Integrative Medicine Research 14 (2025) 101098

Contents lists available at ScienceDirect

Integrative Medicine Research

journal homepage: www.elsevier.com/locate/imr

Review Article

Effectiveness and safety of combined treatment with herbal medicines and palliative chemotherapy for advanced gastric cancer: A systematic review and meta-analysis

Dong-Hyeon Kim [a,b], Soo-Dam Kim [c], Hyeong-Joon Jun [d], Eun-Bin Kwag [b,e], Sang-Won Shin [f], Hwa-Seung Yoo [g], So-Jung Park [a,h,*]

[a] Department of Korean Internal Medicine, Korean Medicine Hospital, Pusan National University, Yangsan, Republic of Korea
[b] Department of Korean Medicine, Graduate School, Daejeon University, Daejeon, Republic of Korea
[c] KM Science Research Division, Korea Institute of Oriental Medicine, Daejeon, Republic of Korea
[d] KM Data Division, Korea Institute of Oriental Medicine, Daejeon, Republic of Korea
[e] Integrative Medicine Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY, United States
[f] Department of Humanities & Social Medicine, School of Korean Medicine, Pusan National University, Yangsan, Republic of Korea
[g] East West Cancer Center, Seoul Korean Medicine Hospital, Daejeon University, Seoul, Republic of Korea
[h] Department of Korean Internal Medicine, School of Korean Medicine, Pusan National University, Yangsan, Republic of Korea

ARTICLE INFO

Keywords:
Advanced gastric cancer
Herbal medicine
Palliative chemotherapy
Meta-analysis

ABSTRACT

Background: Advanced gastric cancer (AGC) is a leading cause of cancer-related death worldwide, and its treatment is complicated by challenges such as high recurrence rates, severe side effects, and the limited effectiveness of current therapies. Herbal medicine (HM) has emerged as an adjunct to palliative chemotherapy (PC), potentially improving the tumor response and reducing side effects. This study involved a meta-analysis to evaluate the effectiveness and safety of HM in palliative therapy for patients with inoperable stage III and IV AGC.
Methods: Ten electronic databases, including PubMed, Embase, the Cochrane Library, CNKI, and ScienceON, were searched until August 2023. The inclusion criteria focused on randomized controlled trials (RCTs) that combined herbal medicine with palliative therapy for patients with AGC. The primary outcomes assessed were tumor response rates, overall survival, adverse drug reactions (ADRs), and patients' quality of life (QoL).
Results: Our meta-analysis of the 101 included RCTs comparing PC alone to PC combined with HM revealed statistically significant improvements in the overall response rate (ORR), disease control rate (DCR), and survival rates, as well as a reduction in adverse drug reactions (ADRs) and an enhancement in the quality of life (QoL) of patients receiving HM in combination with PC ($p < 0.00001$, $I^2 = 0\%$).
Conclusions: The combination of HM with PC significantly increases tumor response and survival rates while reducing overall adverse drug reactions (ADRs) and improving the quality of life (QoL) of patients with stage III and IV AGC. HMs not only improve the efficacy of PC but also help alleviate side effects, including myelosuppression, digestive symptoms, nausea, vomiting, diarrhea, liver and renal injuries, and neurotoxicity.
Protocol registration: PROSPERO, CRD 42022354133.

1. Introduction

Gastric cancer (GC) is the fourth leading cause of cancer-related death and the fifth most common cancer globally as of 2020, according to the Global Cancer Observatory (GCO). The incidence rate of GC in men is twice that in women.[1] Unfortunately, GC has a poor prognosis, with approximately 60% of patients diagnosed with advanced disease worldwide.[2] Once GC progresses to an advanced stage, surgical intervention becomes considerably less feasible, and the disease tends to advance rapidly. Tumors extending into the muscle layer but not invading the surrounding organs are classified as middle-stage gastric cancers, whereas those infiltrating nearby organs are categorized as advanced-stage gastric cancer. Currently, chemotherapy serves as the cornerstone treatment for advanced GC (AGC) and can be divided into three

* Corresponding author at: Department of Korean Internal Medicine, School of Korean Medicine, Pusan National University, Geumoro 20, Mulgeum-eup, Yangsan-si, Gyeongnam, 50612, Republic of Korea.
E-mail address: vivies@hanmail.net (S.-J. Park).

https://doi.org/10.1016/j.imr.2024.101098
Received 18 January 2024; Received in revised form 30 October 2024; Accepted 13 November 2024
Available online 22 November 2024

main categories: palliative chemotherapy (PC), adjuvant chemotherapy, and neoadjuvant chemotherapy. Clinical practice guidelines recommend palliative chemotherapy as a treatment option for patients with incurable or recurrent disease.[3]

Standard chemotherapy for AGC uses targeted agents or cytotoxic drugs according to the National Comprehensive Cancer Network (NCCN) guidelines.[3] Treatment is increasingly standardized and personalized. The initial treatment targets human epidermal growth factor receptor 2 (HER2) in advanced metastatic cases. Common chemotherapy regimens for AGC often include platinum-based therapies. These treatments include combinations such as FOLFOX (folinic acid, fluorouracil [5-Fu] and oxaliplatin), SOX (tegafur [S-1] and oxaliplatin), and XELOX (capecitabine and oxaliplatin). Despite its effectiveness, chemotherapy can cause gastrointestinal reactions, bone marrow suppression, and peripheral neuropathy. These side effects often force patients to modify or discontinue their chemotherapy treatment. Consequently, for patients with inoperable AGC, the median survival rate is < 1 year, and the 5-year survival rate is 6.7%, which is still very low.[1]

Herbal medicine (HM) is widely used as a complementary and alternative therapy for AGC patients in Korea and other East Asian countries, The Society for Integrative Oncology is also deeply interested in this issue.[4,5] However, currently, the development of a standardized herbal treatment plan for AGC is ongoing in Korea.[6-8] The treatment approach for AGC has evolved from the holistic concept provided by traditional medicine to evidence-based treatment methods. Unlike conventional medicine, which often uses the same prescription for patients with the same conditions, traditional Korean medicine utilizes various herbal prescriptions based on pattern identification, making the development of evidence-based treatment methods difficult. This approach aligns with the concept of “different treatments for the same disease,” highlighting the diversity in therapeutic approaches within traditional Korean medicine.[9] However, the traditional approach has shown remarkable results in reducing toxicity, improving treatment efficacy, extending patients’ lifespan, alleviating clinical symptoms, enhancing immunity, and improving quality of life (QoL).[10] Numerous randomized controlled trials (RCTs) utilizing various herbal treatments for patients with AGC have been reported. The aim of this study is to conduct a meta-analysis to evaluate the effectiveness and safety of combining herbal medicine with palliative chemotherapy in the treatment of advanced gastric cancer.

2. Methods

This protocol was registered with The International Prospective Register of Systematic Reviews (PROSPERO: CRD 42022354133). The reporting of this review adheres to the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Supplement 1).[11]

2.1. Inclusion and exclusion criteria

2.1.1. Study types

This review included only randomized controlled trials (RCTs) that explicitly stated the use of randomization.

2.1.2. Participant types

The participants included those diagnosed with TNM stage III-IV gastric cancer, confirmed by pathology, with no restrictions on age or sex.

2.1.3. Intervention types and controls

Studies that combined HMs, such as multi-ingredient formulations, in the intervention group were considered without restrictions on administration. Additionally, studies in which chemotherapy, particularly platinum-based regimens such as FOLFOX, SOX, and XELOX, was used according to NCCN guidelines and HMs were part of the intervention group (compared with chemotherapy alone in the control group) were also included, regardless of the treatment duration or clinical setting.

2.1.4. Outcome measures

The primary outcome was the tumor response, which was assessed according to the Response Evaluation Criteria in Solid Tumors (RECIST[12]) or the WHO Solid Tumor Therapeutic Evaluation Criteria.[13] In particular, the primary outcomes of interest were the objective response rate (ORR) and disease control rate (DCR). The ORR was defined as the sum of patients who achieved a complete response (CR) and partial response (PR), whereas the DCR included patients who experienced a CR, PR, and stable disease (SD).

The secondary outcomes included survival rates, quality of life (QoL), and adverse drug reactions (ADRs). Survival outcomes included overall survival (OS) and 1- to 5-year survival rates. OS was defined as the duration from the initiation of the trial to the recorded date of death from any cause or the date of the last follow-up. QoL was specifically assessed using the Karnofsky Performance Status (KPS) score, where an improvement was defined as an increase in the score of 20 points or more between the pretreatment and posttreatment evaluations. ADRs were also evaluated, and although the grading of side effects according to Common Terminology Criteria for Adverse Events (CTCAE) v5.0[14] was not included, the incidence rate of each ADR reported in the studies was compiled. The ADRs assessed included myelosuppression, neutropenia, thrombocytopenia, anemia, digestive symptoms (nausea, vomiting, and diarrhea), hepatic dysfunction, renal dysfunction, neurotoxicity, and oral mucositis, as recommended by CTCAE v5.0. Studies that reported only the total effective rate or the efficacy of the traditional Chinese medicine (TCM) symptom score were excluded.

2.2. Literature search

We searched ten electronic databases to identify studies on the effectiveness and safety of combining traditional herbal medicine with chemotherapy for patients with advanced gastric cancer (AGC): PubMed, Embase, the Cochrane Library, the Chinese National Knowledge Infrastructure (CNKI), Citation Information by NII (CiNii), ScienceON, the Korean Medical Database (KMBase), Regional Information Sharing Systems (RISS), the Korean Information Service System (KISS), and the Outcome and Assessment Information Set (OASIS). We included randomized controlled trials (RCTs) that compared the combination of herbal medicine with chemotherapy to chemotherapy alone. The search was conducted up to August 2023, using the following search terms: “stomach cancer,” “stomach neoplasms,” “gastric cancer,” “gastrointestinal neoplasms,” and “herbal medicine,” “traditional medicine,” “Korean traditional medicine,” “Chinese traditional medicine,” “East Asian traditional medicine,” and “plants,” along with “randomized controlled trial.”

We limited our search to articles published between January 2010 and August 2023 to ensure that only recent and relevant studies were included, while outdated data were excluded. The detailed search strategy is provided in Supplement 2.

2.3. Study selection

The search results were managed using Endnote version 20, and duplicates were removed. Two independent researchers (DHK and SDK) reviewed the titles and abstracts, excluding studies that did not satisfy the inclusion criteria. The full texts were reviewed, and studies satisfying the criteria were included following a consultation between the two researchers. In cases of disagreement, a third researcher (EBK) resolved the issue. The reasons for excluding studies were documented.

2.4. Data extraction

All the articles were read by two independent researchers (DHK and SDK), who extracted data from the articles according to predefined criteria. The extracted data included the author’s name(s), year of publication, sample size, age, sex, stage, herbal medicine intervention,

chemotherapy intervention, treatment dosage and duration, main outcomes, and adverse effects. When the reported data were insufficient or unclear, the author contacted the first author or corresponding authors by e-mail or telephone to request missing data or clarify the details.

2.5. Risk of bias assessment of the included studies

The Cochrane Risk of Bias (RoB) tool was used to evaluate each included trial.[15] Two reviewers independently assessed multiple domains, including random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, completeness of datasets, selective outcome reporting, and other bias, such as ambiguous reporting, and undisclosed outcomes. The assessment of attrition bias focused on whether each document provided detailed descriptions of the dropouts and whether the dropouts influenced the outcomes. Based on this analysis, a “low RoB” rating was assigned. For the assessment of reporting bias, we primarily checked for the presence of a protocol. If a protocol was absent, we also verified whether a review and approval by an ethics committee was described. Additionally, we examined whether any outcomes were omitted. As a result, if the protocol matched the outcomes, it was rated as a “low RoB” (25 %). In cases where the protocol could not be verified but the results were complete, they were categorized as an “unclear RoB” (75 %). For the assessment of other biases, we focused on the clarity of the reports. Documents with unclear or simplified descriptions that hindered clear communication of the intended meaning were rated as an ”unclear/high RoB.” Each domain was categorized as “low”, “high”, or “unclear”. Discrepancies were resolved through consensus by discussion and, where necessary, consultation with a third reviewer.

Building upon this foundation, our quality of evidence assessment utilized the GRADE system[16] to classify the evidence levels as high, moderate, low, or very low. Initially, RCTs provided high-quality evidence, which could be downgraded due to serious limitations, such as a risk of bias, inconsistency, indirectness, and imprecision. Each potential source of bias was carefully considered in context. For example, domains were not downgraded for a high risk of bias if their overall impact on the study outcomes was minimal or adequately addressed in sensitivity analyses. Similarly, while substantial heterogeneity was observed across studies, it did not necessarily lead to downgrading in the inconsistency domain if it did not significantly affect the overall conclusions of the meta-analysis.

Evidence could also be upgraded based on factors such as a large effect size and dose–response relationship. The resulting GRADE evidence profile provided a structured assessment of the quality of the evidence for each outcome, highlighting both strengths and areas requiring further research.

2.6. Data analysis

The meta-analysis followed the Cochrane Handbook 6.1[17] guidelines and utilized Review Manager (RevMan) v.5.4.1 for Windows (The Nordic Cochran Center, Copenhagen, Denmark). Differences between the intervention and control groups were assessed. For the analysis of clinical efficacy, dichotomous data were assessed by calculating the risk ratio (RR), and continuous data were assessed by calculating the mean difference (MD). Dichotomous and continuous variables are presented as efficacy values with 95% conffidence intervals (CIs). A random-effects model was used to assess combined effect sizes from efficacy variables, and substantial clinical heterogeneity was expected across the included studies based on the diversity among the interventions, study designs, and other conditions. Funnel plots were generated to explore potential publication bias.

3. Results

3.1. Study selection

An initial search of medical databases retrieved 702 studies, with 246 duplicates. After removing duplicates, 438 studies remained, and 202 irrelevant studies were excluded based on the title and abstract review. A total of 236 studies were evaluated, and 135 studies were subsequently excluded for the following reasons: not the target population (n = 30), not an RCT or protocol (n = 28), inappropriate intervention (n = 15), inappropriate outcome (n = 12), or thesis (n = 50). In total, 101 studies[18-118] involving 7744 patients were included in the qualitative synthesis. The study selection process is illustrated in the PRISMA flowchart criteria (Fig. 1).

3.2. Study characteristics

The study characteristics are summarized in Table 1. The included studies were published between 2010 and 2023, with most conducted in mainland China. The experimental groups received PC combined with various HM formulations as supplementary treatments. Among the 101 studies, 70 (69.3%) used HM decoctions, 26 (25.7%) used prescriptions, 3 (3%) used powders, and 2 (2%) used pills. All studies provided detailed descriptions of the components of the prescriptions used (Supplement 3), and the regimens of chemotherapy were described in each study. Among the chemotherapy regimens, FOLFOX was utilized most frequently in 30 studies (29.70%), followed by SOX in 18 studies (17.82%), XELOX in 10 studies (9.90%), DCF in 6 studies (5.94%), and OLF in 5 studies (4.95%). Other regimens were used in 32 studies (31.68%). The treatment durations ranged from 3 to 24 weeks.

3.3. Risk of bias in the included studies

Eighty-nine studies used computer software or random number tables for randomization, whereas 12 studies did not specify their randomization method. Only 10 % of the studies explicitly mentioned allocation concealment. Blinding of participants or personnel was not feasible in most RCTs, as only the experimental group received THM. This approach resulted in a high or unclear risk of performance bias, with many studies rated accordingly. None of the studies provided protocols for selecting results, preventing an assessment of the adherence to a prespecified analysis plan. Consequently, all studies were rated as having concerns or a high risk of bias in this domain (Fig. 2).

3.4. Intervention effects

3.4.1. Assessment of the tumor response

A total of 84 studies[18-38,40-44,47,48,50-53,55-58,61-68,70,72,73,76-81,83-89,94-112,114-118] used RECIST as the primary endpoint to assess the tumor response. However, three studies[29,63,98] did not provide sufficient data on SD, and thus they were excluded from the DCR analysis.

The ORR showed an RR of 1.34 (95% CI: 1.28 to 1.41, $p < 0.00001$, $I^2 = 0\%$, $N = 84$, $n = 6442$). Similarly, the DCR had an RR of 1.12 (95% CI: 1.10 to 1.15, $p < 0.00001$, $I^2 = 0\%$, $N = 81$, $n = 6225$). These results, as shown in Supplement 4, indicate a significant improvement in both the ORR and DCR with the combination of palliative chemotherapy and herbal treatment.

3.4.2. Assessment of the survival rate

A meta-analysis of 10 studies[39,42,46,52,92,95,99,107,109,113] in which REM was used to evaluate 1- to 5-year survival rates revealed significant improvements with HMs and chemotherapy. In the 9 studies[39,42,46,52,92,95,99,107,109] that analyzed the 1-year survival rate, the RR was 1.29 (95% CI: 1.13 to 1.48, p = 0.0003, I^2 = 43%, N = 9,

Table 1
Characteristics of the included trials.

References	Sample size E:C (M/F, Age) / Stage	Herbal medicine	Chemotherapy	Treatment period	Outcome measures	Main results
Wang 2016a[18]	E: 40 (22/18, 56.5) C: 35 (18/17, 56.7)/III-IV	Bazhen Decoction	FOLFOX4	6 weeks	1) RECIST (ORR) 2) RECIST (DCR)	1) RR 1.83 [1.05, 3.19] 2) RR 1.38 [1.01, 1.87]
Li 2014a[19]	E: 40 (28/12, 56.9) C: 32 (20/12, 55.7)/IIIb-IV	Bazhen Decoction (M)	XELOX	8 weeks	1) RECIST (ORR) 2) RECIST DCR) 3) KPS improvement rate	1) RR 1.36 [0.94, 1.99] 2) RR 1.15 [0.93, 1.42] 3) RR 1.68 [0.93, 3.04]
Chen 2018[20]	E: 22 C: 21 (27/19, 53.6)/III-IV	Bazhen Decoction (M)	XELOX	6 weeks	1) RECIST (ORR) 2) RECIST (DCR) 3) KPS score	1) RR 1.07 [0.51, 2.25] 2) RR 1.15 [0.82, 1.60] 3) MD 6.23 [2.98, 9.48]
Yang 2011[21]	E: 24 (11/13, 52) C: 24 (12/12, 53)/IIIb-IV	Bazhen Decoction (M)	DCF	6 weeks	1) RECIST (ORR) 2) RECIST DCR) 3) KPS improvement rate	1) RR 1.36 [0.80, 2.33] 2) RR 1.11 [0.83, 1.49] 3) RR 3.00 [1.13, 7.99]
Zheng 2015[22]	E: 43 (31/12, 60.4) C: 42 (24/18, 59.1)/IV	Buqi Jianwei Decoction	FOLFOX	6 weeks	1) RECIST (ORR) 2) RECIST DCR) 3) KPS improvement rate	1) RR 1.24 [0.64, 2.42] 2) RR 1.29 [0.96, 1.74] 3) RR 2.44 [1.05, 5.69]
Pei 2020[23]	E: 36 (20/16, 56.4) C:36 (19/17, 54.7)/IIIb-IV	Buzhong Yiqi Decoction	TCF	8 weeks	1) RECIST (ORR) 2) RECIST (DCR)	1) RR 1.54 [0.91, 2.60] 2) RR 1.15 [0.90, 1.48]
Qin 2012[24]	E: 27 (19/8, 59.0) C: 26 (20/6, 57.7)/III-IV	Buzhong Yiqi Decoction (M)	SOX	8 weeks	1) RECIST (ORR) 2) RECIST (DCR) 3) KPS score	1) RR 1.05 [0.57, 1.94] 2) RR 1.11 [0.85, 1.44] 3) MD 10.57 [4.33, 16.81]
Wang 2020a[25]	E: 30 (19/11, 50.2) C: 30 (20/10, 49.3)/II-IV	Buzhong Yiqi Decoction (M)	XELOX	6 weeks	1) RECIST (ORR) 2) RECIST (DCR) 3) KPS score	1) RR 1.07 [0.63, 1.81] 2) RR 0.95 [0.64, 1.41] 3) MD 6.80 [2.10, 11.50]
Zhang 2021[26]	E: 45 (31/14, 63.1) C: 45 (30/15, 62.8)/III-IV	Buzhong Yiqi Decoction (M)	DOC	8 weeks	1) RECIST (ORR) 2) RECIST (DCR)	1) RR 1.59 [1.02, 2.48] 2) RR 1.70 [1.25, 2.31]
Wang 2019[27]	E: 50 (30/20, 70.2) C: 50 (32/18, 70.4)/III-IV	Chrysanthemum Pill	S-1	8 weeks	1) RECIST (ORR) 2) RECIST DCR) 3) KPS improvement rate	1) RR 1.17 [0.87, 1.56] 2) RR 1.09 [0.96, 1.25] 3) RR 1.86 [1.11, 3.12]
Dong 2016[28]	E: 36 (24/12, 52) C: 36 (23/13, 53)/IIIb-IV	Dahuangzhechong Pill	SP	20 weeks	1) RECIST (ORR) 2) RECIST (DCR) 3) KPS score	1) RR 1.00 [0.69, 1.45] 2) RR 1.03 [0.85, 1.26] 3) MD 8.50 [5.03, 11.97]
Ding 2021[29]	E: 40 (24/16, 59.4) C: 40 (22/18, 59.1)/IIIb-IV	Dangshen Xiaozheng Quyu Decoction	OLF	6 weeks	1) RECIST (ORR) 2) KPS improvement rate	1) RR 1.18 [0.60, 2.32] 2) RR 1.50 [0.90, 2.51]
Fei 2014[30]	E: 40 (26/14, 58.3) C: 40 (28/12, 56.7)/III-IV	Fuzheng Huayu Prescription	DCF	3 weeks	1) RECIST (ORR) 2) RECIST (DCR)	1) RR 1.60 [1.00, 2.57] 2) RR 1.10 [0.87, 1.38]
Lu 2016[31]	E: 29 C: 28 (30/27, 56.5)/III-IV	Fuzheng Huayu Prescription	XELOX	6 weeks	1) RECIST (ORR) 2) RECIST (DCR)	1) RR 5.79 [1.92, 17.52] 2) RR 1.54 [1.05, 2.27]
Jing 2017[32]	E: 48 C: 48 N/A ($P > 0.05$)/IIIb-IV	Fuzheng Kang'ai Decoction	SOX	6 weeks	1) RECIST (ORR) 2) RECIST (DCR)	1) RR 1.67 [1.01, 2.75] 2) RR 1.26 [1.03, 1.55]
Zhao 2019[33]	E: 46 (29/17, 63.6) C: 46 (31/15, 62.7)/IIIb-IV	Fuzheng Kang'ai Decoction	SOX	6 weeks	1) RECIST (ORR) 2) RECIST (DCR)	1) RR 1.35 [0.84, 2.18] 2) RR 1.24 [1.01, 1.53]
Li 2016a[34]	E: 34 C: 34 (42/26, 46.8)/III-IV	Fuzheng Kang'ai Prescription	mFOLFOX4	8 weeks	1) RECIST (ORR) 2) RECIST (DCR)	1) RR 1.50 [1.05, 2.15] 2) RR 1.00 [0.84, 1.19]
Sun 2020[35]	E: 40 (27/13, 63.1) C: 40 (26/14, 62.7)/III-IV	Self-made Fuzheng Kang'ai Prescription	FOLFOX6	6 weeks	1) RECIST (ORR) 2) RECIST (DCR)	1) RR 2.50 [1.08, 5.79] 2) RR 1.29 [1.02, 1.61]
Liu 2020[36]	E: 49 (28/21, 58.3) C: 49 (29/20, 58.5)/III-IV	Fuzheng Sanjie Prescription	SOX	18 weeks	1) RECIST (ORR) 2) RECIST (DCR)	1) RR 1.37 [1.06, 1.76] 2) RR 1.09 [0.97, 1.23]
Zhu 2016a[37]	E: 45 (31/14, 61.7) C: 45 (33/12, 62.1)/III-IV	Self-made Fuzheng Xiaozheng Decoction	FOLFOX6	6 weeks	1) RECIST (ORR) 2) RECIST (DCR)	1) RR 1.83 [0.74, 4.53] 2) RR 1.33 [1.06, 1.68]
Li 2015[38]	E: 40 (23/17, 54.6) C: 40 (26/14, 55.2)/III-IV	Guben Jiandu Deoction	PFC	8 weeks	1) RECIST (ORR) 2) RECIST (DCR) 3) KPS improvement rate	1) RR 1.45 [0.77, 2.73] 2) RR 1.15 [0.86, 1.54] 3) RR 1.77 [1.05, 2.98]
Niu 2017[39]	E: 100(38/62, 59.6) C: 100(40/60, 58.7)/III-IV	Guipi Decoction	TFL	8 weeks	Survival rate (1y)	RR 1.73 [1.11, 2.70]
Li 2014b[40]	E: 23 (16/7, 62.3) C: 21 (11/10, 56.9)/IV	Guishao Liujunzi Decoction	TS	12 weeks	1) RECIST (ORR) 2) RECIST (DCR) 3) KPS improvement rate	1) RR 1.12 [0.58, 2.14] 2) RR 1.11 [0.75, 1.63] 3) RR 1.83 [0.84, 3.99]
Wang 2018a[41]	E: 60 (34/26, 64.2) C: 60 (31/29, 68.6)/III-IV	Guishao Liujunzi Decoction	SOX	12 weeks	1) RECIST (ORR) 2) RECIST (DCR) 3) KPS improvement rate	1) RR 1.10 [0.86, 1.41] 2) RR 1.02 [0.90, 1.15] 3) RR 1.43 [0.93, 2.19]
Zeng 2020[42]	E: 47 (32/15, 63.4) C:46 (30/16, 63.9)/IIIb-IV	Huazhuo Jiedu Qingyou Prescription	FOLFOX4	24 weeks	1) RECIST (ORR) 2) RECIST (DCR) 3) Survival rate (1y)	1) RR 1.10 [0.86, 1.41] 2) RR 1.02 [0.90, 1.15] 3) RR 1.73 [1.11, 2.70]
Yu 2012[43]	E: 30 (21/9, 64.4) C: 30 (20/10, 62.2)/III-IV	Huoxue Huayu Yangyin Prescription	FOLFOX4	12 weeks	1) RECIST (ORR) 2) RECIST (DCR)	1) RR 1.08 [0.62, 1.89] 2) RR 0.96 [0.78, 1.19]
Shi 2019[44]	E: 30 (19/11, 50.4) C: 30 (16/14, 50.5)/III-IV	Jianpi Fuzheng Decoction	mFOLFOX6	6 weeks	1) RECIST (ORR) 2) RECIST (DCR)	1) RR 1.39 [1.00, 1.94] 2) RR 1.21 [1.00, 1.46]
Huang 2012[45]	E: 40 (29/11, 39.3) C: 40 (31/9, 37.8)/IIIb-IV	Jianpi Fuzheng Decoction	FOLFOX	8 weeks	KPS score	MD 9.90 [4.02, 15.78]
Zhu 2017[46]	E: 35 (19/16, 71.3) C: 35 (20/15, 71.4)/IIIb-IV	Jianpi Fuzheng Decoction	FOLFOX4	8 weeks	1) Survival rate (1y) 2) Survival rate (3y) 3) Overall Survival 4) KPS score	1) RR 1.32 [1.05, 1.65] 2) RR 1.57 [0.97, 2.54] 3) MD 3.50 [3.14, 3.86] 4) MD 7.37 [4.29, 10.45]

(*continued on next page*)

Table 1 (*continued*)

References	Sample size E:C (M/F, Age) / Stage	Herbal medicine	Chemotherapy	Treatment period	Outcome measures	Main results
Xiong 2013[47]	E: 40 C: 40 (39/41, 65.2)/IV	Jianpi Hewei Prescription	FOLFOX4	4 weeks	1) RECIST (ORR) 2) RECIST (DCR) 3) KPS score	1) RR 1.13 [0.66, 1.94] 2) RR 1.03 [0.85, 1.25] 3) MD 8.60 [5.20, 12.00]
Huang 2014[48]	E: 30 (17/13, 53.4) C: 30 (16/14, 53.2)/IV	Jianpi Huayu Decoction	FOLFOX4	8 weeks	1) RECIST (ORR) 2) RECIST (DCR) 3) KPS improvement rate	1) RR 1.17 [0.65, 2.09] 2) RR 1.04 [0.86, 1.25] 3) RR 2.20 [1.27, 3.81]
Liu 2019[49]	E: 48 (26/22, 54.4) C: 48 (25/23, 55.1)/IV	Jianpi Huayu Decoction	FOLFOX4	8 weeks	KPS score	MD 5.31 [3.00, 7.62]
Jia 2018[50]	E: 20 (13/7, 65.3) C: 20 (12/8, 65.2)/III-IV	Jianpi Huayu Prescription	SP	6 weeks	1) RECIST (ORR) 2) RECIST (DCR)	1) RR 1.07 [0.73, 1.57] 2) RR 1.12 [0.91, 1.38]
Zhao 2016[51]	E: 39 (28/11, 57.0) C:39 (26/13, 58.3)/III-IV	Jianpi Huayu Prescription	SOX	6 weeks	1) RECIST (ORR) 2) RECIST (DCR) 3) KPS score	1) RR 1.17 [0.75, 1.82] 2) RR 1.03 [0.86, 1.23] 3) MD 5.70 [2.99, 8.41]
Huang 2016[52]	E: 34 (18/16, 46.5) C: 33 (18/15, 46.7)/IIIb-IV	Jianpi Huoxue Prescription	SOX	8 weeks	1) RECIST (ORR) 2) RECIST (DCR) 3) Survival rate (1y) 4) KPS score	1) RR 1.28 [0.97, 1.69] 2) RR 1.11 [0.92, 1.35] 3) RR 1.86 [1.12, 3.09] 4) MD 9.69 [6.94, 12.44]
Wang 2013[53]	E: 15 C: 15 N/A($P > 0.05$)/IIIb-IV	Jianpi Quyu Decoction	POF	8 weeks	1) RECIST (ORR) 2) RECIST (DCR) 3) KPS score	1) RR 1.20 [0.47, 3.09] 2) RR 1.09 [0.73, 1.62] 3) MD 10.67 [3.01, 18.33]
Meng 2020[54]	E: 45 (32/13, 57.5) C: 45 (30/15, 57.9)/III-IV	Jianpi Quyu Decoction	SOX	6 weeks	KPS score	MD 14.00 [8.54, 19.46]
Chui 2018[55]	E: 40C: 40 (46/34,36~69)/IV	Self-made Jianpi Wenzhong Decoction	DC	6 weeks	1) RECIST (ORR) 2) RECIST (DCR) 3) KPS improvement rate	1) RR 1.27 [0.66, 2.45] 2) RR 1.07 [0.82, 1.40] 3) RR 1.86 [1.15, 3.00]
Zhang 2012[56]	E: 23 C: 23(25/21, 65.6)/IV	Jianpi Xiao'ai Decoction	DLF	12 weeks	1) RECIST (ORR) 2) RECIST (DCR) 3) KPS improvement rate	1) RR 1.60 [0.93, 2.74] 2) RR 1.11 [0.88, 1.39] 3) RR 3.00 [1.13, 7.94]
Wu 2018[57]	E: 28 (15/13, 57.6) C: 22 (12/10, 58.2)/III-IV	Jianpi Xiao'ai Prescription	mFOLFOX6	8 weeks	1) RECIST (ORR) 2) RECIST (DCR) 3) KPS improvement rate	1) RR 1.75 [1.00, 3.04] 2) RR 1.09 [0.86, 1.38] 3) RR 1.57 [0.94, 2.63]
Weng 2020[58]	E: 31 (17/14, 62.3) C: 31 (18/13, 60.3)/III-IV	Jianpi Xiaoji Decoction	SOX	3 weeks	1) RECIST (ORR) 2) RECIST (DCR)	1) RR 1.38 [0.83, 2.31] 2) RR 1.19 [0.88, 1.60]
Chen 2016[59]	E: 30 (25/5, 60.6) C: 30 (27/3, 59.9)/III-IV	Jianpi Xiaopi Decoction	FOLFOX4	8 weeks	KPS score	MD 6.15 [2.62, 9.68]
Chen 2012[60]	E: 30 (21/9, 55.6) C: 30 (24/6, 54.6)/IIIb-IV	Jianpi Yiliu Decoction	FOLFOX	6 weeks	1) KPS score 2) KPS improvement rate	1) MD 5.48 [2.75, 8.21] 2) RR 2.17 [0.95, 4.94]
Ma 2017[61]	E: 40 (25/15, 46.2) C: 40 (23/17, 45.9)/III-IV	Jianpi Yiqi Sanjie Decoction	FOLFOX	8 weeks	1) RECIST (ORR) 2) RECIST (DCR) 3) KPS improvement rate	1) RR 1.63 [1.04, 2.53] 2) RR 1.18 [0.92, 1.51] 3) RR 1.64 [1.00, 2.71]
Wang 2018b[62]	E: 21 (14/7, 65.8) C: 21 (12/9, 66.4)/IV	Jianpi Yiqi Sanjie Decoction	SOX	12 weeks	1) RECIST (ORR) 2) RECIST (DCR)	1) RR 3.00 [0.68, 13.20] 2) RR 1.88 [1.02, 3.45]
Jin 2016[63]	E: 35 (21/14, 56.3) C: 35 (20/15, 57.1)/IV	Jianpi Yiqi Yangyin Huoxue Prescription	DPF	4 weeks	RECIST (ORR)	ORR RR 2.33 [1.43, 3.80]
Lai 2010[64]	E: 25 (20/5, 44) C: 30 (24/6, 48)/IV	Jianpi Yishen Decoction	TFL	8 weeks	1) RECIST (ORR) 2) RECIST (DCR) 3) KPS improvement rate	1) RR 1.20 [0.69, 2.09] 2) RR 1.05 [0.82, 1.34] 3) RR 1.73 [0.89, 3.37]
Wang 2015a[65]	E: 30 (21/9, 70.2) C: 30 (23/7, 72.6)/IIIb-IV	Jianpi Yishen Decoction	PCC	8 weeks	1) RECIST (ORR) 2) RECIST (DCR) 3) KPS improvement rate	1) RR 1.67 [1.00, 2.76] 2) RR 1.12 [0.93, 1.35] 3) RR 2.14 [1.02, 4.49]
Xu 2018[66]	E: 35 (23/12, 71.3) C: 35 (24/11, 70.8)/III-IV	Jianpi Yishen Decoction	PCC	6 weeks	1) RECIST (ORR) 2) RECIST (DCR)	1) RR 1.71 [1.08, 2.73] 2) RR 1.14 [0.96, 1.35]
Zheng 2011[67]	E: 35 (29/6, 64) C: 30 (27/3, 63)/IIIb-IV	Jianpi Yishen Prescription	FOLFOX	6 weeks	1) RECIST (ORR) 2) RECIST (DCR) 3) KPS improvement rate	1) RR 1.07 [0.60, 1.92] 2) RR 1.09 [0.83, 1.43] 3) RR 2.04 [1.05, 3.97]
Wang 2015b[68]	E: 39 (25/14, 49.1) C: 39 (29/10, 50.2)/III-IV	Jianpi Yiwei Decoction	FMC	8 weeks	1) RECIST (ORR) 2) RECIST (DCR) 3) KPS improvement rate	1) RR 2.57 [1.21, 5.45] 2) RR 1.32 [1.07, 1.63] 3) RR 3.17 [1.42, 7.07]
Wang 2011a[69]	E: 34 (22/12,32~75) C: 34 (23/11,34~73)/III-IV	Jianzhong Huashi Decoction	XP	3 weeks	KPS improvement rate	RR 9.00 [2.26, 35.82]
Xing 2017[70]	E: 42 (26/16, 66.9) C: 42 (24/18, 66.1)/III-IV	Self-made Kang'ai Decoction	FOLFOX	8 weeks	1) RECIST (ORR) 2) RECIST (DCR)	1) RR 1.64 [0.99, 2.73] 2) RR 1.18 [1.00, 1.38]
Fang 2018[71]	E: 30 C: 30 (32/28, 55)/IIIb-IV	Lizhong Decoction (M)	XELOX	3 weeks	KPS improvement rate	RR 1.67 [0.87, 3.20]
Feng 2015[72]	E: 31 (NA, 56.9) C: 31 (NA, 57.2)/III-IV	Liujunzi Decoction	DCF	6 weeks	1) RECIST (ORR) 2) RECIST (DCR) 3) KPS improvement rate	1) RR 1.06 [0.67, 1.70] 2) RR 1.00 [0.85, 1.18] 3) RR 2.10 [1.19, 3.69]
Lin 2017[73]	E: 35 (20/15, 53) C: 34 (18/16, 51)/III-IV	Liujunzi Decoction	FOLFOX	4 weeks	1) RECIST (ORR) 2) RECIST (DCR) 3) KPS improvement rate	1) RR 1.02 [0.70, 1.47] 2) RR 0.97 [0.76, 1.25] 3) RR 1.78 [1.06, 3.00]
Fan 2013[74]	E: 19 C: 19 (20/18, 62.3)/III-IV	Liujunzi Decoction	FOLFOX	24 weeks	KPS improvement rate	RR 2.40 [1.05, 5.49]
Wang 2016b[75]	E: 23 (10/13, 67) C: 22 (10/12, 67)/III-IV	Liujunzi Decoction (M)	FOLFOX4	8 weeks	KPS improvement rate	RR 2.80 [1.21, 6.50]

(*continued on next page*)

Table 1 (*continued*)

References	Sample size E:C (M/F, Age) / Stage	Herbal medicine	Chemotherapy	Treatment period	Outcome measures	Main results
Guo 2016[76]	E: 75 (47/28, 56.1) C: 75 (49/26, 55.5)/III-IV	Qiangpi Yiqi Prescription	S-1	24 weeks	1) RECIST (ORR) 2) RECIST (DCR)	1) RR 1.29 [0.84, 1.98] 2) RR 1.10 [0.96, 1.26]
He 2014[77]	E: 22 (15/7, 56.5) C: 22 (16/6, 56.9)/III-IV	Qizhu Prescription	FOLFOX4	12 weeks	1) RECIST (ORR) 2) RECIST (DCR) 3) KPS improvement rate	1) RR 1.50 [0.49, 4.59] 2) RR 1.15 [0.74, 1.81] 3) RR 1.20 [0.66, 2.18]
Zhang 2020a[78]	E: 43 (24/19, 50.4) C: 43 (26/17, 49.1)/III-IV	Shengyang Yiwei Decoction	SOX	9 weeks	1) RECIST (ORR) 2) RECIST (DCR)	1) RR 1.41 [1.00, 1.99] 2) RR 1.13 [0.90, 1.40]
Kong 2021[79]	E: 30 C: 30 (40/20, 60.9)/IIIb-IV	Shenhubanxia Decoction	DOS	9 weeks	1) RECIST (ORR) 2) RECIST (DCR)	1) RR 1.82 [1.07, 3.10] 2) RR 1.13 [0.91, 1.39]
Li 2016b[80]	E: 50 (29/21, 62.2) C: 50 (26/24, 58.7)/III-IV	Shenlingbaizhu Powder	TS	12 weeks	1) RECIST (ORR) 2) RECIST (DCR) 3) KPS improvement rate	1) RR 1.23 [0.82, 1.84] 2) RR 1.11 [0.89, 1.39] 3) RR 1.83 [0.84, 3.99]
Zhang 2017[81]	E: 40 (25/15, 56.7) C: 40 (28/12, 56.2)/III-IV	Shenlingbaizhu Powder	TS	8 weeks	1) RECIST (ORR) 2) RECIST (DCR) 3) KPS improvement rate	1) RR 1.67 [0.95, 2.93] 2) RR 1.27 [0.90, 1.80] 3) RR 2.00 [1.12, 3.56]
Lai 2018[82]	E: 30 (22/8, 45) C: 30 (24/6, 44)/IV	Shenlingbaizhu Powder	TCF	4 weeks	KPS improvement rate	RR 2.29 [1.10, 4.74]
Yu 2019a[83]	E: 45 (27/18, 61.7) C: 45 (25/20, 62.4)/III-IV	Shenyi Jianzhong Decoction	SOX	12 weeks	1) RECIST (ORR) 2) RECIST (DCR)	1) RR 0.92 [0.61, 1.37] 2) RR 1.08 [0.91, 1.28]
Liu 2018[84]	E: 41 (22/19, 50.8) C:41 (21/20, 51.0)/III-IV	Shenyi Jianzhong Decoction	SOX	12 weeks	1) RECIST (ORR) 2) RECIST (DCR)	1) RR 1.19 [0.72, 1.97] 2) RR 1.29 [1.01, 1.63]
Wang 2017[85]	E: 41 (25/16, 52.7) C: 41 (22/19, 53.2)/III-IV	Shenyi Jianzhong Decoction (M)	S-1	12 weeks	1) RECIST (ORR) 2) RECIST (DCR) 3) KPS improvement rate	1) RR 1.04 [0.77, 1.40] 2) RR 1.06 [0.88, 1.27] 3) RR 1.90 [1.01, 3.57]
Yang 2018[86]	E: 40 (21/19, 59.4) C: 40 (23/17, 54.3)/IIIb-IV	Shenyu Yangwei Decoction	XELOX	6 weeks	1) RECIST (ORR) 2) RECIST (DCR) 3) KPS improvement rate	1) RR 1.69 [1.00, 2.87] 2) RR 1.18 [0.92, 1.51] 3) RR 1.63 [1.04, 2.53]
Jia 2019[87]	E: 31 (20/11, 56.8) C: 31 (22/9, 56.8)/III-IV	Shiquandabu Decoction	XELOX	6 weeks	1) RECIST (ORR) 2) RECIST (DCR)	1) RR 1.75 [1.06, 2.90] 2) RR 1.24 [0.93, 1.65]
Cao 2010[88]	E: 51 C: 54 (66/39, 58)/III-IV	Sijunkang'ai Decoction	FOLFOX4	8 weeks	1) RECIST (ORR) 2) RECIST (DCR) 3) KPS improvement rate	1) RR 1.31 [0.78, 2.18] 2) RR 1.20 [0.97, 1.48] 3) RR 1.25 [0.97, 1.60]
Wu 2020[89]	E: 47 (28/19, 55.5) C: 47 (27/20, 56.5)/III-IV	Wei'aining Decoction	FOLFOX6	12 weeks	1) RECIST (ORR) 2) RECIST (DCR)	1) RR 1.26 [0.93, 1.70] 2) RR 1.07 [0.93, 1.25]
Yin 2016[90]	E: 36 (17/19, 61.7) C: 36 (16/20, 62.8)/III-IV	Wei'aining Decoction	FOLFOX	12 weeks	KPS improvement rate	RR 1.83 [0.74, 4.42]
Gu 2020[91]	E: 51 (28/23, 70.1) C: 51 (30/21, 69.7)/III-IV	Wei'aining Decoction	SOX	12 weeks	KPS score	MD 8.59 [6.30, 10.88]
Zhang 2020b[92]	E: 53 C: 53 (59/47, 56.3) /IIIb-IV	Xiangsha Liujunzi Decoction	SOX	4 weeks	1) RECIST (ORR) 2) RECIST (DCR)	1) RR 1.52 [1.06, 2.19] 2) RR 1.27 [1.04, 1.55]
Ni 2015[93]	E: 33 (22/11, 69.3) C: 33 (21/12, 68.9)/III-IV	Xiangsha Liujunzi Decoction	DCF	6 weeks	1) Survival rate (1y) 2) Survival rate (2y) 3) Survival rate (3y)	1) RR 1.35 [0.91, 2.02] 2) RR 1.45 [0.80, 2.64] 3) RR 2.25 [0.77, 6.59]
Tang 2017[94]	E: 24 C: 24 (29/19, 59.8) / III-IV	Xiangsha Liujunzi Decoction	S-1	8 weeks	KPS improvement rate	RR 2.80 [1.20, 6.55]
Li 2016c[95]	E: 40 (21/19, 64.6) C: 40 (22/18, 64.1)/III-IV	Xiangsha Liujunzi Decoction (M)	DCF	3 weeks	1) RECIST (ORR) 2) RECIST (DCR) 3) Survival rate (1y) 4) Survival rate (2y)	1) RR 1.67 [1.13, 2.45] 2) RR 1.27 [1.04, 1.54] 3) RR 1.33 [0.99, 1.79] 4) RR 1.73 [1.58, 2.81]
Tong 2018[96]	E: 38 (21/18, 62.7) C: 37 (24/16, 63.5)/III-IV	Xiangsha Liujunzi Decoction (M)	XELOX	12 weeks	1) RECIST (ORR) 2) RECIST (DCR) 3) KPS improvement rate	1) RR 1.34 [0.61, 2.95] 2) RR 1.23 [0.90, 1.67] 3) RR 2.34 [0.91, 5.98]
Hu 2019[97]	E: 40 (23/17, 57.0) C: 40 (21/19, 57.5)/III-IV	Xiangsha Liujunzi Decoction (M)	XELOX	6 weeks	1) RECIST (ORR) 2) RECIST (DCR)	1) RR 1.20 [0.71, 2.03] 2) RR 1.43 [1.01, 2.02]
Gu 2013[98]	E: 32 (20/12, 54.9) C: 35 (22/13, 52.3) /IIIb-IV	Xiaotan Sanjie Prescription	SOX	16 weeks	RECIST (ORR)	RR 1.30 [0.82, 2.06]
Yu 2018[99]	E: 41 (25/16, 74.2) C: 44 (20/24, 73.5)/III-IV	Yiqi Jianpi Prescription	S-1	16 weeks	1) RECIST (ORR) 2) RECIST (DCR) 3) Survival rate (1y) 4) KPS improvement rate	1) RR 1.17 [0.79, 1.73] 2) RR 1.10 [0.94, 1.29] 3) RR 1.23 [0.92, 1.65] 4) RR 1.56 [1.07, 2.27]
Gao 2019[100]	E: 50 (NA, 68.1) C: 50 (NA, 66.7)/III-IV	Yiqi Jianpi Huaji Prescription	DC	9 weeks	1) RECIST (ORR) 2) RECIST (DCR) 3) KPS score	1) RR 1.25 [0.74, 2.12] 2) RR 1.24 [0.98, 1.58] 3) MD 8.13 [6.21, 10.05]
Bu 2016[101]	E: 20 C: 20 (27/13, 59.5)/III-IV	Yiqi Jianpi Huoxue Decoction	DOF	8 weeks	1) RECIST (ORR) 2) RECIST (DCR) 3) KPS score	1) RR 1.67 [0.75, 3.71] 2) RR 1.12 [0.91, 1.48] 3) MD 5.00 [1.34, 8.66]
Ge 2017[102]	E: 30 (17/13, 59.7) C: 30 (16/14, 58.2)/III-IV	Yiqi Jianpi Huoxue Decoction	FOLFOX	8 weeks	1) RECIST (ORR) 2) RECIST (DCR)	1) RR 1.56 [1.08, 2.26] 2) RR 1.07 [0.96, 1.20]
Jiang 2017[103]	E: 48 (26/22, 60.8) C: 48 (27/21, 60.1)/III-IV	Yiqi Jianpi Huoxue Decoction	FMC	8 weeks	1) RECIST (ORR) 2) RECIST (DCR)	1) RR 1.91 [1.04, 3.51] 2) RR 1.03 [0.78, 1.36]
Pang 2018[104]	E: 40 (25/15, 50.2) C: 40 (22/18, 49.3)/III-IV	Yiqi Jianpi Jiedu Prescription	FOLFOX4	8 weeks	1) RECIST (ORR) 2) RECIST (DCR)	1) RR 2.00 [1.02, 3.91] 2) RR 1.25 [0.99, 1.58]

(*continued on next page*)

Table 1 (*continued*)

References	Sample size E:C (M/F, Age) / Stage	Herbal medicine	Chemotherapy	Treatment period	Outcome measures	Main results
Zhou 2015[105]	E: 15 (10/5, 56.9) C: 14 (9/5, 56.1) /IIIb-IV	Yiqi Jianpi Qingre Huayu Decoction	OLF	8 weeks	1) RECIST (ORR) 2) RECIST (DCR)	1) RR 1.63 [1.02, 2.62] 2) RR 1.08 [0.89, 1.30]
Zhu 2016b[106]	E: 42 (26/16, 58.5) C: 42 (28/14, 57.8)/III-IV	Yiqi Jianpi Yangwei Prescription	DSP	4 weeks	1) RECIST (ORR) 2) RECIST (DCR) 3) KPS score	1) RR 1.43 [0.84, 2.43] 2) RR 1.15 [0.96, 1.39] 3) MD 4.76 [2.48, 7.04]
Xiong 2012[107]	E: 30 (20/10, 64.5) C: 28 (18/10, 63.5)/IIIb-IV	Yiqi Qingdu Huayu Prescription	OLF	24 weeks	1) RECIST (ORR) 2) RECIST (DCR) 3) Survival rate (1y) 4) Survival rate (2y) 5) Survival rate (3y)	1) RR 1.12 [0.58, 2.17] 2) RR 1.14 [0.93, 1.38] 3) RR 1.07 [0.79, 1.46] 4) RR 1.73 [0.80, 2.01] 5) RR 1.49 [0.82, 2.72]
Ma 2018[108]	E: 30 C: 30 (37/23, 57.9) /IIIb-IV	Yiqi Qingre Jiedu Prescription	DCF	6 weeks	1) RECIST (ORR) 2) RECIST (DCR) 3) KPS score 4) KPS improvement rate	1) RR 1.45 [0.82, 2.59] 2) RR 1.27 [1.01, 1.61] 3) MD 1.64 [0.33, 2.95] 4) RR 1.44 [0.73, 2.86]
Ji 2016[109]	E: 26 (15/11, 69.5) C: 26 (16/10, 70.5)/III-IV	Yiqi Shenghua Decoction	FOLFOX	8 weeks	1) RECIST (ORR) 2) RECIST (DCR) 3) Survival rate (1y) 4) Survival rate (3y) 5) Survival rate (5y)	1) RR 1.38 [0.87, 2.20] 2) RR 1.14 [0.92, 1.42] 3) RR 1.04 [0.87, 1.25] 4) RR 1.45 [0.85, 2.50] 5) RR 1.33 [0.54, 3.31]
Wang 2018c[110]	E: 46 (25/21, 62.5) C:49 (30/19, 64.7)/III-IV	Yiqi Yangyin Prescription	XELOX	8 weeks	1) RECIST (ORR) 2) RECIST (DCR) 3) KPS score	1) RR 1.13 [0.89, 1.43] 2) RR 1.04 [0.92, 1.18] 3) MD 4.42 [0.86, 7.98]
Liu 2021[111]	E: 45 (25/20, 59.3) C: 45 (25/20, 60.1)/III-IV	Yiwei Shengyang Decoction (M)	DOF	9 weeks	1) RECIST (ORR) 2) RECIST (DCR)	1) RR 1.67 [1.10, 2.52] 2) RR 1.08 [0.94, 1.24]
Li 2020[112]	E: 49 (32/17, 55.7) C: 49 (31/18, 52.4)/III-IV	Yiwei Xiao'ai Decoction	OLF	9 weeks	1) RECIST (ORR) 2) RECIST (DCR)	1) RR 1.87 [1.15, 3.04] 2) RR 1.08 [0.87, 1.35]
Huang 2020[113]	E: 43 (27/16, 65.9) C: 43 (25/18, 64.3)/III-IV	Yiwei Xiao'ai Decoction	OLF	9 weeks	Survival rate (3y)	RR 1.59 [1.03, 2.45]
Shen 2017[114]	E: 34 (19/15, 54.2) C: 34 (21/13, 56.1) /IIIb-IV	Zhengyang Lilao Decoction	TCF	4 weeks	1) RECIST (ORR) 2) RECIST (DCR) 3) KPS score	1) RR 0.95 [0.61, 1.46] 2) RR 0.97 [0.85, 1.11] 3) MD 10.33 [4.72, 15.94]
Yu 2019b[115]	E: 53 (25/28,67.6) C: 53 (28/25,68.5)/III-IV	Zhengyang Lilao Decoction	Bevacizumab	3 weeks	1) RECIST (ORR) 2) RECIST (DCR) 3) Overall Survival 4) KPS score	1) RR 1.68 [1.11, 2.57] 2) RR 1.44 [1.03, 2.02] 3) MD 5.04 [4.21, 5.87] 4) MD 10.52 [6.02, 15.02]
Wang 2020b[116]	E: 41 (26/15, 57.2) C: 41 (27/14, 58.0)/III-IV	Ziyin Jianpi Quyu Decoction	SOX	12 weeks	1) RECIST (ORR) 2) RECIST (DCR)	1) RR 1.29 [0.74, 2.22] 2) RR 1.10 [0.88, 1.37]
Jiang 2018[117]	E:134(77/57 60.8) C:134(71/63 62.0)/III-IV	Unnamed Decoction	SOX	12 weeks	1) RECIST (ORR) 2) RECIST (DCR)	1) RR 1.28 [1.03, 1.60] 2) RR 1.14 [1.01, 1.29]
Wang 2011b[118]	E: 36 (26/10, 65.8) C: 36 (24/12, 62.4)/III-IV	Unnamed Prescription	FOLFOX4	16 weeks	1) RECIST (ORR) 2) RECIST (DCR) 3) KPS improvement rate	1) RR 1.63 [1.02, 2.62] 2) RR 1.08 [0.89, 1.30] 3) RR 1.52 [1.13, 2.06]

E, experimental; C, control; M, modified; MD, mean difference, RR: Risk Ratio; DC, docetaxel and cisplatin; DCF, docetaxel, cisplatin, and fluorouracil; DLF, cisplatin, leucovorin, and fluorouracil; DOC, docetaxel, oxaliplatin, and capecitabine; DOF, docetaxel, oxaliplatin, and 5-fluorouracil; DOS, docetaxel, oxaliplatin and S-1; DPF, docetaxel, cisplatin, and fluorouracil; DSP, docetaxel, S-1 and cisplatin; FOLFOX, folinic acid, fluorouracil, and oxaliplatin; FMC, fluorouracil, mitomycin, and cisplatin; OLF, oxaliplatin, leucovorin, and fluorouracil; PCC, pirarubicin, capecitabine, and cisplatin; PFC, paclitaxel, fluorouracil and cisplatin; POF, paclitaxel, oxaliplatin, and fluorouracil; SP, S-1 and cisplatin; SOX, S-1 (tegafur, gimeracil, and oteracil) and oxaliplatin; TCF, paclitaxel, cisplatin, and 5-flourouracil; TFL, paclitaxel, fluorouracil and leucovorin; TS, paclitaxel and S-1; XELOX, capecitabine and oxaliplatin; XP, capecitabine and cisplatin.

n = 771). For the 2-year survival rate, which was analyzed in 3 studies,[92,95,107] the RR was 1.40 (95% CI: 1.03 to 1.91, $p = 0.03$, $I^2 = 0\%$, $N = 3$, n = 204). The 3-year survival rate, which was analyzed in 5 studies,[46,92,107,109,113] had an RR of 1.57 (95% CI: 1.23 to 2.00, $p = 0.0003$, $I^2 = 0\%$, $N = 5$, n = 332). No studies reported the 4-year survival rate, and only one study[109] reported the 5-year survival rate, with an RR of 1.33 (95% CI: 0.54 to 3.31, $p = 0.53$, $N = 1$, n = 52). OS was analyzed in 2 studies,[46,115] with an MD of 4.22 months (95% CI: 2.72 to 5.73, $p < 0.00001$, $I^2 = 91\%$, $N = 2$, n = 176) as shown in Supplement 5.

3.4.3. QoL

The meta-analysis indicated a significant improvement in the QoL of patients in the HM plus chemotherapy group. Twenty-two studies[20,24,26,28,45-47,49,51-54,59,60,91,100,101,106,108,110,114,115] included KPS scores, with an MD of 7.19 (95% CI: 5.84 to 8.54, $p < 0.00001$, $I^2 = 76\%$, $N = 22$, $n = 1594$) indicating statistically significant results.

Similarly, the KPS improvement rates were reported in 37 studies[19,21,22,27,29,38,40,41,48,55-57,60,61,64,65,67-69,71-75,77,80-82,85,86,88,90,93,96,99,108,118] and presented an RR of 1.72 (95% CI: 1.56 to 1.89, $p < 0.00001$, $I^2 = 0\%$, $N = 36$, n = 2497). These findings also indicate statistically significant results, as shown in Supplement 6.

3.4.4. Assessment of ADRs

The meta-analysis revealed that patients receiving both HMs and chemotherapy were less likely to experience ADRs such as myelosuppression, neutropenia, thrombocytopenia, anemia, digestive symptoms, nausea, vomiting, diarrhea, hepatic and renal dysfunction, neurotoxicity, and oral mucositis than were those receiving chemotherapy alone (Table 2). These findings highlight a significant reduction in ADRs associated with HM plus chemotherapy treatment.

3.5. Publication bias

The funnel plot of the analysis of studies reporting the tumor response (ORR and DCR) showed central clustering with a rightward skew (Supplement 7). For survival rates, one-year survival rates were similar, whereas two- and three-year survival rates were skewed toward higher values. The literature on publication bias for five-year survival and

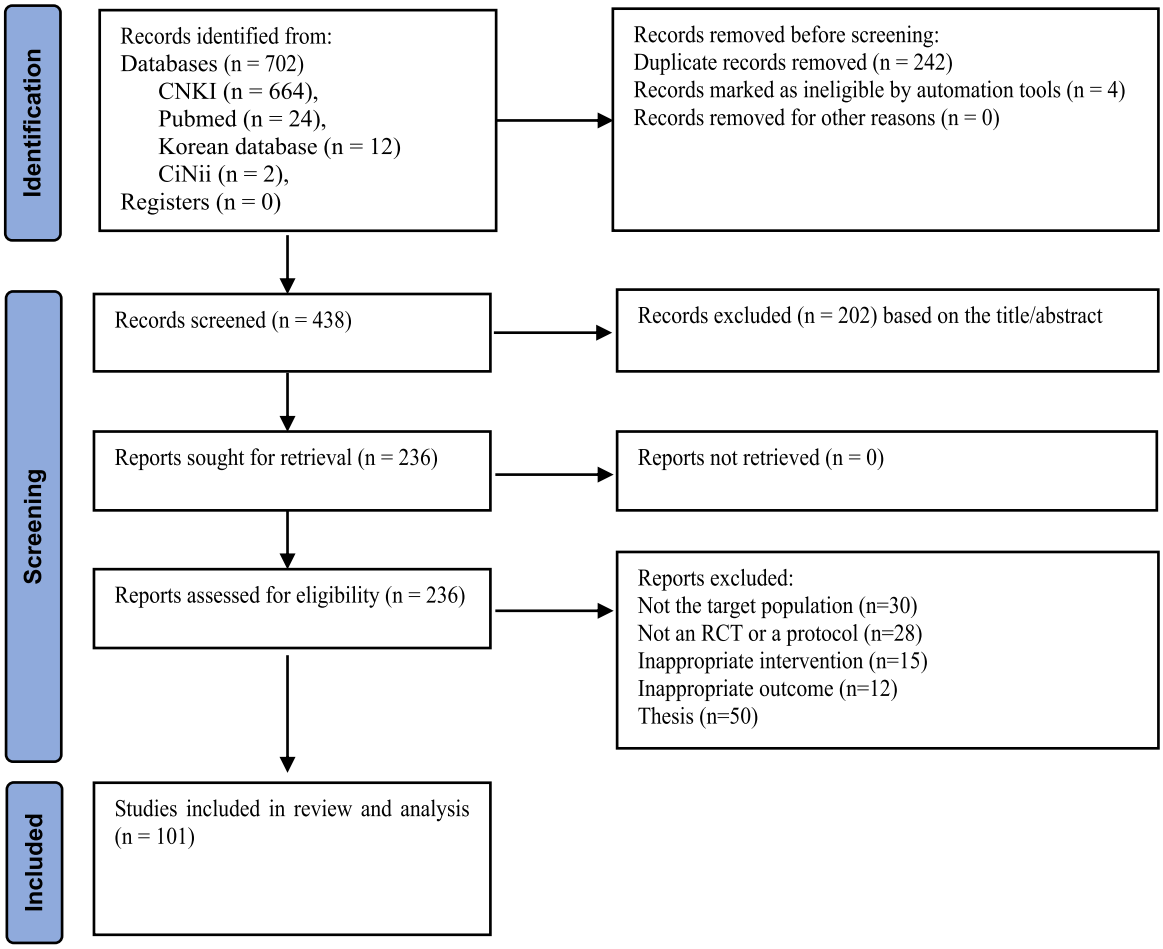
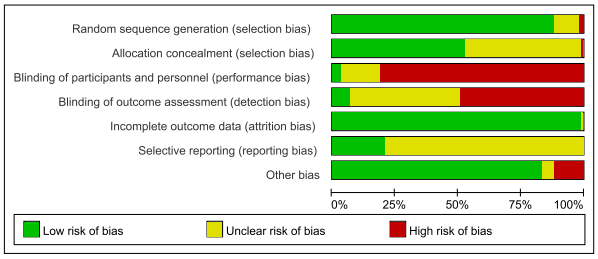


Fig. 1. PRISMA 2020 flow diagram of the included studies.
Abbreviations: CiNii, Citation Information by the National Institute of Informatics; CNKI, China National Knowledge Infrastructure; RCT, randomized controlled trial.

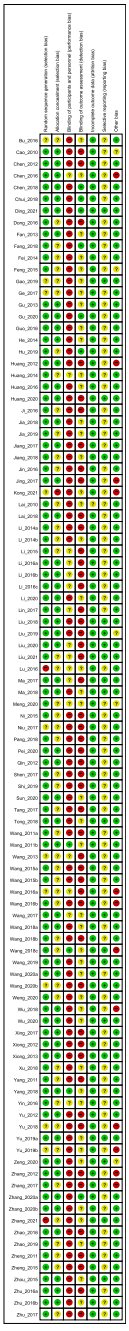
Table 2
The results of meta-analysis of adverse drug reactions of HM+Chemotherapy vs. Chemotherapy with random effect model.

Adverse drug reactions	No of RCTs	HM + Chemo (Events/Total)	Chemotherapy (Events/Total)	Total RR [95% CI]	I^2 (%)	References
Myelosuppression	22	205/887	323/882	0.66 [0.58,0.76]	0	21,29,30,31,33,38,40,41,42,61,62,69,76,79,80,81,91,93,96,104,106,115
Neutropenia	42	500/1648	876/1645	0.60 [0.54,0.66]	41	20,22,24,26,28,35,44,45,46,48,49,51,53,54,55,56,57,59,60,65,70,72,73,77,79,84,85,86,88,91,92,94,97,99,103,107,110,111,112,113,116,117
Anemia	18	185/692	303/692	0.67 [0.59,0.76]	0	26,47,53,55,56,59,60,65,72,73,77,82,85,86,88,92,103,117
Thrombocytopenia	38	295/1472	530/1473	0.57 [0.51,0.64]	0	20,24,26,35,44,45,46,48,49,51,52,53,54,55,56,57,59,60,64,65,70,72,73,78,79,82,84,85,86,91,99,103,110,111,112,113,116,117
Digestive symptoms	21	157/751	335/748	0.49 [0.42,0.58]	0	26,29,30,31,33,35,42,56,57,61,62,79,91,92,93,99,104,106,110,113,116
Nausea and vomiting	44	523/1767	951/1763	0.56 [0.49,0.63]	54	20,21,22,23,28,34,38,40,41,44,45,46,47,51,52,53,54,55,59,64,65,69,70,71,73,76,77,78,80,81,84,85,86,88,93,94,96,97,103,107,111,112,116,117
Diarrhea	28	215/1111	444/1108	0.52 [0.46,0.60]	0	21,28,34,38,40,45,46,47,51,52,53,65,69,71,77,80,81,84,85,88,93,94,96,97,103,107,111,117
Hepatic dysfunction	28	179/1134	294/1131	0.64 [0.55,0.74]	0	22,24,26,31,33,38,40,41,48,49,51,53,55,57,80,81,86,88,93,96,97,99,108,110,112,115,117
Renal dysfunction	13	93/499	159/497	0.64 [0.53,0.77]	4	22,24,26,33,48,49,57,72,86,88,108,112
Neurotoxicity	32	247/1230	457/1184	0.59 [0.53,0.67]	0	20,21,24,26,28,35,41,42,44,46,47,48,49,53,54,55,59,62,64,65,70,77,88,93,103,104,106,107,108,112,116,117
Oral mucositis	14	93/524	145/525	0.68 [0.54,0.86]	0	24,26,28,47,53,65,70,85,86,88,96,104,111,112

RR: Risk Ratio; I^2: Moderate heterogeneity (30% ≤ I^2 ≤ 75%), Low heterogeneity (I^2 ≤ 30%).



(A)



(B)

Fig. 2. Risk of bias (A) graph; (B) summary.

overall survival (OS) is limited. The ADR data showed central clustering with a leftward skew, indicating potential publication bias.

3.6. Certainty of evidence assessment via the GRADE system

The detailed outcomes, effects, and absolute values are presented in Table 3.

The analysis of the tumor response revealed that the DCR was evaluated with "moderate" certainty, whereas the ORR was rated with "low" certainty. The assessment of survival rates indicated that one- to three-year survival rates had "moderate" certainty, whereas the five-year survival rate and OS were rated as "low" certainty. The QoL assessment, which uses the KPS scale, revealed "low" certainty. The certainty of evidence for ADRs varied: myelosuppression, anemia, thrombocytopenia, digestive symptoms, diarrhea, hepatic and renal dysfunction, and oral mucositis were evaluated with "moderate" certainty, whereas neutropenia, nausea and vomiting, and neurotoxicity were rated with "low" certainty.

4. Discussion

4.1. Summary of the evidence

This systematic review and meta-analysis included 101 RCTs including 7,744 patients to evaluate the effects of combining HMs with chemotherapy on the tumor response and survival rates of patients with AGC receiving palliative treatment. The included studies had a moderate to high risk of bias, particularly in terms of allocation concealment and blinding. The combination therapy significantly improved the tumor response rates (ORRs and DCRs) and 1- to 3-year survival rates. Furthermore, the combination therapy reduced various ADRs and improved QoL measures, such as KPS scores. The evidence for the efficacy of combination therapies on the symptoms of AGC patients is limited. However, the results should be interpreted with caution because the risk of bias of the included studies was high or moderate.

4.2. Applicability of the evidence

Our findings suggest that integrating HMs with chemotherapy may be a potential treatment option for AGC, a disease that significantly affects patients' quality of life. The combined therapy of HMs with PC can yield significant outcomes through several mechanisms.

First, this approach adopts a multipronged strategy against tumors, inhibiting tumor growth and enhancing the tumor response by targeting various biological mechanisms in tumor cells simultaneously.[119-122] Second, HMs have the potential to suppress tumor growth and enhance the immune system, either by directly acting on tumor cells or by regulating their activities.[123] Moreover, HMs can mitigate the side effects of various chemotherapeutic agents used in tumor treatment and modulate the immune system to suppress tumor invasion.[124] Third, HMs can improve the overall health status of patients and reduce resistance to anticancer therapy by providing tailored treatment based on individual constitutions and enhancing patients' constitutions and immune systems.[125]

Clinically, the integration of HMs with standard chemotherapy regimens may not only improve the tumor response but also increase overall survival and quality of life by mitigating ADRs such as myelosuppression and gastrointestinal toxicity.

In addition, several HMs frequently used in integrative oncology include Bazhen decoction,[18-21] Buzhong yiqi decoction,[23-26] Liujunzi decoction,[72-75] Xiangsha liujunzi decoction,[92-97] and Shenling baizhu powder.[80-82] These HMs are known for their spleen-strengthening properties, which are believed to support digestive health and vitality. By enhancing spleen function, they may improve nutrient absorption and the energy distribution, which is particularly beneficial for cancer patients undergoing treatment, who often experience compromised energy levels and immune function.

Table 3
Summary of findings with GRADE.

Outcomes	Studies (RCTs)	No. of patients HM+CT (%), CT (%)	Effect (RR & 95% CI)	Absolute Effect (per 1000 & 95% CI)	Certainty of evidence
Tumor Response Assessment					
ORR	84	1800/3231(55.7), 1296/3211(40.4)	RR 1.34 (1.28 to 1.41)	541 more per 1000 (517 more to 569 more)	⨁⨁◯◯ Low [A,B]
DCR	81	2676/3124(85.7), 2310/3101(74.5)	RR 1.12 (1.10 to 1.15)	834 more per 1000 (819 more to 857 more)	⨁⨁⨁◯ Moderate [A]
Survival Rate					
1-year survival rate	9	258/386 (66.8), 190/385 (49.4)	RR 1.29 (1.13 to 1.48)	699 more per 1000 (628 more to 762 more)	⨁⨁⨁◯ Moderate [C]
2-year survival rate	3	54/103 (52.4), 37/101 (36.6)	RR 1.40 (1.03 to 1.91)	526 more per 1000 (387 more to 661 more)	⨁⨁⨁◯ Moderate [A]
3-year survival rate	5	90/167 (53.9), 56/165 (33.9)	RR 1.57 (1.23 to 2.00)	553 more per 1000 (438 more to 662 more)	⨁⨁⨁◯ Moderate [A]
5-year survival rate	1	8/26 (30.8), 6/26 (23.1)	RR 1.33 (0.54 to 3.31)	307 more per 1000 (114 more to 605 more)	⨁⨁◯◯ Low [D,E]
Overall survival	2	88 / 88	–	MD 4.22 higher (2.72 higher to 5.73 higher)	⨁⨁◯◯ Low [F,G]
Quality of Life Assessment					
KPS score	22	797 / 797	–	MD 7.19 higher (5.84 higher to 8.54 higher)	⨁⨁◯◯ Low [B,C]
KPS improvement rate	37	715/1291 (55.4), 391/1278 (30.6)	RR 1.70 (1.55 to 1.85)	520 more per 1000 (476 more to 569 more)	⨁⨁◯◯ Low [A,B]
Adverse Drug Reactions					
Myelosuppression	22	205/887 (23.1), 323/882 (36.6)	RR 0.66 (0.58 to 0.76)	242 fewer per 1000 (278 fewer to 212 fewer)	⨁⨁⨁◯ Moderate [A]
Neutropenia	42	500/1648 (30.3), 876/1645 (53.3)	RR 0.60 (0.54 to 0.66)	320 fewer per 1000 (351 fewer to 288 fewer)	⨁⨁◯◯ Low [A,C]
Anemia	18	185/692 (26.7), 303/692 (43.8)	RR 0.67 (0.59 to 0.76)	293 fewer per 1000 (333 fewer to 258 fewer)	⨁⨁⨁◯ Moderate [A]
Thrombocytopenia	38	295/1472 (20.0), 530/1473 (36.0)	RR 0.57 (0.51 to 0.64)	205 fewer per 1000 (230 fewer to 184 fewer)	⨁⨁⨁◯ Moderate [A]
Digestive symptoms	21	157/751 (20.9), 335/748 (44.8)	RR 0.49 (0.42 to 0.58)	219 fewer per 1000 (260 fewer to 188 fewer)	⨁⨁⨁◯ Moderate [A]
Nausea and vomiting	44	523/1767 (29.6), 951/1763 (53.9)	RR 0.56 (0.49 to 0.63)	302 fewer per 1000 (340 fewer to 264 fewer)	⨁⨁◯◯ Low [A,C]
Diarrhea	28	215/1111 (19.4), 444/1108 (40.1)	RR 0.52 (0.46 to 0.60)	208 fewer per 1000 (240 fewer to 184 fewer)	⨁⨁⨁◯ Moderate [A]
Hepatic dysfunction	27	185/1234 (15.0), 301/1231 (24.5)	RR 0.64 (0.55 to 0.74)	166 fewer per 1000 (192 fewer to 143 fewer)	⨁⨁⨁◯ Moderate [A]
Renal dysfunction	13	93/499 (18.6), 159/497 (32.0)	RR 0.64 (0.53 to 0.77)	205 fewer per 1000 (246 fewer to 170 fewer)	⨁⨁⨁◯ Moderate [A]
Neurotoxicity	32	247/1230 (20.1), 457/1184 (38.6)	RR 0.59 (0.53 to 0.67)	228 fewer per 1000 (259 fewer to 205 fewer)	⨁⨁◯◯ Low [A,B]
Oral mucositis	14	93/524 (17.7), 145/525 (27.6)	RR 0.68 (0.54 to 0.86)	188 fewer per 1000 (238 fewer to 149 fewer)	⨁⨁⨁◯ Moderate [A]

CI, confidence interval; HM, herbal medicine; CT, chemotherapy; MD, mean difference; RCTs, randomized controlled trials; RR, risk ratio; Serious [A], Although the results were statistically significant, the 95% confidence intervals were wide and included the possibility of no effect, raising concerns about the precision of the results; Serious [B], Possible publication bias; Serious [C], Moderate heterogeneity ($30\% \leq I^2 \leq 75\%$); Serious [D], The included study(ies) had a unclear risk of selection, performance biases; Serious [E], The 95% confidence interval overlapped with no effect; Serious [F], Rob Risk of bias may influence the findings; Serious [G], Substantial heterogeneity exists ($I^2 > 75\%$).

Bazhen decoction[126] has shown promise in inhibiting colorectal cancer by targeting key cancer-related genes and pathways, such as the PI3K-AKT and P53 pathways. Additionally, it enhances T-cell activity in the tumor environment, promoting an antitumor immune response. While these findings are related primarily to colorectal cancer, the mechanisms of action of Bazhen decoction may also have implications for AGC. Given the shared pathways involved in tumorigenesis, further research is warranted to explore its potential therapeutic benefits for AGC, as it may similarly enhance the immune response and inhibit tumor progression in this patient population.

Buzhong yiqi decoction[127,128] has been evaluated for its ability to improve immune function and safety when combined with inhibitors targeting the immune checkpoint PD-L1 in animal tumor models. Reports also indicate its effectiveness in improving bowel movement. Its ability to enhance the immune response and improve digestive health suggests that it may serve as a complementary treatment option for patients with AGC, warranting further investigation in clinical settings.

Liujunzi decoction[129-131] and Xiangsha liujunzi decoction[132] have significant advantages in repairing the gastric mucosa and enhancing the efficacy and eradication rate of *Helicobacter pylori* in individuals with chronic atrophic gastritis, thereby reducing recurrence rates. Given the established link between chronic atrophic gastritis and the development of gastric cancer, these decoctions may also play a critical role in preventing progression to AGC. The ability of these herbal formulas to inhibit inflammation, regulate apoptosis, and suppress angiogenesis contributes to their therapeutic potential, suggesting that these herbal formulas could be instrumental in managing gastric health and mitigating the risk of AGC.

Samryeongbaekchul powder[133] contains active ingredients such as quercetin, kaempferol, and β-sitosterol, which target key pathways and regulate tumor-related, metabolism-related, and inflammatory pathways. Given the significant roles that inflammation and metabolic dysregulation play in the progression of AGC, the active compounds in Samryeongbaekchul powder may provide therapeutic benefits in this context. Molecular docking tests revealed that compounds such as pyrolig-

neous acid, stigmasterol, and β-sitosterol bind effectively to target sites, indicating their potential to inhibit tumor growth and support cancer treatment. These findings suggest that integrating Samryeongbaekchul powder into treatment regimens could be beneficial for managing AGC.

This integrated approach offers a more effective treatment for tumors, reducing side effects and enhancing the quality of life of patients, especially those with inoperable AGC. These results suggest a promising integration of traditional and modern therapies, contributing to a more holistic approach to cancer care.

4.3. Quality of the evidence

Although the outcomes of combined HMs and PC are generally positive, several methodological issues compromise their quality. Several studies had methodological limitations, particularly regarding detection and reporting biases, with only 25% having protocols that match their reported outcomes, indicating potential reporting biases. Nevertheless, the consistency of the results across numerous studies strengthens the robustness of these findings.

The significant reductions in ADRs and improvements in QoL metrics provide compelling evidence for the benefits of this combination therapy. Despite the methodological shortcomings, the consistent positive outcomes strengthen the reliability of these findings.

4.4. Agreements and disagreements with other reviews

The results of this systematic review are consistent with previous findings on the combination of HMs and chemotherapy in cancer treatment.[134-136] This combination enhances the tumor response and reduces side effects. Previous studies have focused on platinum-based chemotherapy combined with HMs, and our study aggregated data on all PC treatments, particularly focusing on patients with inoperable AGC. This broader approach allowed us to collect extensive data, indicating that combining HMs with PC is both effective and safe. Our frequency analysis highlights commonly used herbal medicines in AGC treatment, providing insights into their therapeutic roles. This combination not only enhances the tumor response but also reduces toxicity, which aligns with previous reviews.

Despite these benefits, knowledge gaps persist regarding the specific components and interactions of HMs with standard treatments. The meta-analysis revealed 101 different HMs, highlighting the heterogeneity in their compositions. However, despite the differences in each prescription component, we observed that some formulations exerted similar effects within the context of traditional medicine. Importantly, the absence of serious adverse effects of the combination therapy shows the potential for such synergistic treatments.

In summary, integrating HMs with PC offers a promising and safe treatment pathway with the potential to enhance future cancer therapies. However, more comprehensive and standardized research is necessary for broader clinical application.

4.5. Limitations of the review

One limitation of this study is that many of the included studies compared chemotherapy alone to chemotherapy with HMs, often lacking double-blinding or placebo controls due to ethical concerns in life-threatening conditions. These concerns involve the ethical implications of assigning patients to potentially less effective treatments or sham controls.[137] Additionally, the clinical heterogeneity associated with herbal medicine and chemotherapy cannot be overlooked. Meta-analyses ideally require consistency in population, intervention, comparison, and outcome (PICO) criteria. However, our study included a diverse range of herbal prescriptions and chemotherapy regimens for treating AGC patients.

While this approach offered a comprehensive evaluation method and showed the effectiveness and safety of using HMs in AGC patients receiving PC, future studies should adopt a more focused approach. Specifically, conducting meta-analyses that concentrate on specific herbal prescriptions or chemotherapy regimens would provide more granular insights. Moreover, the heterogeneity of the herbal formulations in the included studies adds further complexity to the generalizability of the results. Additionally, clinical studies combining targeted therapies and immune checkpoint inhibitors with HMs are lacking, despite their increasing use in AGC patients.

4.6. Conclusions

Combination therapy may significantly improve the tumor response, survival rates, and quality of life. Additionally, HMs enhance the anticancer effects of PC and reduce side effects such as myelosuppression, digestive symptoms, and neurotoxicity. These findings suggest that this combination therapy could be a valuable approach in integrative oncology. However, the methodological limitations emphasize the need for more rigorous studies to strengthen the evidence base.

CRediT authorship contribution statement

Dong-Hyeon Kim: Formal analysis, Investigation, Data curation, Writing – original draft, Visualization, Project administration. **Soo-Dam Kim:** Formal analysis, Investigation, Writing – original draft. **Hyeong-Joon Jun:** Software, Visualization. **Eun-Bin Kwag:** Validation, Investigation. **Sang-Won Shin:** Methodology, Writing – review & editing. **Hwa-Seung Yoo:** Methodology, Writing – review & editing. **So-Jung Park:** Conceptualization, Writing – review & editing, Supervision, Project administration, Funding acquisition.

Declaration of competing interest

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (grant number: RS-2020-KH093707 and RS-2023-KH139460).

Ethical statement

Not applicable.

Data availability

The data associated with this systematic review can be made available upon reasonable request to the corresponding author.

Deviation from the protocol

The original protocol specified the inclusion of patients undergoing “adjuvant chemotherapy after gastric cancer surgery.” However, we expanded the inclusion criteria to include patients with “inoperable AGC” to address the clinical relevance of palliative chemotherapy interventions for this group. This adjustment was made to better capture the target population most likely to benefit from the intervention. Patients with advanced gastric cancer represent a subgroup with more significant clinical needs, which aligns more closely with the primary objectives of our study.In addition, the term “Traditional Korean medicine” in the protocol has been specified further to “herbal medicine” to enhance the clarity and specificity of the intervention. This change ensures that the study accurately reflects the intervention being administered and

avoids potential ambiguity regarding the scope of treatment.These protocol deviations were implemented after careful consideration and the preservation of study integrity.

This study builds upon findings presented in the author's dissertation, which was submitted to Daejeon University in partial fulfillment of the requirements for the Degree of Korean Medicine in 2024. The manuscript includes substantial revisions, additional analyses, and further discussions to expand upon the original work.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.imr.2024.101098.

Supplement 1. PRISMA 2020 Checklist

Supplement 2. Search strategy

Supplement 3. Herbal medicine prescription

Supplement 4. Overall effect of herbal medicine on chemotherapy-induced overall response rate and disease control rate as risk ratio

Supplement 5. Overall effect of herbal medicine on chemotherapy-induced disease control rate as risk ratio

Supplement 6. Overall effect of herbal medicine on chemotherapy-induced (A) mean difference of KPS score and (B) risk ratio of KPS improvement rate. KPS, Karnofsky Performance Status

Supplement 7. Funnel plot assessing publication bias in (A) tumor response according to RECIST, (B) survival rates, and (C) adverse drug reactions

References

1. Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2021;71(3):209–249.
2. Herbreteau E, Jooste V, Hamza S, et al. Trends in the management of gastric cancer over a 32-year period: a French population-based study. *Gastric Cancer*. 2015;18:129–137.
3. Ajani JA, D'Amico TA, Bentrem DJ, et al. Gastric Cancer, Version 2.2022, NCCN clinical practice guidelines in oncology. *J Natl Compr Canc Netw*. 2022;20(2):167–192.
4. Lu Y, Liu H, Yang K, et al. A comprehensive update: gastrointestinal microflora, gastric cancer and gastric premalignant condition, and intervention by traditional Chinese medicine. *J Zhejiang Univ Sci B*. 2022;23(1):1–18.
5. Zhao CC, et al. Systematic evaluation of a randomized controlled trial of Chinese herbal tonics combined with chemotherapy in the treatment of intermediate and advanced gastric cancer. *Lishizhen Med Mater Med Res*. 2020;31(4):896–899.
6. Kim HR, Jeong HR, Baek DG, et al. Clinical Practice Guidelines of Korean Medicine for Gastric Cancer. *J Kor. Tradit Oncol*. 2014;19(1):1–24.
7. Han GJ, Seong S, Kim SS, et al. Analysis of existing guidelines and randomized, controlled, clinical trials for development of [guideline of clinical trial with herbal medicinal product for gastric cancer]. *J Korean Med*. 2017;38(3):124–142.
8. Song SY, et al. Development of a guidelines of the herbal medicine treatment for gastric cancer on the use of systemic review and delphi technique. *J Korean Tradit Oncol*. 2018;23(1):1–14.
9. Chui ZS. The medical system of Donguibogam is based on the relationship between body, Disease, symptom-complex and recipe. *Korean J Orient Med*. 2009;15(2):125–130.
10. MAO Jun J, et al. Integrative oncology: addressing the global challenges of cancer prevention and treatment. CA: a. *Cancer J Clin*. 2022;72(2):144–164.
11. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. 2021;372:n71. doi:10.1136/bmj.n71.
12. Eisenhauer EA, Therasse P, Bogaerts J, et al. New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1). *Eur J Cancer*. 2009;45(2):228–247.
13. Zhang HL, Liu WC. *Clinical Oncology. Xi'an*. Fourth Military Medical University Publishing House; 2016.
14. National Cancer Institute. Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0. Published November 27, 2017. Available at: https://www.meddra.org/. Accessed November 25, 2024.
15. Higgins JPT The Cochrane Collaboration; 2011:2016.
16. Goldet Gabrielle, Howick Jeremy. Understanding GRADE: an introduction. *J Evid Based Med*. 2013;6.1:50–54.
17. Higgins J, Thomas J, Chandler J, et al. *Cochrane Handbook for Systematic Reviews of Interventions Version*. 6.1; 2020 Available from *www.training.cochrane.org/handbook*.
18. Wang Y, Wu GQ, Wang LF, et al. Clinical study of Ba Zhen Tang combined with FOLFOX4 regimen in the treatment of middle and advanced gastric cancer. *J. Nouth Pharmacy.*. 2016;13(6):40.
19. Li CJ, Shi Y. Clinical observation on 40 cases of advanced gastric cancer treated with chemotherapy by adding and subtracting Bazhen Tang. *Chinese J. Ethnomed Ethnopharm.*. 2014;23(22):70–71.
20. Chen XX, Xiao SX, Hu AQ. Study on the efficacy of combining the XELOX regimen with the Jiawei Bazhen-Tang in the treatment of advanced gastric cancer. *J. Shaanxi Univ Chinese Med*. 2018;41(5):54–57.
21. Yang XF, Liu B, Zhao SQ, et al. Clinical observation of Bazhen decoction combined with DCF regimen on advanced gastric cancer. *Hebei J TCM*. 2011;33(10):1497–1499.
22. Zheng JE. Clinical observation on 43 cases of middle and advanced gastric cancer treated with chemotherapy by Buqi Jianwei Decoction. *J Zhejiang TCM*. 2015;50(2):92–93.
23. Pei JW, Sun TZ, Fu PH, et al. Effects of Buzhong Yiqi Decoction on Th1, Th2 cytokines and Th1/Th2 immune balance in patients with gastric cancer. *C J T C M P*. 2020;35(6):3160–3163.
24. Wang MD, Chen MX. Efficacy of Buzhong Yiqi decoction combined with capecitabine and oxaliplatin in the treatment of advanced gastric cancer. *Chin J Clin Oncol Rehabil*. 2020;27(5):525–527.
25. Zhang QS, Li L. Effect of buzhong yiqi decoction combined with yiwei decoction on the efficacy and quality of life for patients with advanced gastric cancer receiving palliative chemotherapy. *J Sichuan TCM*. 2021;39(3):93–96.
26. Qin XG. Clinical observation of buzhong yiqi decoction combined with sox therapy on the patient with advanced gastric cancer. *J. Practical Tradit Chinese Int Med*. 2012;26(10):39–41.
27. Wang YP, Li QH, Peng Y, et al. Clinical efficacy of Chrysanthemum pill combined with chemotherapy in treatment of advanced gastric cancer and its impact on quality of life. *World J Integr Tradit Western Med*. 2019;14(5):700–703 11.
28. Dong HL. Clinical observation on the treatment of advanced gastric cancer by Dahuangzhechong pill combined with chemotherapy. *Henan Med Res*. 2016;25(7):1289–1290.
29. Ding XJ, Li LY, Zhang SH, et al. Dangshen Xiaowei Quyu decoction with OFL chemotherapy regimen to treat 40 cases of advanced gastric cancer (spleen deficiency and blood stasis syndrome). *Glob Tradit Chinese Med*. 2021;14(3):522–524.
30. Fei YH, Wang NY, Wang J. Clinical study on combination of fuzheng huayu formula with chemotherapy in treating advanced gastric cancer. *Henan Tradit Chinese Med*. 2014;34(11):2182–2183.
31. Lu H, Cai W, Cao TH, et al. Clinical effect observation on 29 cases of advanced gastric cancer treated with Fuzheng Huayu Prescription combined with chemotherapy. *Nei Mongol J. TCM.*. 2016;35(13):93–94.
32. Jing T. Effects of Fuzheng Kang'ai Decoction with chemotherapy on quality of life and immunological indexes of advanced gastric cancer patients. *Shaanxi J. TCM.*. 2017;38(10):1403–1404.
33. Zhao CJ. Effects of Fu Zheng Kang Ai Tang combined with SOX chemotherapy regimen on Chinese medicine evidence score and immune function of advanced gastric cancer patients. *Chronic Pathematol J*. 2019;20(10):1583–1585.
34. Li DC, Xiong YJ. Fuzhengkang'ai Prescription Combined with mFOLFOX4 chemotherapy in treatment of advanced gastric cancer. *ACTA Chinese Med*. 2016;31(9):1253–1257.
35. Sun B, Zhou L, Wang XL, et al. Clinical study of self-made fuzheng kang'ai decoction combined with FOLFOX6 chemotherapy on symptoms, signs and quality of life for patients with stage III-IV gastric cancer. *J Sichuan TCM*. 2020;38(12):101–104.
36. Liu SY, Zhang ZY. Effects of Fu Zheng San Jie Compound combined with chemotherapy on Chinese medicine evidence, tumor markers and immune function in gastric cancer patients. *Hebei J TCM*. 2020;42(3):402–406.
37. Zhu QQ. Effects of Chinese medicine combined with FOLFOX6 regimen chemotherapy on the quality of life of patients with middle and advanced gastric cancer. *Modern J Integrat Tradit Chinese Western Med*. 2016;25(9):996–998.
38. Li JH, Li CY. The clinical curative effect of guben jiedu decoction for the treatment of advanced gastric cancer. *Chinese Archive TCM*. 2015;33(7):1765–1768.
39. Niu SH. Clinical observation on the use of Gui Pi Tang combined with western medicine chemotherapy for advanced gastric cancer. *World Latest Med Inf*. 2017;17(6):145 7.
40. Li X, Li ZP, Liu SL. Clinical study on 23 cases of advanced gastric cancer treated with chemotherapy in combination with Gui Shao Liu Jun Zi Tang. *Jiangsu J. TCM.*. 2014;46(12):19–21.
41. Wang Y, Li ZP, Qian WT, et al. Treated HER2 negative advanced metastatic gastric cancer by combining guishao liujunzi decoction with SOX regimen. *J Anhui Sci. Technol. Univ*. 2018;32(5):48–52.
42. Zeng ZJ, Li MH, Guo SY. Clinical Study on modified huazhuo jiedu qingyou prescription combined with western medicine for advanced gastric cancer with positive helicobacter pylori. *J New Chinese Med*. 2020;52(18):108–112.
43. Yu L, Hou AJ, Wang WH. Combination of "Huoxue Huayu Yangyin Decoction" and FOLFOX4 chemotherapy regimen for advanced gastric cancer: a report of 30 cases. *SH. J. TCM.*. 2012;46(7):47–49.
44. Shi LE Chinese Community Doctors; 2019:104–105.
45. Huang ZF, Wei JS, Li HZ, et al. Impacts on the quality of life and immune function for the patients with gastric cancer at the late stage treated with the selective medication of jianpi fuzheng decoction and chrono chemotherapy. *World J Integr Tradit Western Med*. 2012;7(7):590–593.
46. Zhu ZC, Sun TZ, Hu CH, et al. Clinical observation on the treatment of advanced gastric cancer in the elderly by Jianpi Fuzheng Tang and its effect on survival period. *Shaanxi J TCM*. 2017;38(8):1014–1015 141.
47. Xiong J. Efficacy of TCM spleen righting combination chemotherapy in advanced gastric cancer. *J Med Forum*. 2013;34(9):57–58.
48. Huang JQ, Cao JX. Therapeutic effect of JianpiHuayu decoction combined with chemotherapy in treating 30 cases of advanced gastric cancer with spleen deficiency, phlegm and stasis type. *Hunan J Tradit Chinese Med*. 2014;30(4):53–54.
49. Liu ZW, Wang DL, Peng XF, et al. Effect of jianpi huayu decoction on immune func-

tion and toxicity for patients with gastric cancer before and after chemotherapy. *J. Sichuan TCM.*. 2019;37(10):92–96.
50. Jia YN, Li JP. Analysis of the effect of jianpi huayu decoction combined with chemotherapy in patients with advanced gastric cancer. *China Continu Med Educat*. 2018;10(22):146–148.
51. Zhao XN, Xie WH. Therapeutic efficacy of Jianpi Huayu formula combined with chemotherapy in treating advanced gastric cancer and its effect on quality of life. *Acta Chinese Med Pharmacol*. 2016;44(3):105–108.
52. Huang P, Tao MX, Xu C, et al. Clinical effects of jianpi huoxue decoction combined with chemotherapy on quality of life and immune function in patients with advanced gastric cancer. *J. Hubei Univ Chinese Med*. 2016;18(6):37–39.
53. Wang P, Tang WW. Thirty cases of advanced gastric cancer treated with chemotherapy combined with Jianpi Quyu decoction. *J Changchun Univ TCM*. 2013;29(6):400–401.
54. Meng LF. Effectiveness and toxic side effects, quality of life, and physical condition of Jianpi Quyu Decoction treatment on advanced gastric cancer patients. *J Math Med*. 2020;33(7):1062–1063.
55. Chui QL, Ma DY, Hu YH, et al. Clinical observation of jianpi wenzhong decoction and chemotherapy in treatment of advanced gastric cancer. *Liaon J Tradit Chinese Med*. 2018;45(5):974–976.
56. Zhang SF. Efficacy of Jianpi Xiao'ai Decoction combined with chemotherapy in treating advanced gastric cancer in the elderly. *Guide China Med*. 2012;10(34):280–281.
57. Wu XM, Zhang HJ, Xu YP, et al. Effect of Jianpi xiaoai decoction combined with mFOLFOX6 chemotherapy on tumor attenuation and tumor markers with gastric cancer patients. *Chinese Archive TCM*. 2018;36(6):1435–1438.
58. Weng ML, Wu XL, Song XW, et al. Clinical Study on Jianpi Xiaoji Tang for Advanced Gastric Cancer. *J. New Chinese Med.*. 2020;52(9):114–116.
59. Chen F, Lao GQ, Shi ZY, et al. Impact of Jianpi Xiaopi decoction on the life quality of advanced gastric cancer patients. *Clin J Chinese Med*. 2016;8(3):130–133.
60. Chen QS, Chen Y, Pei RQ, et al. Effects of spleen-enhancing and tumor-suppressing decoction on survival quality of patients with advanced gastric cancer. *Chinese Med Modern Distance Educ China*. 2012;10(12):129–130.
61. Ma Y, Cao JX. Clinical study on 40 cases of gastric cancer with spleen deficiency and phlegm stasis type by Jianpi Yiqi Sanjie Tang. *Guid J Tradit Chinese Med Pharmacol*. 2017;23(21):54–56.
62. Wang L. Effect of Jianpi Yiqi Sanjie decoction combined with chemotherapy in treating stage IV of gastric cancer with syndrome of spleen deficiency phlegm and blood stasis. *Docter*. 2018;3(10):49–50.
63. ZL Jin, Dai GJ, Xu YH. Study on therapeutic efficacy and quality of life of Jianpi Yiqi Yangyin Huoxue Formula combined with modified DCF chemotherapy in patients with advanced gastric cancer. *Guid J Tradit Chinese Med Pharmacol*. 2016;22(5):97–98.
64. Lai YJ, Chen NJ, Wu DH, et al. Clinical observation on 25 cases of advanced gastric cancer treated with chemotherapy by self-formulated Jianpi Yishen Decoction. *FuJian J. TCM.*. 2010;41(5):18–19.
65. Wang BQ, Liu XD. Clinical efficacy and safety observation of Jianpi Yishen Decoction combined with chemotherapy in the treatment of advanced gastric cancer in elderly people. *Acta Chinese Med Pharmacol*. 2015;43(6):97–99.
66. Xu G. The rapeutic effect of jianpi yishen decoction on elderly patients with advanced gastric cancer on the basis of routine chemotherapy. *China Reflexol*. 2018;27(18):181–182.
67. Zheng QH, Chen WG, Wang FL, et al. Observation on the adjuvant therapeutic effect of Jianpi Yishen traditional Chinese medicine on chemotherapy patients with advanced gastric cancer. *J Sichuan TCM*. 2012;30(3):73–74.
68. Wang HL. Clinical research on adjuvant treatment of advanced gastric cancer by Jianpi Yiwei Decoction. *Clinical J Chinese Med*. 2015;7(30):129–130.
69. Wang R, Feng J, Wang YL. Clinical study on 34 cases of advanced gastric cancer treated with " Jian Zhong Hua Shi Decoction" combined with XP regimen. *Jiangsu J TCM*. 2011;43(6):32–33.
70. Xing KJ, Chen CC. Observation on the efficacy of self-proposed Kang'ai decoction in the adjuvant treatment of advanced gastric cancer in the elderly and its effect on patients' immune function and quality of life. *Chinese J Tradit Med Sci Technol*. 2017;24(6):759–760 69.
71. Fang L. Reducing gastrointestinal side effects after chemotherapy for gastric cancer by adding flavors to Lizhong Tang and combining it with dietary therapy formula: 30 cases. *Jiangxi Univ Tradit Chinese Med*. 2018;49(4):55–56.
72. Feng X. Clinical observation on the treatment of progressive gastric cancer with Chinese medicine and DCF chemotherapy regimen. *World Latest Med Inf (Electronic Version)*. 2015;15(54):82 97.
73. Lin H, Wu DH, Yang AL. Clinical observation on the improvement of quality of life of advanced gastric cancer chemotherapy patients by adding Jia Wei Liu Jun Zi Tang. *Strait Pharmaceutical J*. 2017;29(6):152–153.
74. Fan YH. Efficacy of Liujunzi-Tang combined with chemotherapy in the treatment of middle and advanced gastric cancer. *Shaanxi J Tradit Chinese Med*. 2013;34(10):1219–1221.
75. Wang JM. Observation on the clinical efficacy of Liujunzi Tang with chemotherapy in the treatment of middle and advanced gastric cancer. *Health Everyone*. 2016;18:131.
76. Guo J, Wang N. Effect of Qiangpiyiqi decoction combined with S-1 in the treatment of patients with advanced gastric cancer. *Chin J Clin Oncol Rehabil*. 2016;23(1):76–78.
77. He HH, Zhuo DB, Shen H, et al. Clinical observation on 22 cases of advanced gastric cancer patients with chemotherapy failure treated with QiZhuFang combined with FOLFOX4 regimen. *J Tradit Chinese Med*. 2014;55(23):2020–2024.
78. Zhang LH, Zhao CJ, Wu H, et al. Exploration on the effect of shengyang yiwei decoction plus reduction in chemotherapy for advanced gastric cancer patients with wet resistance syndrome of yang deficiency. *World Chinese Med*. 2020;15(24):3792–3796.
79. Kong KK. Efficacy of shenhubanxia decoction combined with chemotherapy in patients with advanced gastric cancer. *Henan Med Res*. 2021;30(13):2463–2465.
80. Li ZP, Xu L, Xue T, et al. Clinical observation on 50 cases of progressive gastric cancer treated with Shen Ling Bai Zhu San combined with TS chemotherapy regimen. *J. TCM.*. 2016;57(16):1393–1396.
81. Zhang YY. Clinical efficacy of Shenlingbaizhusan combined with chemotherapy in treating patients with gastric cancer. *Clin Pharm*. 2017;12(9):39–41.
82. Lai YJ, Huang JR, Wang Y. Effect of Shenlingbaizhu-san on the immunosuppressive status of dose-intensive chemotherapy for gastric cancer. *FuJian J. TCM.*. 2018;49(6):18–19 22.
83. Yu JT. Combination of chemotherapy and traditional Chinese medicine in the treatment of middle- and late-stage gastric cancer: 45 clinical observations. *Chinese J Ethnomed Ethnopharm*. 2019;28(8):110–111 4.
84. Liu GQ. Clinical efficacy and effect on immune function of Sen Yi Jianzhong Tang combined with SOX chemotherapy in the treatment of middle and advanced gastric cancer. *Forum on TCM*. 2018;33(5):40–42.
85. Wang X, Huang YH. Clinical analysis of shenyi jianzhong decoction combined with s-1 in treatment of advanced gastric cancer. *Acta Chinese Med*. 2017;32(10):1844–1848.
86. Yang Y, Ma J, Zhang HY. Clinical study on 40 cases of middle and advanced gastric cancer treated with CapeOX regimen chemotherapy combined with Shen Yu Yang Wei Decoction. *Jiangsu J TCM*. 2018;50(4):40–43.
87. Jia SX, Chen YN, Liao MM, et al. Observation on the efficacy of 31 cases of middle and advanced gastric cancer treated with tonic method. *Zhejiang J. TCM.*. 2019;54(1):31.
88. Cao J. The analysis of Curative Effect of traditional Chinese medicine combined with FOLFOX-4 chemotherapy on Treatment for the patients with advanced gastric cancer. *Liaon J Tradit Chinese Med*. 2010;37(3):493–495.
89. Wu SB. Clinical study on the treatment of middle and advanced gastric cancer with Wei Ai Ning Tang combined with western medicine. *Shaanxi J TCM*. 2020;41(7):894–896.
90. Yin HF, Wang J, Sun X, et al. The effect of Wei Ai Ning Tang on the quality of life of late-stage gastric cancer patients after chemotherapy. *Heilongjiang Med J*. 2016;29(4):702–704.
91. Gu GQ, Zhang BC, Fan YH, et al. Effects of oral administration of traditional Chinese medicine prescription combined with chemotherapy on peripheral blood T-lymphocyte subpopulations and serum MMP-9, TIMP-1 and VEGF expression in elderly gastric cancer patients. *Chinese J Gerontol*. 2020;40(3):526–529.
92. Ni SM, Zeng SH, Chan HL. Clinical efficacy study on palliative treatment of advanced gastric cancer with traditional Chinese medicine. *Chinese Rural Health Serv Administrat*. 2015;35(3):378–379.
93. Tang JQ, Xu MJ. Clinical observation on 24 cases of advanced gastric cancer after applying chemotherapy with S-1 by adding and subtracting Xiangsha Liu Jun Zi Tang. *Hunan J TCM*. 2017;33(5):59–61.
94. Zhang LX, Yang Y, Zhang QN, et al. Effects of Yiqi Jianpi Formula combined with SOX regimen on immune function and therapeutic efficacy in patients with advanced gastric cancer. *Gansu Med J*. 2020;39(4):313–315.
95. Li PK, Li PY. Feasibility and safety of Xiangsha Liu Junzi Tang as adjuvant treatment for advanced gastric cancer. *Nei Mongol J TCM.*. 2016;35(5):12–13.
96. Tong X, Xiao DH, Li M, et al. Clinical observation of the combined treatment of the modified xiangsha liujunzi decoction and XELOX scheme in treatment of the advanced gastric cancer. *World J Integrat Tradit Western Med*. 2018;13(12):1633–1635 52.
97. Hu GP. Exploring the role of Xiangsha Liujunzi Tang combined with YiWei Tang in chemotherapy patients with advanced gastric cancer. *Heilongjiang J Tradit Chinese Med*. 2019;48(2):17–18.
98. Gu QH, Hu B, Zhang XD, et al. Clinical observation on xiaotan sanjie formula combined with chemotherapy for 32 cases of advanced gastric cancer. *J. Tradit Chinese Med*. 2013;54(23):2008–2011 7.
99. Yu GH, Yao Q, Zhang HB, et al. Chinese Herbal Medicine Yiqi Jianpi Prescription combined with S-1 as first-line treatment for 41 cases of advanced gastric cancer. *Beijing J. TCM.*. 2018;37(4):318–320 23.
100. Gao CC, Fan X, Li N. Effects of Yiqi Jianpi Huaji Formula on the efficacy of chemotherapy, patient safety and prognosis of gastric cancer. *Shaanxi J Tradition Chinese Med*. 2019;40(4):475–477.
101. Bu XH. Observation on the effect of combining chemotherapy with Yiqijianpihuoxue-Tang in the treatment of patients with middle and advanced gastric cancer. *J. Contemporary Med Sympos.*. 2016;14(5):16–17.
102. Ge J, Zhu CD. Analysis of the clinical effect of Yiqi Jianpi Huoxue-Tang combined with chemotherapy regimen on middle and advanced gastric cancer. *J. North Pharm*. 2017;14(10):22–23.
103. Jiang XF, Shao CF. Clinical observation on FMC chemotherapy regimen combined with yiqijianpihuoxue tang for advanced gastric cancer. *J. New Chinese Med*. 2017;49(2):124–126.
104. Pang SH. Efficacy of Yiqi Jianpi Jiedu Formula combined with FOLFOX4 in the treatment of advanced gastric cancer. *J. Henan Med Coll*. 2018;30(6):632–635.
105. Zhou KN, Bai SG. The Quality of Randomized Parallel Controlled Study of Chemotherapy in Advanced Gastric Cancer and Improve Survival of Yiqi Jianpi Qingre Huoxue Method. *J Pract Tradit Chinese Inter Med*. 2015;29(7):42–44.
106. Zhu LF, Chen YL, Zhang XL. Effects of Yiqi Jianpi Yangwei Formula on the efficacy and survival quality of advanced gastric cancer patients after chemotherapy. *Guiding J TCM Pharm*. 2016;22(13):81–83.

107. Xiong HN, Tang XL, Yu J, et al. Treatment of 30 cases of middle and advanced gastric cancer with the method of Yiqi Qingdu Huayu prescription. *Shaanxi J TCM*. 2012;33(1):7–10.
108. Ma DY, Liu M. Effect of yiqi qingre jiedu recipe combined with chemotherapy on balance and quality of peripheral blood th17treg cells for patients with advanced gastric cancer. *J. Sichuan of Tradit Chinese Med*. 2018;36(8):83–87.
109. Ji GY. Analysis of clinical value of Yiqi Shenghua Tang combined with chemotherapy in treating elderly gastric cancer. *Chinese J Med Guide.*. 2016;14(32):219–220.
110. Wang JT, Yin Y, Li XT, et al. Clinical observation of yiqi yangyin prescription combined with chemotherapy for advanced gastric cancer and its effect on immune function. *J. New Chinese Med*. 2018;50(11):171–173.
111. Liu GY. Clinical effect of Jiawei Yiwei Shengyang Tang combined with DOF regimen in the treatment of advanced gastric cancer. *Clin Res Pract*. 2021;6(4):135–137.
112. Li YX. Effect of Yi Wei Xiao Ai Decoction in treating spleen deficiency, phlegm and stasis type of gastric cancer and its effect on immune function and serum LAG-3 and DKK-1. *Modern J Integrat TCWM.*. 2020;29(9):962–967.
113. Huang MQ, Wang XH, Ni JL, et al. Synergism, attenuation and survival of Yiwei Xiao'ai Decoction combined with chemotherapy in the treatment of advanced gastric cancer. *World J Integrat Tradit Western Med*. 2020;15(4):597–600 608.
114. Shen GX. Clinical observation on 34 cases of advanced gastric cancer treated with chemotherapy by Zhengyang Lilao Tang. *Hunan J TCM*. 2017;33(4):46–47.
115. Yu JP. Zhengyang lilao decoction combined with bevacizumab chemotherapy in the treatment of advanced gastric cancer for 53 cases. *Chinese Med Modern Distance Educ China*. 2019;17(11):117–118.
116. Wang J. Therapeutic efficacy of Ziyin Jianpi Quyu Decoction in treating stage III-IV gastric cancer and its effect on immune function with SOX chemotherapy. *Chin J Public Health Eng*. 2020;19(4):613–615.
117. Jiang XJ. Clinical observation on 134 cases of advanced gastric cancer treated with chemotherapy combined with traditional Chinese medicine. *Chinese J Ethnomed Ethnopharmac*. 2018;27(12):107–111.
118. Wang X, Sun TZ. A clinical observation of treating advanced gastric cancer in the TCM herbal compound plus chemotherapy. *Clin J Chinese Med*. 2011;3(13):8–10.
119. Chen YC. Exploring the pathogenesis of advanced gastric cancer. *J Changchun Univ TCM.*. 2011;27(6):951–953.
120. Yu JR, Liu YY, Gao YY, et al. Diterpenoid tanshinones inhibit gastric cancer angiogenesis through the PI3K/Akt/mTOR signaling pathway. *J Ethnopharmacol*. 2024;324:117791.
121. Li M, Wang X, Wang Y, et al. Strategies for remodeling the tumor microenvironment using active ingredients of Ginseng—A promising approach for cancer therapy. *Front Pharmacol*. 2021;12:797634.
122. YQ FAN, Ma Z, Zhao LL, et al. Anti-tumor activities and mechanisms of Traditional Chinese medicines formulas: a review. *Biomed Pharmacother*. 2020;132:110820.
123. Ambrose Okem, Charlotte Henstra, et al. A review of the pharmacodynamic effect of chemo-herbal drug combinations therapy for cancer treatment. *Med Drug Discover*. 2023;17:100147.
124. Brianna Lee SH. Chemotherapy: how to reduce its adverse effects while maintaining the potency? *Med Oncol*. 2023;40(3):88.
125. Wei JH, Liu Z, He J, et al. Traditional Chinese medicine reverses cancer multidrug resistance and its mechanism. *Clin Translation Oncol*. 2022;24:471–482.
126. Lu S, Sun XB, Zhou ZB, et al. Mechanism of Bazhen decoction in the treatment of colorectal cancer based on network pharmacology, molecular docking, and experimental validation. *Front Immunol*. 2023;14:1235575.
127. Yang SY, et al. Evaluation of the potential herb-drug interaction between Bojungikki-tang and PD-L1 immunotherapy in a syngeneic mouse model. *Front Pharmacol*. 2023;14:1181263.
128. Kwon HE, Kim JN, Kwon MJ, et al. The traditional medicine bojungikki-tang increases intestinal motility. *Pharmacogn Mag*. 2021;17(5):S1–S8.
129. Zhou M. Network pharmacology approach to investigate the mechanism of modified liu jun zi decoction in the treatment of chronic atrophic gastritis. *Evid-Based Complement Altern Med*. 2022:1–12.
130. Xu CC, Su XL, Fan WY, et al. Study on the mechanism of action of the drug pairing of Oldenlandiae Diffusa Herba and Scutellaria Barbata Herba in the treatment of gastric pre-cancerous lesions based on network pharmacology. *Beijing J Tradit Chinese Med*. 2021;40(8):901–906.
131. Zhang Y, Luo XN, Guo Z. Clinical study of oldenlandia diffusa-scutellaria barbata for the maintenance treatment of malignant tumors. *J Gannan Med Univ*. 2022;42(6):583–586.
132. Zhou EH, Xu EP, Zhang N, et al. XiangshaLiuJunzitang for Prevention and Treatment of Gastric Cancer: a Review. *Chinese J Exp Tradit Med Form*. 2023;29(4):221–227.
133. Ke G, Dong QK, Xiao SR, et al. Molecular mechanism of ShenlingBaizhu powder in treatment of cancer cachexia based on network pharmacology. *J Pharmaceutic Pract Ser*. 2024;42(3):1–9.
134. Cheng MQ, Hu J, Zhao Y, et al. Efficacy and safety of astragalus-containing traditional Chinese medicine combined with platinum-based chemotherapy in advanced gastric cancer: a systematic review and meta-analysis. *Front Oncol*. 2021;11:632168.
135. TAN Y, Wang HP, Xu BW, et al. Chinese herbal medicine combined with oxaliplatin-based chemotherapy for advanced gastric cancer: a systematic review and meta–analysis of contributions of specific medicinal materials to tumor response. *Front Pharmacol*. 2022;13:977708.
136. Li X, Yang G, Li X, et al. Traditional Chinese medicine in cancer care: a review of controlled clinical studies published in Chinese. *PLoS One*. 2013;8(4):e60338.
137. Kim DH, Kim JH, Yoo HS, et al. A Literature Review on the Application of the Propensity Score Matching Method in the Field of Asian Oncology. *J Kor Tradit Oncol*. 2022;27(1):25–36.