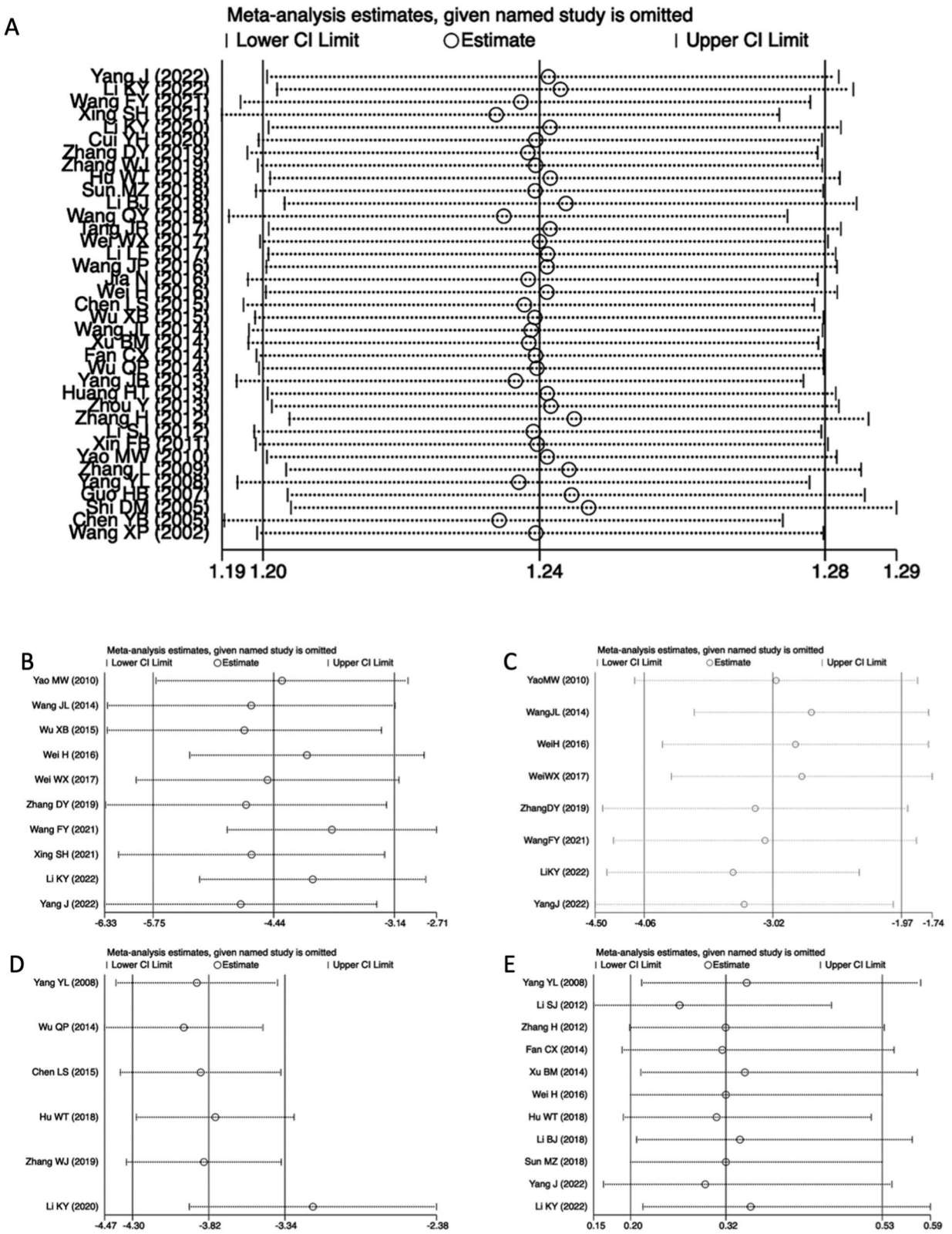

Fig. 10. (A–E)Sensitivity Analysis. A: clinical efficacy; B: Inflammatory factors (TNF- α); C: Inflammatory factors (IL-8); D: TCM symptom score; E: adverse reactions.

research for fine end, and black plum mud and evenly, encryption for pills, such as the size of sycamore. Take 7–9 g each, three times a day. Cold, slippery and smelly food are forbidden."

Wumei Bolus for cold and heat parallel prescription, *Prunus mume (Siebold) Siebold & Zucc* taste acid, warm the body, make ascaris quiet, astringent intestinal, dysentery; *Zanthoxylum bungeanum Maxim* for the characteristic of the xinwen, both drive ascaris and cold; *Aconitum carmichaeli Debx*, *Asarum sieboldii Miq*, *Zingiber oj-jicinale Rosc*, *Cinnamomum cassia Presl* warm viscera and remove cold; *Coptis chinensis Franch* and *Phellodendron chinense Schneid* clear heat and dry dampness; *Panax ginseng C. A. Meyer* and *Angelica sinensis* nourish 'qi' and blood. Wumei Bolus moderate the liver, regulate spleen and stomach, cold the upper, warm the lower, treat abdominal pain, dysentery, and diarrhea. Modern pharmacological studies have confirmed that Wumei Bolus has the effects of anti-inflammatory, antibacterial, anti-tumor, immunosuppression, promoting ulcer healing, regulating gastrointestinal function, and enhancing body immunity [44]. At present, many basic experimental studies have confirmed that Wumei Bolus can treat UC by regulating cytokines and their participating signaling pathways, reducing inflammatory mediators, repairing mucosal barriers, regulating immune function, promoting the recovery of gastrointestinal function, and oxidative damage [4]. Wumei Bolus exert a therapeutic effect on UC by upregulating anti-inflammatory cytokines in UC model rats and downregulating pro-inflammatory cytokines [45]. It can increase the level of serum IL-10 and IL-4 in UC model rats [46] and inhibit the abnormal activity of IL-6/JAK/STAT3 signaling pathway in colonic mucosal tissue of UC model rats, reduces the level of serum IL-8, IL-6 [47,48]. Both Wumei Bolus and their dismantling formulas reduced the content of inflammatory mediators - myeloperoxidase (MPO) and prostaglandin E2 (PGE2) in UC model rats, and the addition and subtraction of Wumei Bolus could be subtracted [49]. The contents of platelet activating factor (PAF) and *P*-selectin in UC model rats were adjusted to reduce the expression of intercellular adhesion molecule (ICAM)-1 [50,51], thereby reducing intestinal mucosal damage. Studies have shown that Wumei Bolus can play the role of downregulating blood adhesion molecules CD_{44} and CD_{54} and restore the immune function of UC model rats by increasing the apoptosis sensitivity of colon tissue $CD4^+$ T cells, reducing inflammatory cytokine secretion [52,53]. Fas/FasL-mediated mass apoptosis of colonic epithelial cells plays an important role in the pathogenesis of UC, and Wumei Bolus can inhibit excessive apoptosis of colonic epithelial cells and promote the repair of the colonic mucosal barrier by inhibiting the activation of the Fas/FasL signaling pathway [54]. Moreover, Wumei Bolus can treat UC by acting on the Notch signaling pathway, which has the key pathway that regulates the differentiation and proliferation of intestinal epithelial cells, participates in the maintenance of intestinal epithelial cells, and maintains the antibacterial activity of intestinal epithelial cells [55]. It was found that the regulation effect of wumei on intestinal flora was mainly reflected in improving the proportion of beneficial bacteria and harmful bacteria and regulating the abundance of intestinal flora. Li YiFei [2,56] constructed a broad-spectrum antibiotic induced intestinal microbiota disorder model in mice and compared the intestinal microbiota of mice before and after umme intervention by 16SrRNA gene sequencing. It is proved that wumei can regulate intestinal flora, change intestinal microecological environment and cure complex digestive system diseases. A large number of clinical and animal experimental studies have confirmed that Wumei Bolus can effectively reduce the levels of serum inflammatory factors, such as IL-8, TNF-α, IL-17, IL-23, etc. [57], and treat UC through multi-target and multi-pathway, with significant clinical efficacy and strong application prospect.

Through systematic and comprehensive retrieval and strict screening, 35 literatures were finally included in this paper, with a total sample size of 2953 cases, including 1512 cases in experimental group and 1441 cases in control group. The results of meta-analysis showed that the total clinical effective rate of Wumei Bolus (Tang) decoctio for the treatment of ulcerative colitis was higher than that of conventional Western medicine group, which could better reduce pro-inflammatory cytokines and improve TCM symptoms, and the incidence of adverse reactions in the experimental group was lower than that in the control group. Moreover, the stability and high reliability between various studies can be used as one of the clinical application methods. However, in the analysis of inflammatory factor results, we found that the heterogeneity was high, and we believe that the difference in treatment course and unit led to large differences in study quality, which may be the reason for the high heterogeneity. It can be used as an effective clinical treatment. It can be considered from both macroscopic and mechanistic aspects that the total clinical effective rate of Wumei Bolus in the treatment of UC is better than that of western medicine alone, and the combined treatment can enhance the clinical efficacy of western medicine and the safety is higher.

This study confirmed that Wumei Bolus could effectively treat UC from the perspective of evidence-based medicine, which provided a basis for clinical application. However, it also had limitations: (1) most of the literatures did not describe the randomized method, blind method was not reported in all the literatures, and the experimental protocol was not described. There was a possibility of selective reporting, and other bias was not described. (2) TCM diagnosis and treatment will increase or decrease according to the symptoms of patients, and there will be differences in therapeutic drugs, and there are differences among different studies; (3) Follow-up of patients, shedding of cases and adverse reactions were not described in most literatures; (4) There was a large difference in outcome indicators, and systematic analysis was not conducted.

Therefore, although this article was able to demonstrate the effectiveness of Wumei Bolus in the treatment of UC, the conclusions of this study still need to be supplemented by more centers, large samples and high-quality RCT studies, to further improve the quality of the study, enhance the credibility and scientific nature of the analysis, and provide more powerful evidence for clinical application.

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Data availability statement

Data included in article/supplementary material/referenced in article.

Author contributions

Zepeng Chen: Wrote the paper, Analyzed and interpreted the data, Conceived and designed the study, Performed the study.
Linhai He: Analyzed data and filtered articles, Performed the study.
Wenwen Tang: Analyzed data and filtered articles, Performed the study.
Qinglong Gu: Analyzed and interpreted the data, Performed the study.
Kuiling Wang: Analyzed data and filtered articles.
Yuji Wang: Analyzed data and filtered articles.
Ruichao Chen: Contributed analysis tools.
Yugen Chen: Conceived and designed the experiments, Contributed analysis tools.
All authors read and approved the final manuscript.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. The authors declare the following financial interests/personal relationships which may be considered as potential competing interests.

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Abbreviations

UC: ulcerative colitis;
WOS: Web of Science;
RCT: Randomized Controlled Trials;
OR: odds ratio;
RR: relative risk;
WMD: weighted mean difference;
SMD: standardized mean difference;
CI: confidence intervals;
5-ASA: 5-aminosalicylic acid;
ORR: overall response rate;
WB: Wumei Bolus;
WD: Wumei Decoction;
SASP: Salicylazosulphapyridine Salazosulfapyridine