World Journal of Gastroenterology

Submit a Manuscript: http://www.wjgnet.com/esps/
Help Desk: http://www.wjgnet.com/esps/helpdesk.aspx
DOI: 10.3748/wjg.v21.i15.4466

World J Gastroenterol 2015 April 21; 21(15): 4466-4490
ISSN 1007-9327 (print) ISSN 2219-2840 (online)

REVIEW

Herbal traditional Chinese medicine and its evidence base in gastrointestinal disorders

Rolf Teschke, Albrecht Wolff, Christian Frenzel, Axel Eickhoff, Johannes Schulze

Rolf Teschke, Axel Eickhoff, Department of Internal Medicine Ⅱ, Division of Gastroenterology and Hepatology, Klinikum Hanau, Teaching Hospital of the Medical Faculty of the Goethe University Frankfurt/Main, D-63450 Hanau, Germany
Albrecht Wolff, Department of Internal Medicine Ⅱ, Division of Gastroenterology, Hepatology and Infectious Diseases, Friedrich Schiller University Jena, D-07747 Jena, Germany
Christian Frenzel, Department of Medicine I, University Medical Center Hamburg Eppendorf, D-20246 Hamburg, Germany
Johannes Schulze, Institute of Industrial, Environmental and Social Medicine, Medical Faculty of the Goethe University Frankfurt/Main, D-60591 Frankfurt/Main, Germany
Author contributions: Teschke R had the idea for this work; Wolff A, Frenzel C and Eickhoff A designed the report and performed the literature search; Eickhoff A and Schulze J analyzed the publications; Schulze J provided the tables; Teschke R and Schulze J wrote the paper.
Conflict-of-interest: None of the authors has a conflict of interest in relation to the preparation of this work.

Correspondence to: Rolf Teschke, MD, Professor, Department of Internal Medicine Ⅱ, Division of Gastroenterology and Hepatology, Klinikum Hanau, Teaching Hospital of the Medical Faculty of the Goethe University Frankfurt/Main, Leimenstrasse 20, D-63450 Hanau, Germany. rolf.teschke@gmx.de
Telephone: +49-61-8121859
Received: November 22, 2014
Peer-review started: November 23, 2014
First decision: January 8, 2015
Revised: January 22, 2015
Accepted: February 11, 2015
Article in press: February 11, 2015
Published online: April 21, 2015

Abstract

Herbal traditional Chinese medicine (TCM) is used to treat several ailments, but its efficiency is poorly documented and hence debated, as opposed to modern medicine commonly providing effective therapies. The aim of this review article is to present a practical reference guide on the role of herbal TCM in managing gastrointestinal disorders, supported by systematic reviews and evidence based trials. A literature search using herbal TCM combined with terms for gastrointestinal disorders in PubMed and the Cochrane database identified publications of herbal TCM trials. Results were analyzed for study type, inclusion criteria, and outcome parameters. Quality of placebo controlled, randomized, double-blind clinical trials was poor, mostly neglecting stringent evidence based diagnostic and therapeutic criteria. Accordingly, appropriate Cochrane reviews and meta-analyses were limited and failed to support valid, clinically relevant evidence based efficiency of herbal TCM in gastrointestinal diseases, including gastroesophageal reflux disease, gastric or duodenal ulcer, dyspepsia, irritable bowel syndrome, ulcerative colitis, and Crohn's disease. In conclusion, the use of herbal TCM to treat various diseases has an interesting philosophical background with a long history, but it received increasing skepticism due to the lack of evidence based efficiency as shown by high quality trials; this has now been summarized for gastrointestinal disorders, with TCM not recommended for most gastrointestinal diseases. Future studies should focus on placebo controlled, randomized, double-blind clinical trials, herbal product quality and standard criteria for diagnosis, treatment, outcome, and assessment of adverse herb reactions. This approach will provide figures of risk/benefit profiles that hopefully are positive for at least some treatment modalities of herbal TCM. Proponents of modern herbal TCM best face these promising challenges of pragmatic

modern medicine by bridging the gap between the two medicinal cultures.

Key words: Evidence based trials; Traditional Chinese medicine; Herbal traditional Chinese medicine; Gastrointestinal disorders

Core tip: This review focuses on evidence based trials of herbal traditional Chinese medicine (TCM) in managing gastrointestinal disorders and presents a practical reference guide on its role for treating these diseases. Overall quality of placebo controlled, randomized, controlled, double-blind clinical trials was poor; mostly neglecting stringent evidence based diagnostic and therapeutic criteria. Accordingly, appropriate Cochrane reviews and meta-analyses were limited and failed to support valid, clinically relevant evidence based efficiency of herbal TCM in most gastrointestinal diseases, including gastroesophageal reflux disease, gastric or duodenal ulcer, dyspepsia, irritable bowel syndrome, ulcerative colitis, and Crohn's disease. Despite its interesting philosophical background with a long history, the general use of herbal TCM to treat various gastrointestinal diseases cannot be recommended due to lacking evidence based efficiency and a negative risk/benefit profile. Thus, substantial skepticism remains, proposing future studies with focus on well performed placebo controlled, randomized, double-blind clinical trials. Herbal product quality and standard criteria for diagnosis, treatment, and outcome should also be considered.

Teschke R, Wolff A, Frenzel C, Eickhoff A, Schulze J. Herbal traditional Chinese medicine and its evidence base in gastrointestinal disorders. *World J Gastroenterol* 2015; 21(15): 4466-4490 Available from: URL: http://www.wjgnet.com/1007-9327/full/v21/i15/4466.htm DOI: http://dx.doi.org/10.3748/wjg.v21.i15.4466

INTRODUCTION

Plants have been used for medicinal purposes long before recorded history in many parts of the world[1-7]. In China, traditional Chinese herbal medicine (TCM) emerged[2,7] and influenced the traditional herbal medicine in Japan[2], called Kampo medicine[8], and in various other Asian countries such as South Korea[9]. The overall increasing popularity of herbal TCM led to substantial interest in laboratory and clinical studies on herbal TCM to evaluate its efficiency in various ailments and to elucidate mechanisms of its actions[2-4,7,9-13]. However, ancient herbal TCM is increasingly seen critically due to concerns of efficiency[13], safety[14], and herbal product quality[15-17]. Herbal TCM has high economic contribution to our society with special financial benefits for herbal TCM producers, providers, and healers. Considering this economic impact, the resulting costs as burden for consumers and society have to be justified.

In this article, we highlight the history and principles of the ancient TCM philosophy proposed as therapeutic cornerstones of herbal TCM, which is preferred by some interested patients as opposed to modern medical treatment. We focus on gastrointestinal disorders and the evidence for ancient herbal TCM therapy options.

LITERATURE SEARCH

Clinical studies for the efficiency of TCM and herbal TCM were identified by searching PubMed and Cochrane clinical studies using "traditional Chinese medicine", "herbal traditional Chinese medicine" and additional keywords denoting gastrointestinal symptoms or diseases of organs such as the gall bladder, liver, pancreas, esophagus, stomach, small intestine, and colon. Results were individually checked whether they described clinical studies with herbal TCM treatment. In order to identify all relevant publications, PubMed was additionally searched for all publications with TCM preparations as described in the clinical studies; again, search results were individually checked for relevant clinical studies. The last three volumes of the Journal of Traditional Chinese Medicine were manually searched for publications of herbal TCM preparations used in gastrointestinal diseases. Neither strategy revealed additional clinical trials.

All results were analyzed whether they reported clinical studies using accepted diagnostic criteria for both the presence of the disease and the treatment effects with herbal TCM preparations. We excluded all studies without at least one accepted diagnostic standard (*e.g.*, diagnostic criteria exclusively based on TCM symptom categorization); we also excluded studies investigating basic pathological mechanisms in healthy volunteers, clinical trials using chemically defined compounds, and clinical trials using nonherbal treatments such as acupuncture or moxibustion. All studies with the full text publication in Chinese only were evaluated by the English language abstract.

Criteria of study quality

The following criteria were used: characterization of herbal preparation and comparative treatment, diagnostic criteria for presence of disease, randomization of participants, blinding of patients and physicians, criteria for therapeutic improvement, and statistical evaluation of data. The levels for individual trials were taken from the criteria defined by the Oxford Center for Evidence Based Medicine (EBM)[18,19], with level Ⅰ: randomized clinical trial; level Ⅱ: non-randomized experimental study; level Ⅲ: non-randomized non-experimental high quality study; and level Ⅳ: observation or opinion.

Table 1 Consolidated standards of reporting trial criteria and level of adherence in herbal traditional Chinese medicine treatment clinical trials

Item	Criterion	Adherence
Group allocation	Randomization	Often claimed; specifics are rarely reported
Hypothesis	Prospective formulation	Rarely reported
Parameter	Primary, secondary outcome	Rarely reported; often inclusion of parameters irrelevant to the initial question
Patients, Treatment time	Selection, rationale for duration	Mostly given
Intervention, control	Herbal composition, placebo	Often lacking, even for drugs under consideration
Blinding	Physician, patient blinding	Often lacking
Data evaluation	Statistical methods	Often lacking. In a lot of publications the reanalysis is impossible or gives different results
	Data selection	Often only report of criteria which are statistically significant. Rarely report of data being comparable
	Data presentation	Often no data for range, standard deviation, confidence interval or relative risk presented
		Often no distinction between "in group" effects and "between group" effects
Interpretation	Conclusions	Often overoptimistic. Lack of consideration for results not fitting the initial assumption

Data compilation and modification from a previous report[30]. CONSORT: Consolidated standards of reporting trials; TCM: Traditional Chinese medicine.

EBM

Principles

EBM has been developed to apply the best available information to individual clinical problems[20]. Thus, publications including clinical trials first have to be evaluated to recognize bias in clinical studies deriving from inappropriate patient selection, randomization, treatment parameter identification, data evaluation or data presentation[21]; only unbiased trials may be used for EBM. The aim of EBM thus is to select the best patient care based on trusted data; the best data are results from randomized controlled trials or clinical controlled trials[21,22]. These trials compare the effects of competing therapy options; ideally, neither patient nor physician is aware of the treatment nature (blinding)[23,24]. Quite often, no placebo controlled, randomized, double blinded clinical trial has been performed for specific problems. In these cases, clinical decisions must be aided by evidence of a lower level, *i.e.*, by results from non-randomized clinical trials or clinical cohort studies; the evaluation of these studies has to consider the resulting limitations for open clinical studies. There is consensus that placebo controlled, randomized, double-blind clinical trials are the gold standard to obtain valid results of treatment efficiency.

Cochrane collaboration, consolidated standards of reporting trials criteria

Based on the proposition of Archibald Lemon Cochrane[25], EBM groups worldwide founded the Cochrane collaboration in 1993 to provide systematic reviews for medical problems in diagnosis and therapy. Randomization and blinding are a prerequisite for including studies into a Cochrane review, which also have covered clinical trials on TCM[26-29]. A more recent study on TCM treatment[29] uncovered that a large number of "randomized" TCM studies in effect were not randomized since "the authors had misunderstood the randomization procedure"[29]. Both EBM and the Cochrane collaboration efforts resulted in guidelines for planning and reporting randomized clinical trials[24,30]. The medical community has adopted the quality criteria as consolidated standards of reporting trials (CONSORT) criteria. These criteria were adapted and used in this review also to assess the clinical trials or cohort studies included in our evaluation (Table 1).

TCM

General considerations

TCM comprises various different practices[10,31], including herbal medicine[10,14,31-37], acupuncture[11,31-33], moxibustion as a variant of acupuncture with local heat therapy[31,33], massage[31,33] as Tui Na, the therapeutic massage[10,13], dietary therapy[10,31], physical exercise such as shadow boxing[31], and Qigong[33]. According to clinical trials performed in mainland China, the focus of TCM is on herbal remedies (90.3%), followed by acupuncture (4.4%), massage (3.8%), moxibustion (1.2%), Qigong (0.1%), and other therapies (0.2%)[33].

TCM has been used by Chinese communities from ancient times[2] and dates back more than 2500 years[10]. A cornerstone of TCM was the introduction of acupuncture in Western countries in the 1600s[31]. Another major contribution of TCM to general health issues was variolation developed in the 16th century in China as a method to immunize against smallpox[31]. TCM became an integral part of Chinese health care; in 2006, the TCM sector provided health care for over 200 million outpatients and 7 million inpatients, accounting for 10%-20% of the health care in China[31]. In the United States, according to the 2007 National Health Interview Survey that included a comprehensive survey on the use of complementary health approaches, an estimated 3.1 million United States adults had used acupuncture in the previous year[10].

Most of the principles of TCM were derived from the philosophical ideas developed from Taoism and Confucianism[10,31]. Ancient beliefs on which TCM is based include: the human body is a miniature version

of a larger, surrounding universe; harmony between two opposing forces, called yin and yang, supports health, and disease results from an imbalance between these forces; five elements - fire, earth, wood, metal, and water - symbolically represent all phenomena, including the stages of human life, and explain the functioning of the body and how it changes during disease; Qi, a vital energy that flows through the body, performs multiple functions in maintaining health[10]. The TCM philosophy created curiosity and skepticism in Western countries, since transparency is lacking. A pragmatic approach to successfully transfer TCM philosophy into valid treatment modalities of modern medicine should postulate clear evidence criteria for therapeutic efficiency, prove the absence of major adverse reactions and provide a positive benefit: risk profile.

In a 2007 review, the quality of reported randomized controlled trials (RCTs) of TCM efficiency was considered poor, based on an analysis of trial results published from 1999 to 2004[33]. This study identified 37252 Chinese language articles in TCM journals published in mainland China. Clinical trials were recognized in 26263/37252 articles, corresponding to 70.5%. Among these 26263 clinical trials, 7422 were initially identified as RCTs, equivalent to 28.3%, but of the 7422 trials only 1329 (17.9%) were truly randomized[33].

Some important methodological components of the RCTs were incompletely reported, such as sample size calculation (reported in 1.1% of RCTs), randomization sequence (7.8%), allocation concealment (0.3%), implementation of the random allocation sequence (0%), and intention to treat analysis (0%)[33]. All reports were searched according to guidelines of the Cochrane Centre, and a comprehensive quality assessment of each RCT was completed using a modified version of the CONSORT checklist[33]. Overall, publications of TCM trials are abundant (10000[32] to 26263[33] publications), but their scientific quality is limited.

The poor quality of many TCM RCTs[33] was continuously discussed in various reports during the last decades[13,31,32,36]; most Cochrane systematic reviews of TCM are inconclusive, due specifically to poor methodology and heterogeneity of the studies reviewed[13]. Similarly, 19/26 acupuncture reviews concluded that there was not enough good quality trials to make a definitive conclusion of its efficiency[13]. This particular situation is difficult to reconcile when evidence for efficiency is a crucial criterion. It is well recognized that planning and performing RCTs, data analysis and compilation are cumbersome, time consuming, and expensive[13], with additional efforts to be put into editorial and reviewing work.

Unless strict criteria are applied for clinical trials of alternative medicinal systems including TCM, these studies will not be accepted as valid. For most analyses, including those evaluated in this review, major quality criteria are violated, including primary research hypothesis formulation, clinical inclusion criteria and outcome parameters, and appropriate statistical analysis.

Although these quality shortcomings of TCM RCTs are well recognized[29,36] and amply documented, even recent studies employ a design of treating both verum and control groups with "established" drugs and adding a Chinese herbal preparation in the verum group[37]. Although this design may have its merits for special clinical problems like efficiency of comedications, they do not allow conclusions about the treatment efficiency of the added herbal preparation.

Another major problem is inconsistent reporting. Whereas group differences before and after treatment have to de documented to prove the efficiency of any treatment ("in group" effects; difference of change within groups), clinical trials are constructed to detect differences between groups with different therapeutic approaches ("between groups" effects, difference between groups without reference to treatment). Therefore, results must strictly separate between the effectivity of a treatment shown by changes in parameter(s) before and after treatment, and indicate the difference between groups. Current clinical studies are designed either to prove superiority of a new drug, or to show equal effectivity of two different drugs (noninferiority design)[38]. Especially for studies comparing herbal preparations with synthetic drugs, it seems prudent to begin with a noninferiority study design; in contrast, nearly all recent Chinese language studies claim superiority of TCM preparations to synthetic drugs. This peculiarity is highlighted in multiple Cochrane reviews of herbal TCM preparations or acupuncture; these reviews also identify no or a very low number of high quality clinical studies[26-29,39].

Specific features of herbal TCM

China is rich in plants[34-42], which favored the development of a diverse herbal TCM. About 13000 herbal preparations are used and are listed in the Chinese Materia Medica (CMM) and are available in China[34,38], being officially recognized and described in detail by the Chinese Pharmacopeia[34,37], including herbs commonly used, regional variations and folk medicine variants. The Chinese Materia Medica[37] is a reference book that also describes details of thousands of plant preparations[10], including some nonbotanical elements (animal parts and minerals)[10,34,41,42] that are incorrectly classified as herbal medicines[34]. Outside of China, only around 500 Chinese herbs are commonly used[34].

Thousands of medicinal plants in China produce an abundance of different chemicals. With the nature as a potent manufacturer of potential drugs, this treasure has led to the development of some chemically defined drugs including artemisinin and ephedrine. Failure of valid clinical studies based on EBM criteria may have prevented the detection of more pharmacologically

active principles and compounds, missing the innovation power of herbal TCM[41]. This situation is different from other countries and cultures with herbal traditional medicine, where plants were used as a source of drugs and resulted in the development of, *e.g.*, acetylic salicylic acid, atropine, codeine, colchicine, coumarins, digoxin, morphine, and quinine[41,42].

The use of herbs is considered an essential part of the TCM philosophy and its proposed therapeutic principles to improve or stabilize health conditions[10]; it takes a holistic view involving activating systems and self-regulating connections enhancing resistance to human diseases[43]. TCM philosophy classifies the causes of illness as symptoms of diseases from abnormal interactions or imbalances in the human system[44]; published diagnostic criteria, however, are poorly defined[31], difficult to ascertain in a Western health care setting and substantially different from the diagnostic approach of Western medicine. Since functional imbalance and specific manifestations of disease are described as "syndrome complex", the concept of syndrome differentiation is important in the TCM diagnostics[44]. Consequently, the use of herbal TCM initially requires an appropriate recognition of the patient's TCM symptoms; the TCM diagnosis should identify the correct symptom complex, usually by a TCM practitioner familiar with the principles of herbal TCM[35]. Ideally, the TCM provider is a physician, as in China; qualification requirements may be less strict in other countries such as Germany, where TCM providers commonly are nonmedical healers and only rarely general practitioners[42].

Herbal TCM is based on long local experience and original treatment principles[40], described in general terms without detailed characterization of herbs and diseases as compared to drug and disease descriptions by modern medicine[10,40]. While modern medicine was developed from physiology and biochemistry, the mode of action of modern drugs are understood at cellular and molecular levels, and the therapeutic efficiency is proven by valid studies[43]. For herbal TCM these criteria do not (yet) apply[40-43].

According to ancient TCM philosophy, in herbal TCM therapy herbs are prescribed tailored to the patient's symptoms, signs and constitution; the original Chinese formulae are often modified, but details of this tailoring are rarely available[43]. As a result, herbal TCM formulae of modified prescriptions continue to appear and are applied without any systematic evaluation[43]. These highly individualized herbal TCM prescriptions create problems in clinical trials of herbal TCM preparations since EBM criteria are hardly applicable, if treatment modalities differ from patient to patient[43]. Stratification of treatment for study purposes is also difficult, since most indications and contraindications of herbal TCM therapies are solely based on experience and documented in ancient books[43].

In line with ancient herbal TCM philosophy, numerous herbal TCM products are mixtures of different herbs, commonly with up to six herbs[14,39] or more[14]; typically there is a primary herb referred to as the "King"[39] or "Monarch"[34] herb. The other constituents, called also "Minister", "Assistant", or "Envoy"[34], are believed to function as modifiers of toxicity[34,39]; to synergistically increase the King herb effects[14]; to improve the immune function[39]; or to strengthen certain aspects of actions[39]. Other aspects classify herbal TCM as having high, moderate or low toxicity[40]. In the Chinese Pharmacopeia[37], herbs are described as mildly toxic to highly toxic, with 59 items of CMM in the latter category[34,37]. Since robust experimental data are lacking, the herbal TCM philosophy related to toxic elements is elusive; although known for a long time[40], it also appears that the question of herbal toxicity has not yet been fully appraised. Also, the use of nonherbal items (animal parts or heavy metals) as elements of the ancient herbal TCM philosophy is elusive[10,14,34,40,41]; animal parts often used are Bai Hua She (venom of the Chinese viper *Agkistrodon acutus*), Jiang Can (dried larvae of *Bombyx Batryticatus*, infected by *Batrytis bassiana*), Ling Yang Qing Fei (antelope horn), Liyu Danzhi (carp juice), Quan Xie (dry polypides of the scorpion *Buthus martensii*), Sang Hwang (*Phellinus lihnteus*, mushroom), Song Rong (*Agaricus blazei*, Himematsutake as Japanese Kampo Medicine, mushroom), Wu Gong (dried polypites of the centipede *Scolopendra subspinipes mutilans*), Wu Shao She (parts of the snake *Zaocys dhumnades*), and Yu Dan (fish gallbladder)[14,41].

EBM of reported herbal TCM trials

EBM criteria have rarely been applied in trials of ancient herbal TCM, as discussed in detail in the present review with reference to many reports[13,26-29,31-33,36,40-43]. Consequently, efficiency of these treatment modalities remains unproven and does not warrant a recommendation for their common use to treat patients, considering also the known risks including life-threatening hepatotoxic reactions[39-42], which should not be downplayed[42]. In particular, the present data of herbal TCM trials and risk evaluations provide no evidence for a positive benefit/risk profile[42]. The aim should be to initiate new strategies to integrate herbal TCM into modern medicine[42,38].

Perspectives of modern herbal TCM

Ancient herbal TCM and modern medicine have evolved under different empirical, theoretical, philosophical, and cultural conditions, in an attempt to establish cornerstones of valid diagnostic and therapeutic principles and to provide efficient healthcare. However, mainstream opinion suggests that the current situation of ancient herbal TCM is poor and disappointing[42], requiring substantial improvements[10-17,31-36,38-43] with the tentative aim to develop a pragmatic modern herbal TCM[42,38] that meets the needs of modern

Table 2 Clinical trials with herbal traditional Chinese medicine preparations for gastroesophageal reflux disease and esophagitis

Ref.	Patients	Intervention	Control	Outcome	Remarks
Zhang *et al*[52], 2012	186 pat.; GERD, no diagnostic criteria	64 pat.; 3 × 6 g Dalitong + 20 mg rabeprazole; 4 wk	61 pat.; 20 mg rabeprazole (control 1) 61 pat.; 3 × 10 mg domperidon + 20 mg rabeprazole (control 2); 4 wk	Intervention significantly better; unclear whether a comparison is within or between groups	No randomi-zation criteria → cohort study
Li *et al*[53], 2011	120 pat.; non- erosive reflux disease, no diag-nostic criteria	60 pat.; 3 × 10 g Tongjiang capsules; 4 wk	60 pat.; 3 × 5 mg mosapride citrate; 4 wk	For scores: in-tervention sig-nificantly better - only in PPP cal-culation; unclear whether a comparison is within or between groups	Relevant data were not available; ill defined scoring system. OR in-cluding 1 is significant
Xu *et al*[55], 2007	116 pat.; GERD	Integrated Chinese + Western medicine; no further data	Western medicine, no further data	Better long term significant effects, no significant short term effects	Inconsistent data pre-sentation
Xu *et al*[56], 2006	78 pat.; laryngopharyn-gitis by GERD, ENT diag- nostic criteria	1 dose/d Banxia Xiexing Tang; 4 wk	2 × 6 g/d Linsang Liyan Wan, 4 wk	Variety of cumulative scores; treatment is more effective	No comparative treat-ment
Zhong *et al*[54], 2005	75 pat.; reflux esophagitis	45 pat; 1 dose/d Jiangni Hewei decoction; 8 wk	30 pat; omeprazole 20 mg/d, 8 wk	No difference in cure rate, total efficiency, symptoms, gastroscopy score. Significantly lower recur-rence rate in verum group	Low patient number
Ghen *et al*[51], 2004	63 pat.; GERD, no diag-nostic criteria	30 pat.; 2 × 100 mL ZhiZhu pills; 8 wk	33 pat.; 2 × 150 mg ranitidine + 2 × 10 mg cisapride; 8 wk	Unclear whether a comparison is within or between groups; "significant improvement in all criteria"	Conclusions cannot be reproduced
Hao *et al*[57], 1998	42 pat.; GERD, diagno-sis by TCM criteria	42 pat.; Yunqitang Ⅰ, Ⅱ, Ⅲ; 4 wk	No control therapy given	"Yunqitang is effective" by TCM scoring system	

GERD: Gastroesophageal reflux disease; TCM: Traditional Chinese medicine.

medicine and possibly combines the two medicinal cultures[38,42,44-46] by bridging the gap between the herbal TCM and Western medicine[45]. Present shortcomings of ancient TCM include insufficient EBM based RCTs supporting therapeutic efficiency, major adverse effects, poor herbal TCM product quality and lack of innovation power to develop new drugs from herbal TCM, inadequate standardization, categorization, and regulation, and intransparent and not validated diagnostic criteria to establish a clinical diagnosis.

Therefore, new approaches are necessary to establish a modern herbal TCM[38,42] with its fascinating and encouraging perspectives, also regarding new drugs to be developed from herbs of TCM[42]. These new approaches should cover herbal TCM products with proven therapeutic efficiency in line with the requirements of EBM criteria and a favorable benefit/risk profile[42], ensuring product standardization and regulatory surveillance[35,43], and an effective ADR system to regulatory agencies[35]. Special scrutiny should be placed on correctly labeling of ingredients[35] and absence of toxins (aflatoxins, bacteria, and heavy metals), nonbotanical ingredients [34,41,42], and mislabeled herbs[35,36]. Until substantial progress is made establishing a modern herbal TCM, risks should be identified, not ignored[42].

GASTROINTESTINAL DISORDERS

We focused on evaluation of the evidence for efficient TCM preparations in the clinically relevant gastrointestinal disorders, thereby excluding diseases such as esophageal carcinoma[29,47], gastric carcinoma[48], pancreatic carcinoma[49], or pancreatitis[26]. Our review covers the main indications gastroesophageal reflux disease (GERD) and esophagitis, gastritis, gastric and duodenal ulcer, inflammatory bowel disease, hepatitis, biliary diseases as well as the common tumor entities of the colon and liver carcinoma, and the exclusion diagnoses dyspepsia and irritable bowel syndrome (IBS).

GERD and esophagitis

Since 2000, no Cochrane review covered gastro-esophageal reflux or esophagitis, considering Cochrane summaries and the search terms "traditional Chinese medicine" OR "Chinese herbal" AND "esophagitis" OR "reflux", except one review on GERD in asthma patients[50]; their trial database presents six relevant trials, which are included in Table 2. For treatment of GERD, seven publications compared herbal TCM preparations with ranitidine + cisapride[51], domperidone[52], mosapride[53], omeprazole[54], Western medicine[55], or the herbal TCM preparation Lingsan Liyan Wan[56]. A seventh study did not specify the comparative treatment[57]. Five studies were available in Chinese only[51,52,54,56,57] and were thus evaluated as abstracts; only the studies of Li *et al*[53] and Xu *et al*[55] were available in an English language version.

In none of these GERD studies, details were given to diagnostic criteria of modern medicine like the Los Angeles classification of severity[58], the Savary-

Miller-classification[59], or the MUSE-classification[60]; none described a randomization process. Hao *et al*[57] did not use a control group at all but compared the efficiency of the herbal TCM Yunqitang for patient groups with differing diagnostic criteria derived from TCM. Furthermore, no two studies used the same herbal TCM preparation. Only one publication listed the ingredients of the intervention herbal TCM Banxia Xiexin Tang[56]; for the other five preparations, no recipe could be identified.

All studies used "TCM symptom scores" to measure the efficiency of the intervention. Again, no publication specified these symptom scores, except Xu[56] who used a semiquantitative scoring system for laryngitis; Xu *et al*[55] did not detail the herbal TCM preparation. No publication reported endoscopic or histologic data, or results from pH-metry, but all publications claimed significantly better improvement in symptom scores.

Taken together, no trial can be rated as a randomized blinded clinical study, and five studies may qualify as open cohort studies[51,52,54,55,57]. Thus, no evidence is currently available in GERD trials to support the equivalency of herbal TCM preparations to established treatments like proton pump inhibitors (PPI). Similar results were obtained by Zhao *et al*[50], who reviewed herbal TCM for nonacute bronchial asthma complicated by gastroesophageal reflux and also concluded that currently no proven benefit can be derived from published studies.

Gastritis

A PubMed search for clinical trials using the items "Chinese herbal" AND "gastritis" retrieved 23 results. Of these, 16 publications were included in Table 3; only two studies[61,62] were reported as randomized trials. All studies originated in China, and only one report was available in English[63]. In nine studies, two different herbal TCM preparations were compared[63-71], and in only four trials, herbal TCM preparations were compared to Western medications: cimetidine[72]; triple therapy[73]; and domperidone[74,75]. In two studies, triple therapy was given in both groups, together with the herbal TCM preparations Junghua Weikang[61] or Wen Wei Chu[62]. In these 16 trials, 13 different herbal TCM preparations were tested, the three preparations Jinghua Weikang[61,74], Kang Wei[66,73], and Wen Wei Chu[62,63] were used twice, and three publications did not specify the herbal TCM preparation used[67,72,76].

All studies reported significantly better results in the verum group, nearly always for clinical symptoms. In most publications, criteria for "total efficiency" were not provided, and some trials[63,66,71] specified symptoms classified by the TCM system rather than Western clinical symptoms. In no publication (including the English ones) were sufficient data given to confirm the statistical calculations. Herbal TCM Kangwei granules were tested in two studies against herbal TCM Weifuchun[66] and bismuth triple therapy[73]. Herbal TCM Wenweishu was evaluated in one study as verum (in addition to pantoprazole, clarithromycine, and metronidazole as triple therapy) and found to improve symptom relief compared to herbal TCM therapy only[62]; in another study, Wenweishu was used as control therapy tested against the herbal TCM Yiweikang, and found inferior to the verum in symptom relief[63].

Taken together, no randomized study has been performed to test herbal TCM preparations head on against Western gastritis therapy. No study has tested herbal TCM against PPIs; in recent studies describing PPI treatment, this drug was given in both groups[61,62]. Only Chen *et al*[73] tested herbal TCM Kang Wei granules against a quadruple therapy and reported significant better improvement in TCM symptoms, without providing data for other parameters. Further ambiguities derive from incomplete description of symptom scores or a mixture of differences within one treatment group with differences between verum and control group.

Future studies should emphasize characterization of patient diagnoses included in these studies, careful selection of the control therapy, outcome definition at the start of the study, and clear data presentation.

Gastric and duodenal ulcers

Efficiency studies of herbal TCM preparations for patients with gastric or duodenal ulcers have only rarely been reported. Among 46 PubMed hits, 17 publications were identified (Table 4), which described clinical studies or clinical reports related to treatment with herbal TCM; nine trials were identified in the Cochrane clinical trials database relating to gastric ulcer and ten trials related to duodenal ulcers. Except Zhou *et al*[77], all studies are available only in Chinese and were evaluated from their English language abstracts. All studies were published in journals devoted to TCM or Chinese medicine.

Five trials were published as randomized[61,62,78-80]; specific details about blinding were mentioned only by Zhou *et al*[81], whereas all other studies did not describe blinding or used a design not amenable to blinding. Among the 17 trials included in Table 3, the study of Zhou *et al*[81] was the only one not describing significantly superior therapeutic effects of herbal TCM preparations. Four studies included patients with duodenal ulcers[61,80,82,83], five trials patients with gastric ulcer[62,77,79,84,85], and eight studies peptic ulcer[78,81,86-90]; the diagnosis was usually proven by endoscopy, for peptic ulcer the location remains unclear.

Among the studies published before 2008, ten trials compared herbal TCM preparations against chemically defined drugs, including famotidine[82,84], ranitidine[77,80,90], cimetidine[86,87,89,91], and bismuth aluminate[83]. All four recent studies used an "add-on" design, comparing a Western standard treatment with a herbal TCM preparation added to this regime; this

Table 3 Clinical trials with herbal traditional Chinese medicine preparations for gastritis

Ref.	Patients	Intervention	Control	Outcome	Remarks
Hu *et al*[61], 2012	565 pat.; gastritis or duodenal ulcer, gastroscopy	LAC (see con- trol), + 3 caps. 2/d Jinghua Weikang, 7 d, then Jinghua Weikang for 14 more days	30 mg lansopra- zole, 1000 mg amoxicilline, 500 mg clarithromycine (LAC) 2/d, 7 d, then lansoprazole 30 mg 1/d for 14 more days; or LAC + 220 mg bismuth citrate 2/d, 7 d, then bismuth citrate for 14 more days	^{14}C-urea test - no difference (abstract unclear). Similar efficiency, better symptomatic improvement (bloating, belching)	11 hospitals; data presentation in abstract unclear. All gastritis patients were included in the intervention group
Li *et al*[64], 2011	150 pat.; chronic atrophic gastritis	120 pat.; Wei Yan serial recipe (WYSR) Ⅰ - Ⅳ; no dose given, 2 × 3 mo	30 pat.; Weifuchun pills; no dose given, 2 × 3 mo	WYSR is superior to control in total effective rate, symptoms, pathology. No difference in HIF, vEGF	Improved precancerous lesions
Li *et al*[65], 2011	229 pat.; chronic atrophic gastritis	119 pat.; Hua Zhuo Jiedu recipe, no dose given; 2 × 3 mo	110 pat.; Weifuchun tablets; no dose given; 2 × 3 mo	Significantly better: pathological results, tumor markers. No difference in acid secretion	No rationale or parameter selection
Hu *et al*[62], 2010	642 pat.; chronic gastritis or gastric ulcer + *H. pylori*	196 pat.; PCM + Wenweishu 224 pat.; PCM + Yangweishu; 7 d	222 pat.; 40 mg bid pantoprazole, 500 mg bid clarithromycine, 400 mg bid metronidazole (PCM); 7 d	Better symptom relief, no difference in *H. pylori* eradication	No parameter for symptoms given
Hu *et al*[63], 2008	67 pat.; chronic gastritis + TCM symptoms; gastroscopy	42 pat.; 4 × 0.5 g, tid Yiweikang capsules; 2 mo	25 pat.; 4 caps. tid; Wenweishu; 2 mo	Improved symptoms in verum; no difference in *H. pylori* eradication	Diagnostically not homogenous; control in this group is verum in 2010 publication[62]
Zeng *et al*[74], 2006	90 pat.; chronic gastritis	80 mg or 160 mg Jinghua Weikang	3 × 10 mg/d domperidone; 14_d. No group size given	Unclear whether in group or be-tween group differences	Data presentation insufficient
Wu *et al*[66], 2005	68 pat.; chronic atrophic gastritis + TCM symptoms	36 pat.; Kangwei granules, 2 × 12 wk. No dose given	32 pat.; Weifuchun, 2 × 12 wk. No dose given	Gastroscopy, pathology significantly improved, symptoms n.s.	Parameters not specified
Xia[67], 2004	98 pat.; chronic gastritis	Herbal pairs; patient number, dose and treatment duration not given	Banxia Xiexin Tang decoction, pat. number, dose and treatment duration not given	Treatment is superior	No explanation given
Chen *et al*[73], 2003	362 pat.; gastropathy with *H. pylori* infection	288 pat.; Kang Wei granules. No further data given	74 pat.; triple therapy plus bismuth (De Nol)	Improves symptoms of TCM classification	No data given for diagnosis, intervention type and results
Ji *et al*[68], 1999	226 pat.; gastritis with *H. pylori* infection	136 pat.; Xialian Yiyou capsule, 4 wk. Dose not given	90 pat.; Lizhu Dele capsules, 4 wk. Dose not given	Significant improvement in clinical symptoms	
Lu *et al*[69], 1998	75 pat.; chronic atrophic gastritis	45 pat.; Wei Shu capsules; 6 mo. Dose not given	30 pat.; Wei Ning granules; 6 mo. Dose not given	Atrophy, metaplasia, dysplasia significantly improved	No data specification
Zhong *et al*[70], 1997	202 pat.; chronic gastritis, intestinal metaplasia	117 pat.; modified Shijinzu decoction, 3 mo; dose not given	85 pat.; Weimeisu, 3 mo; dose not given	Treatment group significantly better	No data specification
Yin *et al*[71], 1996	143 pat.; chronic gastritis by EGD, + TCM symptoms	75 pat.; Piweiping caps. Ⅰ, Ⅱ, Ⅲ, Ⅳ; 3-6 mo. Dose not given	68 pat.; Sanjiu Weitai; 3-6 mo; dose not given	Significantly better cure rate, symptom score, biochemical parameter	Some parameters do not make sense (lymphocyte transformation test, cAMP, DNA)
Li *et al*[75], 1995	200 pat.; chronic atrophic gastritis	Gastrosia con-valescens; no data of pat. number, dose and duration	Domperidon; no data on patient number, dose and duration of treatment	Significantly superior to control	No parameter specified
Long *et al*[72], 1994	Verru-cous gas-tritis, no further informa-tion	Combined TCM + Western medicine; no further information	Western medicine (furazolidone, cimetidine); no further information	Combination is significantly better than WM alone	Insufficient data presentation
Liu *et al*[76], 1992	138 pat.; intestinal metaplasia; 104 pat.; atypical metaplasia	Xiao Wei Yan powder, 5-7 g/tid; 2-4 mo; no pat. number	No information; not treated?	Verum is effective	No description of control group

H. pylori: *Helicobacter pylori*; PCM: Pantoprazole, clarithromycine and metronidazole triple therapy; TCM: Traditional Chinese medicine.

Table 4 Clinical trials with herbal traditional Chinese medicine preparations for gastric or duodenal ulcers

Ref.	Patients	Intervention	Control	Outcome	Remarks
Hu *et al*[61], 2012	565 pat.; duodenal ulcer or gastritis, gastroscopy	LAC (see control), + 3 caps. 2/d Jinghua Weikang, 7 d, then Jinghua Weikang for 14 more days	30 mg lansoprazole, 1000 mg amoxicilline, 500 mg clarithromycine (LAC) 2/d, 7 d, then lansoprazole 30 mg 1/d for 14 more days; or LAC + 220 mg bismuth citrate 2/d, 7 d, then bismuth citrate for 14 more days	^{14}C-urea test - no difference (abstract unclear). Similar efficiency, better symptomatic improvement (bloating, belching)	11 hospitals; data presentation in abstract unclear. All gastritis patients were included in the intervention group. Study also included under "gastritis"
Hu *et al*[62], 2010	642 pat.; chronic gastritis or gastric ulcer + *H. pylori*	196 pat.; PCM + Wenweishu 224 pat.; PCM + Yangweishu; 7 d	222 pat.; 40 mg bid pantoprazole, 500 mg bid clarithromycine, 400 mg bid metronidazole (PCM); 7 d	Better symptom relief, no difference in eradication	No parameter for symptoms given
Zhang *et al*[78], 2009	46 pat.; active peptic ulcer, no *H. pylori* infections	Yiqi Huoxue formula + omeprazole, 5_wk. No information on patient number, dosage	Omeprazole, 5 wk. No information on patient number, dosage	bFGF, vEGF in-creased in treatment, histological improvement. No difference in recurrence	Scant data description
Deng *et al*[79], 2007	60 pat.; gastric ulcer, after 1 wk triple therapy	Qifang Weitong powder + omeprazole, 5 wk. No further details	Omeprazole, 5 wk. No further details	Mucosa thickness, glandular morphology improved (significant)	Scant data description
Lin *et al*[84], 2007	56 pat.; gastric ulcer + TCM symptom	26 pat.; Jianwei Yuyang granule, 4 wk. No further data	30 pat.; famotidine + sucralfat, 4 wk. No further data	Compliance, symptom integral sign. better; ulcer healing, clinical effects n.s.	Incomplete results description
Zhou *et al*[77], 2007	50 pat.; acute gastric ulcer + TCM symptoms	30 pat.; 1 dose/d in 2 × 100 mL solution; Jianpi Qingre Huayu recipe; 8 wk	20 pat.; 2 × 300 mg ranitidine; 8 wk	Effective rate n.s.; cure rate significant better. Sign. differences in T lymphocyte subsets	Randomized, statistics implausible, irrelevant parameters
Zhou *et al*[81], 2005	120 pat.; peptic ulcer, 10 controls no ulcer	6 groups, no clear description of treatment (ranitidine, Jianweiyuyang granules)	No description of control group	Combination improves symptoms and syndrome. No effect on ulcer healing, *H. pylori* eradication	No description of groups and intervention
Ji *et al*[82], 2006	200 pat.; duodenal ulcer	100 pat.; 160 mg Jinghua Weikang capsule 3/d; 4 wk	100 pat.; 20 mg famotidine 2/d; 4 wk	*H. pylori* eradication, anorexia, eructation, incidence of UAW sig. better, remission, healing n.s.	Only *P* values are given
Zhang *et al*[80], 2005	438 pat.; duodenal ulcer	330 pat.; Haigui Yuyang capsule, 6 wk. No dose given	108 pat.; ranitidine, 6 wk. No dose given	No difference between groups; only distension better in verum	"Double blind, double dummy, randomized"
He *et al*[85], 2001	120 pat.; gastric ulcer	60 pat.; Qingwei Zhitong pill. No dose or duration	60 pat.; Sifangwei tablet. No dose or duration	Better ulcer healing, no difference in TCM symptoms	Unclear description
Wan *et al*[86], 1996	200 pat.; peptic ulcer	Yuyang powder, no further data	Cimetidine, no further data	Cure rate n.s., recurrence significantly better	Scant data presented
Yang *et al*[87], 1995	150 pat.; peptic ulcer	Bushen Kangkui decoction; no further details	Cimetidine; no further details	Cure rate n.s., recurrence significantly better	Scant data presented
Li *et al*[88], 1995	80 children; peptic ulcer	Unspecified treatment for 8 wk	No control	Effective after 8 wk (92% cure rate)	(empirical recipe)
Yang *et al*[83], 1994	80 pat.; duodenal ulcer	Kuiyangqing pills; duration, dose not given	32 pat.; bismuth aluminate. No dose, duration	Effective treatment	Unclear group description, no parameter for efficiency, outdated control therapy
Ma and Guo[89], 1992	508 pat.; intractable peptic ulcer	260 pat.; 50 g/d Chuanjia Weidan; 4 wk	248 pat.; 800 mg/d cimetidine; 4 wk	Cure rates similar, *H. pylori* eradication, relapse superior	
Li and Yin[90], 1991	494 pat. (?); peptic ulcer	354 pat.; Jian Wei Yu Yang tablets. No further data	140 pat.; ranitidine, no further data	Treatment superior in cure rate	Scant data presented
Zhou *et al*[91], 1991	Not defined, peptic ulcer	Wei Yang An	Cimetidine, no further data	Short term effects similar, in long term Wei Yang An superior	No data presented

bFGF: Basic fibroblast growth factor; *H. Pylori*: *Helicobacter pylori*; PCM: Pantoprazole, clarithromycine, metronidazole; vEGF: Vascular endothelial growth factor.

study design is not suited to elucidate the therapeutic effect of the added herbal TCM decoction on ulcer healing. The herbal TCM Jianghua Weikang was evaluated in two studies[61,77]; in both, it improved bloating and belching, without eradication of *H. pylori* infection. The herbal TCM Jianwei Yuyang was studied in three trials[81,84,90]; whereas Li and Yin[90] reported significant better cure rates compared to ranitidine, Lin *et al*[84] and Zhou *et al*[81] mentioned only symptomatic improvement compared to famotidine, but no control treatment could be identified from their abstract[81].

All four recent randomized studies[61,62,78,79] used a design comparing herbal TCM plus Western medicine against Western medicine, a study design that cannot

Table 5 Clinical trials with herbal traditional Chinese medicine preparations for inflammatory bowel disease

Ref.	Patients	Treatment	Control	Outcome	Remarks
Liao *et al*[94], 2009	39 pat.; Crohn's disease, postoperative	21 pat.; poly- glycoside of Tripterygium wilfordii, 2 wk	18 pat.; sal azosulfapyridine, 2 wk	Endoscopic recurrence significant better in treatment group	No dose given; 3 dropouts, 2 noncompliance (treatment group)
Han *et al*[95], 2014	120 pat.; mild to moderate UC	60 pat.; Jianpi suppository, dose not given, 2 × 15 d	60 pat.; mesalazine orally, dose not given	Hemorheology, *P*-selectin better improved	Randomized; unclear whether group differences exist
He *et al*[96], 2012	60 pat.; mild to moderate UC, with inner DHAS	30 pat.; 1 dose Qingchang Huashi recipe in 2 × 150 mL, 8 wk	30 pat.; 1 g/qid mesalazine, 8_wk	Symptoms sign, coloscopic, pathological results n.s.	
Fukunaga *et al*[97], 2012	30 pat.; intractable UC	15 pat.; 0.1 g/d Xilei San supp., 2 wk	15 pat.; pla- cebo supp., 2 wk	Verum group with remission P = 0.04 at day 14 and 180. Significant histology, endoscopy	
Zhou *et al*[98], 2012	53 pat.; mild to moderate UC, large intestine DHAS	27 pat.; Qing-chang Huashi recipe oral + Guanchang recipe dermal;Fuzheng Qing-chang recipe oral in remission, 3 mo	26 pat.; 4 × 1 g/d mesalazine, 4 × 0.5 g/d in remission, 3 mo	Diarrhea, blood, pus in stool sign. better	No data given for control group, only P values
Gong *et al*[92], 2012; Yang *et al*[93], 2014	320 pat.; active UC, with DHAS	240 pat.; Fu- fangkushen colon-coated capsule, 8 wk	80 pat.; mesalazine enteric coated tablets, 8 wk	Clinical response, remission, mucosal healing, Mayo scores n.s.	Double blind, double dummy
Tong *et al*[99], 2011	160 pat.; UC with internal DHAS	120 pat.; composite sophora	40 pat.; mesalazine slow release granules, 8 wk	Sign. in Chinese symptom score, mucus + pus stool; others n.s.	Double blind, double dummy
Tong *et al*[100], 2010	126 pat.; UC, DHAS	colon-soluble capsules, 8 wk composite sophora colon soluble capsule: 42 pat. 6 caps, 3 ×/d; 42 pat. 4 caps., 3 ×/d; 8 w	42 pat.; 4 tbl., mesalazine 3 × /d (3 g/d), 8 wk	No significant differences, with tendency for herbal TCM	
Ling *et al*[102], 2010	78 pat.; inflammatory bowel disease	A: 26 pat.; herbal TCM oral and as enema; B: 27 pat.; enema only, 1 mo	25 pat.; Western medicine; 1 mo	A > B = C: main symptoms, coloscopic score, pathology; B > C: tenesms	Randomized controlled trial; scant data presentation
Chen *et al*[101], 1994	153 pat.; intractable UC	Jian Pi Ling tablets; retention ene- ma Radix Sophorae Flavescentis, Flos Sophora (RSF-FS) decoction; 3 mo	A: Salicylazosulfapyridine (SASP), retention enema dexamethasone; 3 mo B: placebo + RSF-FS, 3 mo	Curative rates, effective rates significant better. Immunology normalized in verum group	Doses not given, claimed double blind

DHAS: Damp heat accumulation syndrome; TCM: Traditional Chinese medicine; UC: Ulcerative colitis.

prove the efficiency of herbal TCM on ulcer healing. Zhang *et al*[80] using a comparison of the herbal TCM Haigui Yuyang capsules against ranitidine for 6 wk did not find differences in the outcome parameters (Table 4). For symptom relief, some herbal TCM preparations may be useful. Further studies should focus on pathologically defined diagnoses, homogenous patient cohorts, prespecified objective outcome parameters, and unambiguous data presentation.

Inflammatory bowel disease

Besides infectious diseases, ulcerative colitis and Crohn's disease are clinically important gastrointestinal diseases. In contrast, no review was found in the Cochrane library using the search items herbal TCM AND colitis or Crohn's disease, and only ten clinical trials were found. In PubMed, this strategy retrieved 29 publications. Ten relevant trials were identified (Table 5), one trial was published twice[92,93]. Only one publication specifically included patients with Crohn's disease[94], eight trials considered ulcerative colitis patients[92,95-101], and in one study[102], patients with inflammatory bowel disease were included. Five studies used additionally the "damp heat accumulation syndrome" from the Chinese syndrome system[92,96,98-100]. Six trials were performed against 4 × 1 g mesalazine[92,95,96,98-100], two studies against salazosulfapyridine[94,101], and one study against an unspecified Western medicine[102]. Only Fukunaga *et al*[97] used a placebo controlled study design.

Except the study of He *et al*[96], all other trials were described as randomized, five of these studies also as blinded[92,97,99-101], and only Tong *et al*[100] described the randomization. Qingchang Huashi[96,98] and Composite Sophora[99,100] were studied twice. For Composite Sophora, the group described significant better results only for TCM symptoms; for Qingchang, He *et al*[96] found no significant changes in symptom scores, whereas Zhou *et al*[98], adding Guanchang treatment, reported reduced incidences of diarrhea, blood and pus

in stool.

Taken together, herbal TCM may offer improvement in some TCM syndrome scores. But no well conducted study showed significant superiority; for well designed studies, improvements were similar between groups.

Hepatitis

PubMed using "herbal TCM" and "hepatitis" identified 63 publications marked as clinical trials. Manual search identified 28 clinical studies, using established parameters for disease definition and efficiency parameters (Table 6). Searching the Cochrane library for clinical trials retrieved three reviews on herbal Chinese medicines and chronic hepatitis B[103], chronic hepatitis[104], and HBV carriers[105]; 86 clinical trials were listed, with no additional publication identified in this search. As Chinese language publications only, 16 articles were available and were evaluated by the abstract; twelve English language articles, including one study published in both languages[106,107], were analyzed in full text. Only twelve publications[108-119] did not derive from Chinese hospitals for TCM; all three trials from Western institutions[114,118,119] failed to determine any positive effects from herbal TCM mixtures.

Eleven studies[110,120-129] used a design in which a herbal TCM preparation was used in addition to a Western medication, such as interferon (IFN)-α[120], virustatic drugs[121-123,125,128], or other not specified "routine treatments"[110,124,126]. Most studies were not randomized or used ill defined patient cohorts, comprising chronic hepatitis and liver failure. In most trials, HBV patients were included, and only Hu *et al*[124] described a study in HBV patients with acute-on-chronic liver failure; HCV infected patients were included in four studies[112,114,119,130], nonalcoholic steatohepatitis patients in one trial[129].

Rarely studies reported on the effects of the same herbal TCM preparation. Fushen Huayu was investigated in three trials with four publications [106,108,117,123], salvia injections in three older trials[107,116,131], and CH100 in two studies[112,119]. No two studies used a comparable design (for Fushen Huayu one study each compared to placebo or Heluoshugan, one used an add-on design to lamivudine), so positive findings have not been confirmed. As was seen in all other symptoms and diseases, most of the studies reported superiority of herbal TCM preparations; however, data presentation often was incomplete. Add-on design studies with herbal TCM given in one arm to another drug (virustatic drugs, IFN) in both arms cannot prove herbal TCM effects on hepatitis[110,120-129], and one study reports inconsistent prevention[113]. Among other problems were inappropriate control treatments with polyene phosphatidylcholine or colchicine, missing composition of verum or placebo drugs, or small group sizes. A major problem with interpreting the studies resulted from incomplete data presentation. In about half of the studies included in this analysis, it remained unclear whether a comparison was done in one treatment group comparing the patients before and after treatment, or whether a difference was calculated between groups after treatment; in the study of Qiu *et al*[122], treatment and placebo group description appears to be switched. Better designed studies like good randomization[106] failed to show differences, as was the case in nearly all studies from non-Chinese groups[112,114,115,117,118]. Currently, no evidence has been provided for the efficiency of herbal TCM in viral hepatitis eradication; however, some studies suggest improvement in subjective symptoms. It remains unclear whether this effect can be reproduced. Overall, no consistent proof for the efficiency of TCM preparations in acute or chronic hepatitis, or on amelioration of hepatitis related liver fibrosis[132-138] has been provided.

Biliary diseases

To identify clinical trials with patients suffering from noninfectious biliary diseases, the key words herbal TCM and gall bladder, bile, or biliary were used. In PubMed, 14 publications were identified, from which six were judged relevant to the review. Six reviews were found in the Cochrane library; only the study of Gan *et al*[139] covering cholelithiasis was relevant to biliary diseases. Among the eight trials identified in this database (Table 7)[136,139-145], only one study[136] was related to noninfectious biliary diseases. Two studies[140,141] described cholelithiasis patients, the study by Ma *et al*[140] did not mention clinical parameters and therefore was not included. Four of the six studies[141-144] claimed randomization, and no study blinded the participants or physicians. Only Tong *et al*[143] mentioned histological confirmation for the diagnosis of primary biliary cirrhosis. Four of the studies used an add-on design with ursodeoxycholic acid[142,143,145] or a nonspecified Western medicine[136] in both groups, and Fuzheng Huayu capsules[142], Tongdan decoction[143], or Ganyan Ⅳ[136] given additionally in the verum group; Jiang *et al*[145] did not specify the herbal TCM preparation used. None of the studies was well designed or placebo controlled; thus, no evidence exists for the efficiency of herbal TCM in biliary diseases, in accordance with Gan *et al*[139].

Colon carcinoma

In PubMed, 75 clinical trial publications were retrieved using the key words herbal TCM and colon carcinoma; we excluded all *in vitro* investigations and trials investigating pharmacokinetic effects on cytostatic compounds; only five clinical trials remained with clinically relevant end points. The Cochrane Library did not contain a review or clinical trial describing clinical effects of herbal TCM in colon cancer patients. All trials were published in Chinese, with only the English abstract available for evaluation (Table 8). Three

Table 6 Clinical trials with herbal traditional Chinese medicine preparations for hepatitis

Ref.	Patients	Treatment	Control	Outcome	Remarks
Deng *et al*[108], 2012	180 pat.; liver cirrhosis with HBV infection	90 pat.; Fuzheng Huayu tablet, 6 mo	90 pat.; placebo, 6 mo	Anxiety, depression, social deficit improved; levels of cirrhosis, coagulation, splenomegaly improved	
Wang *et al*[132], 2012	60 pat.; chronic HBV infection	40 pat.;8 capsules 3 ×/d Xinganbao capsule, 6 mo	20 pat.; 5 tablets 3 ×/d Heluo Shugan tablet, 6 mo	Lowered laboratory values, histological parameters in 21/40 treatment patients	
Mao *et al*[120], 2012	288 pat.; HBeAg positive	125 pat.; 5_MU IFNα1b + Yixuesheng capsules, 3 mo	163 pat.; 5 MU IFNα1b	Significant better treatment at 3 and 12 mo, not at 24 mo	22 patients lost in control group
Zhang *et al*[121], 2012	164 pat.; HBeAg-positive chronic HBV	Entecavir + Shenxian Yiganling, dose and duration missing	Entecavir, dose and duration not given	Unchanged: ALT, undetectable virus load; Conversion rate better in treatment group	Insufficient data presentation
Qiu *et al*[122], 2012	240 pat.; HBeAg-positive chronic hepatitis	10 mg/d adefovir dipivoxil, duration and patient number not given	10 mg/d adefovir dipivoxil + Baihua Xianglian Detoxification recipe 2 ×/d, duration and patient number not given	In nearly all comparisons treatment group is better	Strange definition of treatment and control group, unclear whether differences within a group or between groups were compared
Tang *et al*[123], 2012	80 pat.; chronic HBV hepatitis	37 pat.; lamivudine + Fu Zheng Huayu capsules, 6 mo; later lamivudine monotherapy indefinitely	43 pat.; lamivudine, indefinitely	No differences between groups for ALT, AST, virus load; better TGF-β1/BMP-7 ratio; pathology: treatment group better	
Hu *et al*[124], 2012	98 pat.; acute on chronic liver failure	66 pat.; "classic Western treatment" + high dose herbs, 12 wk	32 pat.; "classic Western treatment", 12 wk	Treatment improves survival, laboratory values improved	Herbs selected by personal preference, no randomization
Zhou *et al*[133], 2011	84 pat.; chronic HBV hepatitis with cirrhosis	1 dose 2 ×/d Xiaozhang recipe; 12 mo	Fuzheng Huayu capsule, 5 pills, 3 ×/d, 12 mo	No difference between groups	Indirect comparison, unclear presentation of results
Deng *et al*[130], 2011	24 pat.; chronic HCV infection	24 pat.; 2.5 g 3 ×/d Sho-Sai So To; 12 mo	No control group	Mixed effects on liver enzymes, histology, virus load	Cohort study
Tang *et al*[125], 2010	57 pat.; chronic HBV, HBeAg positive	Entecavir + Yidu recipe, 6 mo. Dose and patient number not given	Entecavir, 6 mo; dose and patient number not given	No difference in HBeAg conversion, HBV-DNA values; improved ALT, AST, HBV-DNA, symptoms	7 dropouts, no distribution given; different data for HBV-DNA; no percentages given
Li *et al*[126], 2010	60 pat.; severe chronic HBV infection	30 pat.; "conventional integrative medicine" + Huchang Jiedu decoction enema 1/d; 3 wk	30 pat.; "conventional integrative medicine", 3 wk	Better values than control group for ALT, AST, bilirubin, globulines, endotoxin, prothrombin, cholesterol, calcium	
Liang *et al*[127], 2010	104 pat.; chronic HBV hepatitis	54 pat.; routine therapy + Danqi Huogan capsule; 3 mo; dose not given	50 pat.; "routine therapy", 3 mo, dose not given	Improved symptoms and signs, decreased HK, blood viscosity, plasma viscosity, RBC aggregation	Unfamiliar parameters, no specific data given
Tang *et al*[109], 2009	208 pat.; chronic viral hepatitis	116 pat.; Astragali compound, 2 mo	92 pat.; "other drugs in regular clinical use", 2 mo	Clinical efficiency, seroconversion better in treatment group	Unspecified controls, no percentages and SD
Chi *et al*[128], 2009	405 pat.; chronic HBV infection	220 pat.; lamivudine + Chai Shao Liu Jun Tang, 18 mo	185 pat.; lamivudine, 18 mo	ALT, HBeAg, HBV-DNA suppression, mutation in treatment group better	Numbers don't add up
Xiao *et al*[110], 2007	57 pat.; chronic HBV infection + cirrhosis	45 pat.; routine medication + Kang Gang Qian granule, dose and duration not given	12 pat.; "routine medication", dose and duration not given	Treatment group better in liver function, laboratory and pathology parameters	Small control group
Wang[129], 2007	80 pat.; NASH	50 pat.; Yiqi Huoxue recipe + polyene phosphatidylcholine capsules, 3 mo	30 pat.; polyene phosphatidylcholine capsules, 3 mo	Superior in syndrome, function, blood lipids, ultrasound	Randomized according to their visit; no values given
Yang *et al*[111], 2006	115 pat.; HBeAg or HBV-DNA positive hepatitis	Fufang Huangqi granule + lamivudine, 24 wk	Fufang Huangqi granule, 24 wk	TCM is superior to second (control) group	In results the group assignment is unclear
Mollison *et al*[112], 2006	97 pat.; chronic HCV hepatitis	61 pat.; CH100 herbal remedy, 24 wk; 24 wk follow-up	30 pat.; placebo for 24 wk, 24 wk follow-up	No difference on viral titer, liver enzymes	Reduced pain in CH100 group, quality of life parameters similar
Chen *et al*[113], 2006	90 pat.; HBV-DNA, HBsAg, HBeAg positive	49 pat.; Bu Shen Granule (BSG) + Marine Injection, 1 yr	41 pat.; lamivudine, 1 yr	Clinical parameters are significantly better; reverse ratios are n.s.	The calculations appear to be skewed (42.6 to 61 - n.s.; 42.6%-36.2% sign)
Liu *et al*[106], 2005	216 pat.; chronic HBV infection with liver cirrhosis	110 pat.; 5 × 1.6 g 3 ×/d Fuzhenghuayu capsule, 24 wk, 12 wk follow-up	106 pat.; 5 × 0.93 g 3 ×/d Heluoshugan capsule, 24 wk, 12 wk follow-up	No difference in fibrotic scores, suppresses inflammation, improves fibrosis "reverse rate"	Randomized, comparison of 2 herbal TCM preparations

Ye *et al*[131], 2005	120 pat.; HBV plus cirrhosis, 60 pat. compensated, 60 decomp	60 pat.; decompensated: 8, 16 or 24 mL Salvia injection, 60 d	60 pat.; compensated: 8, 16, 24 mL Salvia injection, 60 d	Dose dependent improvement in all signs, symptoms and lab values Compensated cirrhosis > decompensated	No exact data given
Yang *et al*[138], 2003	60 pat.; hepatic fibrosis and jaundice	30 pat.; 654-2 injection, "Gan Xian Tui Huang recipe", no dose, 3 mo	30 pat.; routine treatment, 3 mo	Significant improvement in treatment group in clinical and lab values	No specific data provided
Long *et al*[134], 2004	120 pat.; chronic HBV	60 pat.; 100 mg/d matrine i.m., + conventional liver protection; 90 d	60 pat.; conventional liver protection: glucurone, inosine, Vit B compound, caryophyllene	Significant: symptoms and signs, liver function, serum conversion HBeAg, HBV-DNA	Unclear, whether within or in between group differences are reported
Jakkula *et al*[114], 2004	45 pat.; chronic HCV infection, fatigue	10 g/d fixed comb of 10 herbs; 12 wk	10 g/d placebo, 12 wk	No difference for symptoms, laboratory values, virus load	
Zhang *et al*[115], 2004	50 pat.; chronic HBV infection with cirrhosis	36 pat.; 2 ×/d Zhaoyangwan oral, 3 mo	14 pat.; 3 mU IFN i.m., 3/wk, 3 mo	No effect on serum enzymes, virus reduction, significant changes in lymphocyte subtypes, complement	Not blinded; IFN dose given incorrectly (3 MU)
Li *et al*[135], 2003	56 pat.; HBV infection, liver fibrosis	30 pat.; Da Ding Feng Zhu decoction, 3 mo; dose not given	26 pat.; colchicine, 3 mo; dose not given	Effective for hyaluronic acid, procollagen Ⅲ, collagen Ⅳ-C, laminin	Inappropriate control, no percentages given
Liu *et al*[116], 2002	77 pat.; chronic HBV with fibrosis	30 pat.; 2 × 3 tabl./d, each 30 mg salvianolic acid B + 1 MU IFNa 1/d for 1 mo, then 3/wk; 6 mo	30 pat.; placebo, 6 mo	Lower US score, claim of better reduction in fibrosis	17 pat. excluded; unclear application, calculations cannot be reproduced
Chen *et al*[117], 2000	94 pat.; HBsAg pos.	45 pat.; 400 mg kurorinone i.m./d, 3 mo	49 pat.; 3 MU IFNα, 1 mo 1/d, then 3/wk for 2 mo	No significant difference (CR 31% treatment, 45% IFN)	
Akbar *et al*[118], 1998	20 pat.; Child A chronic hepatitis	9 pat.; 3 × 7.5 mg HpPro oral, 1 wk	11 pat.; mix of known drugs, 1 wk	Significant lower AST and ALT only at some time points	Crossover design, no control specified
Batey *et al*[119], 1998	44 pat.; chronic HCV	20 pat.; 5 tbl. 3 ×/d CH-100, 6 mo	20 pat.; 5 tbl. 3 ×/d placebo, 6 mo	ALT improvement significant	4 dropouts; scant data presentation
Hu *et al*[136], 1996	116 pat.; CAH with bilirubinemia	60 pat.; Ganyan Ⅳ	56 pat.; Western medicine	Decreased jaundice, ALT	No data given, only percentages

ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; CAH: Chronic active hepatitis; HBV: Hepatitis B virus; HCV: Hepatitis C virus; NASH: Nonalcoholic steatohepatitis; TCM: Traditional Chinese medicine; US: Ultrasound.

studies[146-148] included colon carcinoma patients only, whereas Guo[149] evaluated intestinal cancers, and Li[150] evaluated patients with digestive tract cancers. In four studies[147-150], a herbal TCM preparation was added to standard chemotherapy; Zhou[146] treated colon cancer patients either with the proprietary Zhao Weitiao No 3 preparation alone or in combination with oxaliplatin + 5-FU. All five studies found improvement in symptoms, whereas tumor size or recurrence was only described by Zhou[146] with smaller tumors in the chemotherapy group. Herbal TCM preparations are not effective against colon carcinoma; they may provide some symptomatic relief especially for symptom scores in the Chinese symptom score systems[147].

Hepatocellular carcinoma

A PubMed search using the key words TCM and hepatocellular carcinoma (HCC) retrieved 36 results, 21 of which were judged relevant. One recent clinical study with Jinlong capsules containing herbal preparations plus snake parts was excluded[151]. The Cochrane library did not list a relevant review; ten trials are quoted in the Cochrane library, all of them already retrieved by the PubMed search. Two other studies[152,153] are included in Table 9; both studies investigated the use of Sho Saiko To, a herbal mixture with antitumor activity *in vitro*, to prevent HCC development in liver cirrhosis patients.

Recent trials investigated the palliative use[154-158], or the adjuvant use of herbal TCM preparations after curative treatment[152,159-163]; more than half of the 23 studies used an add-on design with all patients treated with TACE[159,164-167], microwave ablation[152,160,161], or surgery[159,162], and the verum group additionally received herbal TCM preparations. There was no treatment in the control group in the study of Lin *et al*[167] and some older studies[152,168,169].

Besides Sho Saiko To, studied as a chemopreventive agent[152], only Ganji decoction was evaluated twice by Tian *et al*[164] and Wang *et al*[165]. Both studies used an identical design with four weeks courses of TACE plus Ganji decoction in the treatment group; Tian *et al*[164] reported a better tumor regression in the control group, but better survival in the treatment group, whereas Wang *et al*[165] published an improved long-term survival. Older studies reported significantly better outcome in the treatment groups, but clinical trials with larger cohorts and better design

Table 7 Clinical trials with herbal traditional Chinese medicine preparations for biliary diseases

Ref.	Patients	Treatment	Control	Outcome	Remarks
Wu *et al*[142], 2012	80 pat.; PBC	40 pat.; UDCA, Fuzheng Huayu capsule; no dose; 48 wk	40 pat.; UDCA, no dose; 48 wk	Significant: itching, fatigue, liver enzymes, IgG, IgM, antibodies, blood flow	Most parameters significant only at one of four time points
Tong *et al*[143], 2012	60 pat.; PBC, histology	30 pat.; UDCA, Tongdan decoction; no dose; 24 wk	30 pat.; UDCA, no dose; 24 wk	IgM, IgG decreased after 2 yr, less inflammation after 3 yr	No percentages, no scoring system
Qi *et al*[144], 2009	160 pat.; chronic cholecystitis	80 pat.; Dan An Tang, no dose, no duration	80 pat.; Xiao Yan Li Dan Pian, no dose, no duration	Tr.: total effective rate 95%, control 80% significant	Dan An Tang: cholecystitis relieving; Xiao Yan bile draining
Jiang and He[145], 2003	16 pat.; PBC	No pat. number; UDCA + "some Chinese herbs", no duration, no dose	No pat. number; UDCA, no dose, no duration	No results that can be interpreted	Conclusions not based on results. Clinical observation
Hu *et al*[136], 1996	116 pat., CAH with bilirubinemia	60 pat.; Ganyan Ⅳ	56 pat.; Western medicine	Decreased jaundice, ALT	No actual data given, only percentages
Cui *et al*[141], 1989	89 pat.; extrahepatic jaundice	No pat. number; Li Dan Ling; no dose, or duration	No pat. number; "control group"; no dose, or duration	Herbal TCM better for incomplete obstruction, worse for complete	No data presented

PBC: Primary biliary cholangitis; TCM: Traditional Chinese medicine; UDCA: Ursodeoxycholic acid.

Table 8 Clinical trials with herbal traditional Chinese medicine preparations for colon carcinoma

Ref.	Patients	Treatment	Control	Outcome	Remarks
Zhou *et al*[146], 2009	163 pat.; colon carcinoma, no information on stage	105 pat.; 40 mL/d Zhao's Weitiao No. 3, 30 d = 1 cycle, 4-6 cycles	58 pat.; 40 mL/d Zhao's Weitiao No. 3 + OLF protocol, cycles as treatment	For tumor mass, CEA control is better, for symptom and QoL treatment is better	Assignment according to patients wish; OLF: oxaliplatin, 5-FU + leucovorin. Conclusions incorrect
Liu *et al*[147], 2005	64 pat.; colon carcinoma postoperatively	43 pat.; chemotherapy + Jianpi Huoxue herbs, 3 mo, no dose given	21 pat.; chemotherapy, 3 mo	Remission 39.5% treatment, 33.3 control; Pi deficiency treatment $P < 0.01$	Randomized study; effects only in Chinese symptoms
Guo[149], 1999	68 pat.; large intestinal cancer	38 pat.; chemotherapy + Fu Zheng Yiai decoction, no dose, duration	30 pat.; chemotherapy, no dose, duration	Physical strength, survival time, rate, recurrence sign better	No specific data given
Cao *et al*[148], 1994	79 pat.; diverse advanced carcinoma incl. colon carcinoma	LAK/IL-2 + Lycium Barbarum polysaccharides; no dose, duration	LKA/IL-2	Response rate, remission, NK, LAK cell activity sign. better	4 dropouts. No specific data
Li[150], 1992	176 pat.; malignant tumor of digestive tract	Chemotherapy + Shen Qi injection, no further details given	Chemotherapy, no further details given	No leukocyte decrease, improved cellular immunological function	No specific data given

LKA: Lymphokine activated killer cells; OLF: Oxaliplatin, leucovorin, 5-fluorouracil; QoL: Quality of life.

cannot confirm anticarcinogenic effects of herbal TCM. Most studies describe symptomatic relief and improvement in the quality of life[154,161,165-167,170-172]. Herbal TCM preparations may improve some subjective symptoms[172-176]. This effect is seen with all 16 described herbal TCM preparations as well as in the four studies using individual[166,170] or nonspecified herbal TCM preparations[162,173], so no active ingredient has yet been identified.

Dyspepsia

A PubMed search for herbal TCM and dyspepsia retrieved 25 clinical trials; the Cochrane database identified 18 clinical trials. Thirteen clinical trials and cohort studies are included in Table 10; twelve trials originated in China, and one in Japan. Seven studies randomized the participants[177-183], four studies used a placebo controlled design[178,180,184], or an untreated control group[185], and one study did not report on control patients[186]. Whereas only Xiao Pi-I was tested in three trials as herbal TCM preparation[177,181,183], domperidone was used as control drug in five studies[179,181,183,187,188], only Liu *et al*[177] tested against mosapride. In two trials, two different herbal TCM preparations were compared[182,189]. The diagnostic criteria for functional dyspepsia were not consistent; four trials used TCM scoring systems[178,180,182,189], two studies[179,188] considered anxiety or depression comorbidity, and Liu *et al*[177] and other article preferred gastric dyskinesia criteria. No study employed scores like the Glasgow dyspepsia severity score of modern medicine[190].

In accordance with the results of a Cochrane review of Xiaoyao San for dyspepsia[190,191], some herbal TCM preparations may provide benefit for functional dyspepsia patients. Xiao *et al*[179] showed superiority

Table 9 Clinical trials with herbal traditional Chinese medicine preparations for primary hepatocellular carcinoma

Ref.	Patients	Treatment	Control	Outcome	Remarks
Huang *et al*[154], 2013	68 pat.; HCC, stage ⅢA, ⅢB, palliative treatment	32 pat.; BST + Xiaoaiping inj., dose not given, 30 d	36 pat., BST	RECIST, immune function, QoL Karnofsky scale: significant for immune function, immediate therapeutic effect	China classification system. Kaplan-Meyer: First 20 wk no difference (-40%)
Zhai *et al*[159], 2013	379 pat.; HCC after hepatectomy	185 pat.; 50 mL/d Cinobufacini injection 10 d/mo, 12 mo + 4.5 g bid Jie Du granule, 6 mo	190 pat.; TACE pirarubicin, mitomycin C, once	Herbal TCM prolongs time to recurrence (P = 0.048)	5 dropouts for ITT in verum, 6 dropouts in control. After 14 mo, no further difference
Zhao *et al*[160], 2012	60 pat.; HCC, after microwave ablation therapy	30 pat.; Fuzheng Yiliu recipe, 6 mo, dose not given	30 pat.; additional treatment	Liver function, fibrosis, immune function improved	Data given only for lymphocytes
Tian *et al*[164], 2010	97 pat.; primary HCC or CCC	49 pat.; TACE + Ganji Decoction; dose not given, 4 wk; multiple cycles	48 pat.; TACE with mitomycin C, THP, 5-FU	Tumor regression in control better; survival better in test group	Intervention: no cytostatic agents in TACE. No Kaplan Meier shown
Yen *et al*[155], 2009 Saif *et al*[158], 2010	42 pat.; unresectable HCC	42 pat.; 750 mg capecitabine + PHY906	Dose escalation study	Improved survival to historical control (?)	No histology
Wang *et al*[165], 2009	77 pat.; advanced HCC	40 pat.; TACE + Ganji recipe, dose not given, 4 wk (1 course)	37 pat.; TACE	Survival not different at 3 mo, thereafter different; QoL improved	
Hou and Lu[166], 2009	67 pat.; mid advanced HCC	35 pat.; TACE (gemcitabin, cisplatin) + TCM according to symptoms; 4 wk	32 pat.; TACE (gemcitabin, cisplatin)	QoL, CT/MRT, immune system. No differences described	Ambiguous data presentation
Chen *et al*[170], 2007	82 pat.; HCC, after TACE	45 pat.; complex prescription of Chinese crude drugs, 4 wk	37 pat.; routine liver protection, 4 wk	Symptoms improved in therapy group	No differentiation of drugs
Wu *et al*[171], 2005	61 pat.; HCC	33 pat.; local DDP application (TACE?) + Xiaoshui decoction, 2 mo	28 pat.; DDP application (TACE?)	Ascites, QoL, survival, symptoms: all significant, except QoL	Unclear basic treatment (DDP)
Lao[174], 2005	122 pat.; HCC, after TACE	62 pat.; 150 mg/d matrine injection, 2 wk	60 pat.; "some other hepatinica", 2 wk	Enzyme levels are increased, no clear group allocation	TACE not speci-fied; effects between groups not clearly described
Lin *et al*[172], 2005	72 pat.; HCC Ⅱ or Ⅲ; with histology and microwave coagulation	36 pat.; 20 mL Shenqi mixture, 3 ×/wk, 1 mo	36 pat.; no additional treatment	Significant: cure rate, Karnofsky score, lymphocytes, AFP, Chinese symptom score	Microwave treatment: 2 times 60 W, 800 s 1/wk
Feng *et al*[161], 2005	80 pat.; HCC after TACE	20 pat.; dexamethasone + ginsenosides, dose, duration not given	20 pat.; each dexamethasone, ginsenosides or placebo; no dose, no duration	Treatment lowered nausea, vomiting, fever, pain, bone marrow inhibition	TACE not specified; no numbers given
Lin *et al*[167], 2005	85 pat.; middle advanced HCC	52 pat.; TACE with HCPT, + Shentao Ruangan pill	33 pat.; TACE with HCPT	No difference: tumor size; significant: survival, Chinese symptom score	HCPT: hydroxy- camptothecine
Zhang *et al*[175], 2004	65 pat.; ad vanced HCC	32 pat.; regular protective therapy + Jia Wei Si Jun Zi Tang; no dose or duration	33 pat.; regular protective therapy; no dose or duration	Sigificant improvement in treatment group; "superior in curative effect"	ICGR15: indocyanine green retention 15 min; intervention treatment mentioned, but not described
Chen *et al*[156], 2003	100 pat.; moderate and advanced HCC	50 pat.; Cino bufacini injection, no further information	50 pat.; no further information	Every parameter improved in Cinobufacini injection group	No individual parameter reported
Shao *et al*[176], 2001	60 pat.; middle advanced liver cancer; after TACE	30 pat.; Gan'ai No. Ⅰ and No. Ⅱ, no dose or duration given	30 pat.; no further details	Improved survival, recurrence rate, tumor shrinking, AFP, leukocytes	No treatment details
Xu *et al*[173], 2001	120 pat.; HCC, after resection	61 pat.; herbal TCM for Chinese symptoms, no type, dose, duration	59 pat.; no further treatment	ALT, AST, albumin, γ-GT, bilirubin improved	Unclear whether within or between group differences were reported
Wang[162], 1998	108 pat.; HCC embolism chemotherapy	40 pat.; each herbal TCM preparations, no type duration, dose	40 pat.; no further treatment	Survival rate, short term effects significant	No specific data, no treatment details
Zheng *et al*[163], 1998	106 pat.; HCC	56 pat.; embolization with Bletilla striata angioembolus, follow-up 4 yr	50 pat.; embolization with Gelfoam, follow-up 4 yr	All clinical parameters better than in control	
Han *et al*[169], 1997	HCC with radiotherapy, no further data available	Xuefu Zhuyu decoction, no details on pat. number, dose, duration	No treatment	Survival significantly improved, metastasis not improved	"showed coordinate effect with radiotherapy"
Peng *et al*[157], 1993	Late stage HCC	4–8 mL Salvia miltiorrhizae composita; no pat. number given	No treatment description given	Sign. difference between groups	No description of treatment and results

Oka *et al*[152], 1995	260 pat.; HCC in cirrhosis	130 pat.; conventional drugs + 7.5 g/d Sho Saiko To (TJ-9), 5 yr	130 pat.; no treatment	Survival prolonged (n.s., P = 0.053), for HBs-negative pat. significant	Randomized, prospective, not blinded
Yamamoto *et al*[153], 1989	260 pat.; HCC in cirrhosis, matched pairs	130 pat.; 7.5 g/d of Sho Saiko To, 34 mo	130 pat.; conventional medicine, 34 mo	Sign. lower incidence of HCC (9 *vs* 17)	

BST: Best supportive treatment; CCC: Cholangiolarcellular carcinoma; HCPT: Hydroxycamptothecine; HCC: Hepatocellular carcinoma; QoL: Quality of life; RECIST: Response Evaluation Criteria In Solid Tumors; TACE: Transarterial chemoembolization; THP: Tetrahydropyranyladriamycine.

Table 10 Clinical trials with herbal traditional Chinese medicine preparations for dyspepsia

Ref.	Patients	Treatment	Control	Outcome	Remarks
Liu *et al*[177], 2013	180 pat.; functional dyspepsia (FD), as postprandial distress syndrome	90 pat.; Xiao Pi- Ⅱ, 100 mL, 3 ×/d, 2 wk	90 pat.; 5 mg mosapride 3 ×/d, 2 wk	3D-ultrasound, questionnaire: bloating, eructation, gastric liquid emptying rate fullness P < 0.05	Not blinded, gastric emptying by 3D-ultrasound, randomized
Zhang *et al*[178], 2013	162 pat; FD with spleen deficiency and qi stagnation	108 pat.; gastrosis No.1 compound, no dose; 4 wk, 4 wk follow-up	54 pat.; placebo, no dose, 4 wk	Symptomatic improvement (P < 0.01)	No scores given; randomized
Xiao and Li[179], 2013	89 pat.; FD + anxiety or depression	23 pat.; modified Banxia Houpo decoction (MBHD); no dose given; 4 wk	22 pat.; domperidone, no dose; 22 pat., St. John's Wort, no dose; 4 wk each	Domperidon + St. John's Wort most effective, domperidone ineffective. Few significant differences (MBHD *vs* domperidone)	HAMA, HAMD, FD symptom scoring system, randomized
Zhang *et al*[181], 2013	160 pat.; FD + spleen deficiency and qi stagnation	106 pat.; Liu Jun Zi decoction in 2 × 150 mL water; 4 wk, 4 wk follow-up	54 pat.; placebo in 2 × 150 mL water; 4 wk, 4 wk follow-up	Dyspepsia symptom score, barium emptying markers; TCM group P < 0.01	7 dropouts (5 verum, 2 placebo). Careful conclusions, appropriate, randomized
Li *et al*[187], 2013	134 pat.; FD	66 pat.; Xiaopi-I, no dose given, 4 wk	68 pat.; 10 mg 3 ×/d domperidone; 4 wk	Not visible whether there were differences between groups	6 dropout verum, 8 dropout domperidone, randomized
Fan *et al*[180], 2012	170 pat.; FD	Unknown number; individual therapy by Chinese medical syndrome ty- ping; no dose, 4 wk	34 pat.; domperidone or esomeprazole, no dose, 4 wk?	Symptom score, healing rate, effectivity, SF-36 score, physical and mental component summary: n.s.	16 drop outs in verum, 4 drop outs in control. Conclusions are not supported
Wu *et al*[182], 2011	163 pat.; FD + spleen deficiency and qi stagnation, Rome Ⅱ	83 pat.; IFC-A pills, 6 g/tid, 4 wk	80 pat.; IFC-S, 6 g/tid, 4 wk	IFC-A better than IFC-S on symptom scale (authors scale)	Randomized, double blind. 3 drop outs. Drug difference Citrus aurantis *vs* Camellia sinensis
Xia *et al*[183], 2008	63 pat.; FD	33 pat.; Hewei Xiaopi capsule, dose not given, for 4 wk	30 pat.; domperidone, dose not given, 4 wk	Clinical symptoms-n.s.; EGG: less waves in treated group, 41.9 ± 18.2 *vs* 50.9 ± 16.0	Clinical symp-toms, electrogastrogram randomized
Gao *et al*[186], 2007	32 pat.; FD, dyskinesia	Qingre Liqi granule; no dose given, 6 d	No control group	All parameters improved, correlation between gastric emptying time and symptoms	Cohort study
Zhao and Gan[188], 2005	73 pat.; FD + depression, anxiety	Unknown number, Xinwei decoction,unknown dose, 8 wk	Unknown number, domperidone or placebo, unknown dose, 8 wk	Symptom score, total effectivity in TCM sign. better than domperidone, this better than placebo	Curing rate in TCM 70%
Ge *et al*[189], 2002	100 pat.; functional dyspepsia, TCM symptom	50 pat.; Jian Weishu capsules, decocted separately	50 pat.; Jian Weishu capsules, decocted together	No difference in effects	Claims effectiveness of the herbal TCM preparation
Gu *et al*[185], 1998	64 pat.; FD	20 pat.; 3 × 100 mL/d Weihuigui decoction; 14 d	44 pat.; no treatment	Improves clinical symptoms, gastric emptying time, no data	
Tatsuta and Ishii[184], 1993	42 pat.; chronic idiopathic dyspepsia	22 pat.; Liu Jun Zi Tang (TJ-43) 2.5 g 3 ×/d; 7 d	20 pat.; placebo, no dose given, 7 d	No change in pain, sign for fullness, heartburn, belching and nausea	Gastric emptying by acetaminophen serum conc. No changes in pain at all. Randomized

EGG: Electrogastrogram; FD: Functional dyspepsia; HAMA: Hamilton anxiety scale; HAMD: Hamilton depression scale; MBHD: Modified Banxia Houpo decoction; SF36: Short Form 36 life scale questionnaire.

Table 11 Clinical trials with herbal traditional Chinese medicine preparations for irritable bowel syndrome

Ref.	Patients	Treatment	Control	Outcome	Remarks
Su *et al*[200], 2013	240 pat.; IBS-D, Rome Ⅲ criteria	120 pat.; modified Sishen Wan, dose not given, 4 wk	120 pat.; Chao Maiya, dose not given, 4 wk	Significant better in treatment group for effective rate, cure rate, recurrence	Randomized; 4 dropouts in therapy, 12 dropouts in placebo; cure rate defined as lack of symptoms
Bian *et al*[202], 2013	120 pat.; IBS-C, Rome Ⅲ	60 pat.; 7.5 g bid Ma Zi Ren Wan,18 wk	60 pat.; placebo, 18 wk	After 10 wk good effect, declining afterwards	Randomized, blinded; well conducted study
Huang *et al*[210], 2011	90 pat.; IBS-C, long term care	45 pat.; 1.5 (mild), 3 (moderate) or 4.5 g/d (severe) CCH1 powder, 8 wk. 27 remaining at 12 wk	45 pat.; placebo (no details), 8 w. 31 remaining after 12 wk	After 4 and 8 wk: increased bowel movement, reduced enema use, rescue laxative. After 12 wk: only reduced rescue laxative	Randomized, double blind, placebo controlled. 12 dropout CCH1, 11 dropouts placebo; 9 withdrawals
Cheng *et al*[203], 2011	120 pat.; IBS-C, excessive constipation by Rome Ⅲ and TCM	60 pat.; Hemp Seed pill 7.5 g/bid, 8 wk, follow-up 8 wk	60 pat.; placebo (Dextrin, tea essence, gardenin, caramel)	During treatment sign improvement, after follow-up n.s.	Randomized, double blind. 7-10 dropouts.
Gao *et al*[207], 2010	80 pat.; IBS-D	40 pat.; Jianpi Tiaogan Wen Shen recipe, dose not given, 4 wk	40 pat.; pinaverium bromide, dose not given, 4 wk	No difference in effective rate, cure rate; less mucus, better long term of verum ($P < 0.01$)	3 dropouts in verum, 4 dropouts in control
Zhang *et al*[197], 2010	360 pat.; IBS-D	180 pat.(?); Chinese medicine-syndrome differentiation therapy, dose not given, 4 wk	180 pat. (?); pinaverium bromide, dose not given, 4 wk	TCM significantly superior	No information on dropout, dose, symptom scores
Jia *et al*[204], 2010	132 pat.; constipation with conventional and TCM criteria	44 pat.; 70 mg tid Yun Chang capsule, 2 wk	44 pat.; placebo tid 2 wk	Symptom score improvement in both YCC groups, no dose difference	11 dropouts; well designed study
Zhang[212], 2009	80 pat.; functional constipation	43 pat.; 105 mg tid YCC 40 pat.; 5 g/d compound plantain-senna Granule, 2 wk	40 pat.; 5 g/d starch placebo, 2 wk	Stool frequency and property, clinical symptom scores, transit time sign. improved	
Pan *et al*[195], 2009	120 pat.; IBS-D Rome Ⅲ	80 pat.; 2 pkg/d Tongxie Yaofang granules, 4 wk	40 pat.; 3 × 2 tbl/d Miyarisam, 4 wk	No difference in symptoms; sign. increase in mast cell activation (6 pat. per group)	Miyarisam is described as placebo; 3 dropouts in intervention group
Gao *et al*[205], 2009	104 pat.; IBS-D	78 pat.; 4 caps. tid Changjishu	26 pat.; 3 caps. tid glutamine compound enteric capsule, 3 wk	All clinical scores sign. improved	
Wu and Zhang[198], 2008	125 pat.; IBS-D	Soft elastic capsule, 3 wk 2 groups:	pinaverium 50 mg, oryzanol 10 mg, and bifid triple viable 420 mg, 3/d, 4 wk	SF 36: in 6 of 8 scores TCM superior	
Lv and Wang[201], 2008	58 pat.; IBS-C	TCM therapy not specified, TCM selected patented herbs, dose and number not given; 4 wk 30 pat.; Tongyouqing, no dose given, 4 wk	28 pat.; 6 mg qid tegaserod maleate; 4 wk	Symptom score better in treatment group	Scant data
Wang *et al*[214], 2007	216 children; with constipation	105 pat.; 20 g/d Forlax, 2 wk	111 pat.; 15 mL/d lactulose, 2 wk	Significant: bowel movement, stool consistency, complete clinical remission, abdominal pain	
Zhang *et al*[206], 2007	198 pat.; IBS	66 pat.; 1.2 g tid Dinggui oil, 2 wk;	66 pat.; 5 g tid placebo, 2 wk	High dose is effective (54% effective), low dose 28.8%, placebo 21.9%	Randomized double blind, placebo controlled
Wang *et al*[209], 2006	60 pat.; IBS-D, Rome Ⅱ	66 pat. 0.8 g tid Dinggui oil, 2 wk 30 pat.; 3 × 5 g/d Tong Xiening granule, 3 wk	30 pat.; 3 × 5 g/d placebo, 3 wk	NPIS scale: improvement in some pain parameters	Randomized, double blind, well controlled study
Leung *et al*[196], 2006	119 pat.; IBS-D, Rome Ⅱ, + TCM criteria	60 pat.; Tong Xie Yao Fang, no dose; 8 wk; 8 wk follow-up	59 pat.; placebo, no dose; 8 wk, 8 wk follow-up	Significant improvement in bowel frequency, initial pain relief; other parameters (BSS, SF36) n.s.	14 (verum) 10 dropouts; randomized, blinded, well conducted
Yu *et al*[216], 2005 Shen *et al*[208], 2003	47 pat.; IBS-C, Rome criteria 45 pat.; IBS-D	24 pat.; 2 × 100 mL/d modified Sinisan, 8 wk No number; compound Changjitai; no dose, no duration	23 pat.; 3 × 10 mg cisapride tabl., 8 wk No number; pinaverium bromide, no dose, no duration	Symptom score, rectal tolerance vol. sign. improved Defecation episodes, stool quality, tenesms, distension sign. better (83% > 73%)	Cisapride as control improves gastric emptying Statistics not reproducible

Bensoussan[193,194], 2001	116 pat.; IBS, Rome criteria	38 pat.; individualized herbs, 43 pat. standard formula; 16 wk	35 pat.; placebo; 16 wk	Both treatment groups better than placebo on key outcome parameters; no difference between treatment groups	Proof of principle study

BSS: Bowel symptom score; FD: Functional dyspepsia; IBS-D: Irritable bowel syndrome, diarrhoeic type; IBS-C: Irritable bowel syndrome, constipation type; NPIS: Numeric pain intensity scale; SF-36: Short Form 36 life style questionnaire; TCM: Traditional Chinese medicine; YCC: Yun Chang capsule.

of St. John's Wort extract over modified Banxia Hupo decoction in dyspepsia patients with anxiety or depression; other publications reported improvement in all scores and symptoms, measured without adequate data presentation[189].

IBS

Besides dyspepsia, IBS is a diagnosis of exclusion with abdominal pain rather than eructation. IBS is clinically subdivided with diarrhea or constipation as symptoms; therefore, PubMed and Cochrane libraries were searched for IBS with both diarrhea and constipation. For herbal TCM and constipation, three Cochrane reviews are identified, with Liu *et al*[192] analyzing clinical trials of constipation and herbal medicines in general. Additionally, 33 clinical trials are included in the database. A PubMed search with IBS and herbal TCM identified 20 publications, with eleven relevant publications. Searching for constipation identified 51 publications; eight of them were judged relevant (Table 11). All relevant clinical trials for IBS and herbal TCM were found both in PubMed and Cochrane database searches. Bensoussan *et al*[193,194] studied Chinese patients in Sydney; whereas all other trials were performed in China, mostly in TCM hospitals.

Except Tong Xie Yao Fang which was used in two trials[195,196], no herbal TCM preparation was studied more than once. Three trials[193,197,198] did not specify the type of herbal TCM preparation used. IBS - like dyspepsia - is a diagnosis of exclusion; for classification ROME criteria of Western medicine[199] can be used; this has been confirmed for nine studies[193,195,196,200-204]; also in nine trials, TCM symptom definitions have been used as inclusion criteria[193,196,198,200,203-206]. Most studies were reported as randomized (15/19 studies) and blinded (11/19 studies). Whereas 7/8 studies in IBS constipation type were placebo controlled, pinaverium[197,198,207,208], Chao Maiya[200], Miyarisam[195], and glutamine compound[205] were used as control treatment in IBS with diarrhea. Liu[192] could not identify valid evidence for herbal TCM preparations being effective in constipated IBS patients. Most studies found some symptomatic improvement during the treatment period[195,196,203,204,206,207,209,210], including the Australian study[193,194,211]. However, since this effect was seen with all preparations, especially in older studies[212-216], it may be speculated that this improvement is not due to specific herbal preparations but mediated by nonspecific factors.

CONCLUSION

The use of herbal TCM to treat various diseases has an interesting philosophical basis with a long history, but its negative benefit/risk profile has raised objections about its efficiency. This also has been confirmed for gastrointestinal disorders in the present review, even when analyzing all published clinical trials, since placebo controlled, randomized, double blinded trials are lacking for nearly all preparations and indications. The quality of these studies overall is poor and does not allow a recommendation for its general use in gastrointestinal diseases. Future clinical studies should adhere to accepted standards of placebo controlled, randomized, double-blind clinical trials, also considering issues of herbal product quality and standard criteria of diagnoses and treatment endpoints. A modern herbal TCM should meet these requirements of modern medicine and bridge the gap between these two medicinal cultures.

REFERENCES

1 **Major RH**. History of Medicine. Charles C Thomas, editor. Springfield: Thomas Publisher, 1954
2 **WHO**. IARC Monographs Vol. 82. Introduction: History of use of traditional herbal medicines, 2002. Available from: URL: http://monographs.iarc.fr/ENG/Monographs/vol82/mono82-6A.pdf
3 **WHO**. Traditional medicine: Definitions. Available from: URL: http://www.who.int/medicines/areas/traditional/definitions/en/
4 **WHO**. General Guidelines for Methodologies on Research and Evaluation of Traditional Medicine, 2000. Available from: URL: http://whqlibdoc.who.int/hq/2000/WHO_EDM_TRM_2000.1.pdf?ua=1
5 **MHRA**. Herbal medicines regulation: Registered traditional herbal medicines. Available from: URL: http://www.mhra.gov.uk/Howweregulate/Medicines/Herbalmedicinesregulation/RegisteredTraditionalHerbalMedicines/
6 **EMA**. Herbal medicinal products. Available from: URL: http://ec.europa.eu/health/human-use/herbal-medicines/index_en.htm
7 **Raghavendra HL**, Yogesh HS, Gopalakrishna B, Chardrashkhar VM, Sathish Kumar BP, Kumar V. An overview of herbal medicine. *Int J Pharmaceut Sci* 2009; **1**: 1-20
8 **Nishimura K**, Plotnikoff GA, Watanabe K. Kampo medicine as an integrative medicine in Japan. *JMAJ* 2009; **52**: 147-149
9 **Park HL**, Lee HS, Shin BC, Liu JP, Shang Q, Yamashita H, Lim B. Traditional medicine in china, Korea, and Japan: a brief introduction and comparison. *Evid Based Complement Alternat Med* 2012; **2012**: 429103 [PMID: 23133492 DOI: 10.1155/2012/429103]
10 **National Institutes of Health**; National Center for Complementary and Alternative medicine. Traditional Chinese medicine: An introduction. Last update 10 January 2014. Available from: URL: http://nccam.nih.gov/health/whatiscam/chinesemed.htm
11 The essentials of traditional Chinese herbal medicine. Available

from: URL: http://www.china.org.cn/english/MATERIAL/185685.htm
12 **Medical Center**; NYU Langone: Herbal medicine. Available from: URL: http://www.med.nyu.edu/content?ChunkIID=37432
13 **Manheimer E**, Wieland S, Kimbrough E, Cheng K, Berman BM. Evidence from the Cochrane Collaboration for Traditional Chinese Medicine therapies. *J Altern Complement Med* 2009; **15**: 1001-1014 [PMID: 19757977 DOI: 10.1089/acm.2008.0414]
14 **Teschke R**, Wolff A, Frenzel C, Schulze J. Review article: Herbal hepatotoxicity--an update on traditional Chinese medicine preparations. *Aliment Pharmacol Ther* 2014; **40**: 32-50 [PMID: 24844799]
15 **National Institutes of Health and LiverTox**. Drug record. Chi R Yun (Breynia officinalis). Last updated 25 October 2013. Available from: URL: http://livertox.nih.gov/ChiRYun.htm
16 **Posadzki P**, Watson L, Ernst E. Contamination and adulteration of herbal medicinal products (HMPs): an overview of systematic reviews. *Eur J Clin Pharmacol* 2013; **69**: 295-307 [PMID: 22843016 DOI: 10.10007/s00228-012-1353-z]
17 **Ernst E**. Adulteration of Chinese herbal medicines with synthetic drugs: a systematic review. *J Intern Med* 2002; **252**: 107-113 [PMID: 12190885 DOI: 10.1046/j.1365-2796.2002.00999.x]
18 **Harewood GC**, Hendrick LM. Prospective, controlled assessment of the impact of formal evidence-based medicine teaching workshop on ability to appraise the medical literature. *Ir J Med Sci* 2010; **179**: 91-94 [PMID: 19707728 DOI: 10.1007/s11845-009-0411-8]
19 **Higgins JPT**, Green S. Cochrane Handbook for Systematic Reviews of Interventions. version 5.1.0: The Cochrane Collaboration, 2011
20 **Sackett DL**, Rosenberg WM, Gray JA, Haynes RB, Richardson WS. Evidence based medicine: what it is and what it isn't. *BMJ* 1996; **312**: 71-72 [PMID: 8555924 DOI: 10.1136/bmj.312.7023.71]
21 **Pannucci CJ**, Wilkins EG. Identifying and avoiding bias in research. *Plast Reconstr Surg* 2010; **126**: 619-625 [PMID: 20679844 DOI: 10.1097/PRS.0b013e3181de24bc]
22 **Guyatt GH**, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, Schünemann HJ. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ* 2008; **336**: 924-926 [PMID: 18436948 DOI: 10.1136/bmj.470347.AD]
23 **Kirk-Smith MD**, Stretch DD. Evidence-based medicine and randomized double-blind clinical trials: a study of flawed implementation. *J Eval Clin Pract* 2001; **7**: 119-123 [PMID: 11489037 DOI: 10.1046/j.1365-2753.2001.00270.x]
24 **Begg C**, Cho M, Eastwood S, Horton R, Moher D, Olkin I, Pitkin R, Rennie D, Schulz KF, Simel D, Stroup DF. Improving the quality of reporting of randomized controlled trials. The CONSORT statement. *JAMA* 1996; **276**: 637-639 [PMID: 8773637 DOI: 10.1001/jama.1996.03540080059030]
25 **Cochrane AL**. Effectiveness and efficiency: Random reflections on health services. Nuffield Provincial Hospital Trust, 1972
26 **Wang Q**, Guo Z, Zhao P, Wang Y, Gan T, Yang J. Chinese herbal medicines for acute pancreatitis. *Cochrane Database of Systematic Reviews* 2005; **1**: CD003631
27 **Yang J**, Zhu L, Wu Z, Wang Y. Chinese herbal medicines for induction of remission in advanced or late gastric cancer. *Cochrane Database of Systematic Reviews* 2013; **4**: CD005096
28 **Liu ZL**, Xie LZ, Zhu J, Li GQ, Grant SJ, Liu JP. Herbal medicines for fatty liver diseases. *Cochrane Database of Systematic Reviews* 2013; **8**: CD009059
29 **Wei X**, Chen Z, Yang X, Wu T. Chinese herbal medicines for esophageal cancer. *Cochrane Database of Systematic Reviews* 2009; **4**: CD004520
30 **Ioannidis JP**, Evans SJ, Gøtzsche PC, O'Neill RT, Altman DG, Schulz K, Moher D. Better reporting of harms in randomized trials: an extension of the CONSORT statement. *Ann Intern Med* 2004; **141**: 781-788 [PMID: 15545678 DOI: 10.7326/0003-4819-141-10-200411160-00009]
31 **Tang JL**, Liu BY, Ma KW. Traditional Chinese medicine. *Lancet* 2008; **372**: 1938-1940 [PMID: 18930523 DOI: 10.1016/S0140-6736(09)62131-0]
32 **Tang JL**, Zhan SY, Ernst E. Review of randomised controlled trials of traditional Chinese medicine. *BMJ* 1999; **319**: 160-161 [PMID: 10406751 DOI: 10.1136/bmj.319.7203.160]
33 **Wang G**, Mao B, Xiong ZY, Fan T, Chen XD, Wang L, Liu GJ, Liu J, Guo J, Chang J, Wu TX, Li TQ. The quality of reporting of randomized controlled trials of traditional Chinese medicine: a survey of 13 randomly selected journals from mainland China. *Clin Ther* 2007; **29**: 1456-1467 [PMID: 17825697 DOI: 10.1016/j.clinthera.2007.07.023]
34 **Shaw D**. Toxicological risks of Chinese herbs. *Planta Med* 2010; **76**: 2012-2018 [PMID: 21077025]
35 **Zhang L**, Yan J, Liu X, Ye Z, Yang X, Meyboom R, Chan K, Shaw D, Duez P. Pharmacovigilance practice and risk control of Traditional Chinese Medicine drugs in China: current status and future perspective. *J Ethnopharmacol* 2012; **140**: 519-525 [PMID: 22374080 DOI: 10.1016/j.jep.2012.01.058]
36 **Ernst E**. Methodological aspects of Traditional Chinese Medicine (TCM). *Ann Acad Med Singapore* 2006; **35**: 773-774 [PMID: 17160191]
37 Pharmacopoeia of the People's Republic of China, Vol. 1. Beijing: Peoples Medical Publishing House, 2005
38 **Chan K**. Chinese medicinal materials and their interface with Western medical concepts. *J Ethnopharmacol* 2005; **96**: 1-18 [PMID: 15588645 DOI: 10.1016/j.jep.2004.09.019]
39 **Bunchorntavakul C**, Reddy KR. Review article: herbal and dietary supplement hepatotoxicity. *Aliment Pharmacol Ther* 2013; **37**: 3-17 [PMID: 23121117 DOI: 10.1111/apt.12109]
40 **Ma X**, Peng JH, Hu YY. Chinese herbal medicine-induced liver injury. *J Clin Translat Hepatol* 2014; **2**: 170-175 [DOI: 10.14218/JCTH.2014.00009]
41 **Teschke R**. Traditional Chinese Medicine induced liver injury. *J Clin Translat Hepatol* 2014; **2**: 80-94 [DOI: 10.14218/JCTH.2014.00003]
42 **Teschke R**, Wolff A, Frenzel C, Schulze J. Letter: Herbal hepatotoxicity--an update on traditional Chinese medicine preparations; authors' reply. *Aliment Pharmacol Ther* 2014; **40**: 738-740 [PMID: 25123394 DOI: 10.1111/apt.12887]
43 **Lai JN**, Tang JL, Wang JD. Observational studies on evaluating the safety and adverse effects of traditional chinese medicine. *Evid Based Complement Alternat Med* 2013; **2013**: 697893 [PMID: 24159351 DOI: 10.1155/2013/697893]
44 **Zhao L**, Nicholson JK, Lu A, Wang Z, Tang H, Holmes E, Shen J, Zhang X, Li JV, Lindon JC. Targeting the human genome-microbiome axis for drug discovery: inspirations from global systems biology and traditional Chinese medicine. *J Proteome Res* 2012; **11**: 3509-3519 [PMID: 22624854 DOI: 10.1021/pr3001628]
45 **Li J**, Lu C, Jiang M, Niu X, Guo H, Li L, Bian Z, Lin N, Lu A. Traditional chinese medicine-based network pharmacology could lead to new multicompound drug discovery. *Evid Based Complement Alternat Med* 2012; **2012**: 149762 [PMID: 23346189 DOI: 10.1155/2012/149762]
46 **Pelkonen O**, Xu Q, Fan TP. Why is Research on Herbal Medicinal Products Important and How Can We Improve Its Quality? *J Tradit Complement Med* 2014; **4**: 1-7 [PMID: 24872927 DOI: 10.4103/2225-4110.124323]
47 **Lin H**, Liu J, Zhang Y. Developments in cancer prevention and treatment using traditional Chinese medicine. *Front Med* 2011; **5**: 127-133 [PMID: 21695616 DOI: 10.1007/s11684-011-0137-7]
48 **Hu J**, Zhang J, Zhao W, Zhang Y, Zhang L, Shang H. Cochrane systematic reviews of Chinese herbal medicines: an overview. *PLoS One* 2011; **6**: e28696 [PMID: 22174870 DOI: 10.1371/journal.pone.0028696]
49 **Li X**, Yang G, Li X, Zhang Y, Yang J, Chang J, Sun X, Zhou X, Guo Y, Xu Y, Liu J, Bensoussan A. Traditional Chinese medicine in cancer care: a review of controlled clinical studies published in chinese. *PLoS One* 2013; **8**: e60338 [PMID: 23560092 DOI: 10.1371/journal.pone.0060338]

50 **Zhao YH**, Liu ZI, Li LH, Jiang SH, Shi CH. Systematic review of randomized controlled trials of traditional Chinese medicine treatment of non-acute bronchial asthma complicated by gastroesophageal reflux. *J Tradit Chin Med* 2012; **32**: 12-18 [PMID: 22594096 DOI: 10.1016/S0254-6272(12)60025-9]

51 **Ghen JY**, Qiu JR, Pan F. [Clinical observation on treatment of gastro-esophageal reflux with modified zhizhu pill]. *Zhongguo Zhongxiyi Jiehe Zazhi* 2004; **24**: 25-27 [PMID: 14976884]

52 **Zhang Q**, Tan XP, Wang WZ. [Clinical effects of dalitong granule combined proton pump inhibitors on gastroesophageal reflux disease]. *Zhongguo Zhongxiyi Jiehe Zazhi* 2012; **32**: 464-467 [PMID: 22803423]

53 **Li BS**, Li ZH, Tang XD, Zhang LY, Zhao YP, Bian LQ, Zhang YQ, Wang P, Wang FY. A randomized, controlled, double-blinded and double-dummy trial of the effect of tongjiang granule on the nonerosive reflux disease of and Gan-Wei incoordination syndrome. *Chin J Integr Med* 2011; **17**: 339-345 [PMID: 21611896 DOI: 10.1007/s11655-011-0724-0]

54 **Zhong Y**, Zhou H, Zhong L. [Clinical observation on jiangni hewei decoction in treatment of 45 patients with reflux esophagitis]. *Zhongguo Zhongxiyi Jiehe Zazhi* 2005; **25**: 876-879 [PMID: 16313106]

55 **Xu G**. Treatment of reflux laryngopharyngitis with modified banxia xiexin tang (Pinellia decoction for draining the heart)--a report of 40 cases. *J Tradit Chin Med* 2006; **26**: 127-131 [PMID: 16817279]

56 **Xu HR**, Bo P, Yuan Y. [Study on integrated Chinese and Western therapy and criterion for efficacy evaluation of gastroesophageal reflux disease--a clinical observation on 116 cases]. *Zhongguo Zhongxiyi Jiehe Zazhi* 2007; **27**: 204-207 [PMID: 17432676]

57 **Hao Y**, Sun X, Zhang J. [Effects of Yunqitang on both esophageal mucosal morphology and esophageal motility in reflux esophagitis patients]. *Zhongguo Zhongxiyi Jiehe Zazhi* 1998; **18**: 345-347 [PMID: 11477908]

58 **Lundell LR**, Dent J, Bennett JR, Blum AL, Armstrong D, Galmiche JP, Johnson F, Hongo M, Richter JE, Spechler SJ, Tytgat GN, Wallin L. Endoscopic assessment of oesophagitis: clinical and functional correlates and further validation of the Los Angeles classification. *Gut* 1999; **45**: 172-180 [PMID: 10403727 DOI: 10.1136/gut.45.2.172]

59 An evidence-based appraisal of reflux disease management--the Genval Workshop Report. *Gut* 1999; **44** Suppl 2: S1-S16 [PMID: 10741335 DOI: 10.1136/gut.44.2008.S1]

60 **Armstrong D**. Endoscopic evaluation of gastro-esophageal reflux disease. *Yale J Biol Med* 1999; **72**: 93-100 [PMID: 10780570]

61 **Hu FL**, Cheng H, Zhang XZ, An HJ, Sheng JQ, Lü NH, Xie Y, Chen ZS, Xu JM, Hu NZ, Zheng PY, Zhang L, Zhang LX, Zhang SS, Tao L, Zhang ZY, Cui MH, Yang GB, Wang BM, Jiang K, Yang Q, Gao HJ. [Jinghuaweikang capsules combined with triple therapy in the treatment of Helicobacter pylori associated gastritis and duodenal ulcer and analysis of antibiotic resistance: a multicenter, randomized, controlled, clinical study]. *Zhonghua Yixue Zazhi* 2012; **92**: 679-684 [PMID: 22781295]

62 **Hu FL**. [A multicenter study of Chinese patent medicine wenweishu/yangweishu in the treatment of Helicobacter pylori positive patients with chronic gastritis and peptic ulcer]. *Zhonghua Yixue Zazhi* 2010; **90**: 75-78 [PMID: 20356485]

63 **Hu L**, Hu X, Yang M, Xie H, Xiang Y. Clinical effects of the method for warming the middle-jiao and strengthening the spleen on gastric mucosa repair in chronic gastritis patients. *J Tradit Chin Med* 2008; **28**: 189-192 [PMID: 19004201 DOI: 10.1016/S0254-6272(08)60044-8]

64 **Li Y**, Xu JK, Uu XR. [Clinical and pathological study of weiyan serial recipes in the treatment of gastric precancerous lesions]. *Zhongguo Zhongxiyi Jiehe Zazhi* 2011; **31**: 1635-1638 [PMID: 22384550]

65 **Li DG**, Du YR, Guo M. [Effect of huazhuo jiedu recipe on gastric juice compositions and tumor markers in patients with chronic atrophic gastritic precancerosis]. *Zhongguo Zhongxiyi Jiehe Zazhi* 2011; **31**: 496-499 [PMID: 21608221]

66 **Wu YN**, Chen YB, Wang WF, Tu Z. [Clinical study on effects of kangwei granule on precancerous lesion in patients with chronic atrophic gastritis]. *Zhongguo Zhongxiyi Jiehe Zazhi* 2005; **25**: 836-839 [PMID: 16248251]

67 **Xia J**. Medicinal herbs used in pairs for treatment of 98 cases of chronic gastritis. *J Tradit Chin Med* 2004; **24**: 208-209 [PMID: 15510804]

68 **Ji A**, Zhao W, Wang Z. [Clinical and experimental study on treatment of Helicobacter pylori infected gastritis by xialian yiyou capsule]. *Zhongguo Zhongxiyi Jiehe Zazhi* 1999; **19**: 595-598 [PMID: 11783172]

69 **Lu W**, Shan Z, Shen H. [Clinical study of weishu capsule in treating precancerous lesions of chronic atrophic gastritis]. *Zhongguo Zhongxiyi Jiehe Zazhi* 1998; **18**: 721-723 [PMID: 11475717]

70 **Zhong WR**, Huang YX, Cui JP. [Clinical study on modified sijunzi decoction in treating intestinal metaplasia of gastric mucosa]. *Zhongguo Zhongxiyi Jiehe Zazhi* 1997; **17**: 462-464 [PMID: 10322830]

71 **Yin GY**, He XF, Du YQ. [Clinical study on the piweiping capsule in treating patients with metaplasia of gastric mucosa]. *Zhongguo Zhongxiyi Jiehe Zazhi* 1996; **16**: 283-286 [PMID: 9387720]

72 **Long DS**, Li CM, Yang QG. [Clinical observation on verrucous gastritis with combined therapy of traditional Chinese and Western medicine]. *Zhongguo Zhongxiyi Jiehe Zazhi* 1994; **14**: 150-151, 132-133 [PMID: 7950183]

73 **Chen F**, Wei B, Yao W, Luo X. Kang wei granules in treatment of gastropathy related to Helicobacter pylori infection. *J Tradit Chin Med* 2003; **23**: 27-31 [PMID: 12747192]

74 **Zeng J**, Zuo XL, Wei W. [Clinical study on treatment of chronic superficial gastritis with jinghua weikang capsule]. *Zhongguo Zhongxiyi Jiehe Zazhi* 2006; **26**: 517-520 [PMID: 16841668]

75 **Li CY**, Shi XY, Zhou SJ. [Clinical and experimental study on gastrosia convalescens in treating chronic atrophic gastritis]. *Zhongguo Zhongxiyi Jiehe Zazhi* 1995; **15**: 21-24 [PMID: 7767060]

76 **Liu XR**, Han WQ, Sun DR. [Treatment of intestinal metaplasia and atypical hyperplasia of gastric mucosa with xiao wei yan powder]. *Zhongguo Zhongxiyi Jiehe Zazhi* 1992; **12**: 602-603, 580 [PMID: 1302542]

77 **Zhou FS**, Hu LJ, Wang RJ, Huang ZX, Luo Q. Study on clinical effect and mechanism of jianpi qingre huayu recipe. *Chin J Integr Med* 2007; **13**: 22-26 [PMID: 17578313 DOI: 10.1007/s11655-007-0022-z]

78 **Zhang WP**, Ge HN, Guo JW. [Effect of yiqi huoxue formula on healing quality and recurrence rate of peptic ulcer]. *Zhongguo Zhongxiyi Jiehe Zazhi* 2009; **29**: 1081-1084 [PMID: 20214327]

79 **Deng C**, Luo WS, Li GX. [Morphological observation on gastric mucosa membrane of patients with gastric ulcer treated with combined use of Qifang Weitong Powder and omeprazole]. *Zhongguo Zhongxiyi Jiehe Zazhi* 2007; **27**: 610-612 [PMID: 17717919]

80 **Zhang RM**, Wang L, Chen GY, Mao B, Chang J, Zhang Y, Li TQ, Gong M, Wang YQ, Feng WJ, Li XW. [Randomized controlled trial on haiguiyuyang capsule in the treatment of duodenal ulcer]. *Sichuan Daxue Xuebao Yixueban* 2005; **36**: 233-236 [PMID: 15807275]

81 **Zhou B**, Li JB, Cai GX, Ling JH, Dai XP. [Therapeutic effects of the combination of traditional Chinese medicine and western medicine on patients with peptic ulcers]. *Zhongnan Daxue Xuebao Yixueban* 2005; **30**: 714-718 [PMID: 16708818]

82 **Ji F**, Chen JY, Chen JX. [Comparative study on Jinghua Weikang Capsule and famotidine in treating duodenal ulcer]. *Zhongguo Zhongxiyi Jiehe Zazhi* 2006; **26**: 357-360 [PMID: 16689009]

83 **Yang ZW**, Gao YG, Zhang H. [Clinical observation on 80 cases with duodenal bulbar ulcer treated with kuiyangqing pill]. *Zhongguo Zhongxiyi Jiehe Zazhi* 1994; **14**: 152-153, 133 [PMID:

7950184]
84 **Lin Y**, Liao SS, Zhou YJ. [Clinical study on effect of Jianwei Yuyang Granule in treating patients with gastric ulcer]. *Zhongguo Zhongxiyi Jiehe Zazhi* 2007; **27**: 606-609 [PMID: 17717918]
85 **He LZ**, Zhang Q, Wang SC. [Clinical study on treatment of gastric ulcer with qingwei zhitong pill]. *Zhongguo Zhongxiyi Jiehe Zazhi* 2001; **21**: 422-423 [PMID: 12577435]
86 **Wan QX**, Wang Y, Wang D. [Clinical and experimental studies of yuyang powder in treatment of peptic ulcer]. *Zhongguo Zhongxiyi Jiehe Zazhi* 1996; **16**: 78-80 [PMID: 8762418]
87 **Yang Y**, Yu KY, Zeng XC. [Clinical study on treatment of peptic ulcer with bushen kangkui decoction]. *Zhongguo Zhongxiyi Jiehe Zazhi* 1995; **15**: 583-585 [PMID: 8704420]
88 **Li S**, Chen Z, Yan H, Wang Q. Clinical observation on 80 children with peptic ulcer treated primarily by traditional Chinese medicine. *J Tradit Chin Med* 1995; **15**: 14-17 [PMID: 7783454]
89 **Ma LS**, Guo TM. [Combined traditional Chinese and Western medicine in the treatment of intractable ulcer]. *Zhongguo Zhongxiyi Jiehe Zazhi* 1992; **12**: 524-526, 516 [PMID: 1298466]
90 **Li JB**, Jin YQ. [Treatment of peptic ulcer with jian-wei yu-wang tablets]. *Zhongxiyi Jiehe Zazhi* 1991; **11**: 141-143, 131-132 [PMID: 2065391]
91 **Zhou Z**, Hu Y, Pi D, Fan S, Yang Z, Wang Z, Gao J, Peng Q, Yao S, Liu L. Clinical and experimental observations on treatment of peptic ulcer with wei yang an (easing peptic-ulcer) capsule. *J Tradit Chin Med* 1991; **11**: 34-39 [PMID: 1861510]
92 **Gong Y**, Zha Q, Li L, Liu Y, Yang B, Liu L, Lu A, Lin Y, Jiang M. Efficacy and safety of Fufangkushen colon-coated capsule in the treatment of ulcerative colitis compared with mesalazine: a double-blinded and randomized study. *J Ethnopharmacol* 2012; **141**: 592-598 [PMID: 21911045 DOI: 10.1016/j.jep.2011.08.057]
93 **Gong Y**, Zha Q, Li L, Liu Y, Yang B, Liu L, Lu A, Lin Y, Jiang M. Efficacy and safety of Fufangkushen colon-coated capsule in the treatment of ulcerative colitis compared with mesalazine: a double-blinded and randomized study. *Dt Z Akupunktur* 2014; **57**: 20-21 [DOI: 10.1016/J.DZA.2014.05.006]
94 **Liao NS**, Ren JA, Fan CG, Wang GF, Zhao YZ, Li JS. [Efficacy of polyglycosides of Tripterygium wilfordii in preventing postoperative recurrence of Crohn disease]. *Zhonghua Weichang Waike Zazhi* 2009; **12**: 167-169 [PMID: 19296254]
95 **Han J**, Wang J, Wang JH. Effects of jianpi herbal suppository on hemorheology and CD62p in patients with ulcerative colitis. *J Tradit Chin Med* 2014; **34**: 155-158 [PMID: 24783925 DOI: 10.1016/S0254-6272(14)60070-4]
96 **He HH**, Shen H, Zheng K. [Observation of the curative effect of qingchang huashi recipe for treating active ulcerative colitis of inner-accumulation of damp-heat syndrome]. *Zhongguo Zhongxiyi Jiehe Zazhi* 2012; **32**: 1598-1601 [PMID: 23469594]
97 **Fukunaga K**, Ohda Y, Hida N, Iimuro M, Yokoyama Y, Kamikozuru K, Nagase K, Nakamura S, Miwa H, Matsumoto T. Placebo controlled evaluation of Xilei San, a herbal preparation in patients with intractable ulcerative proctitis. *J Gastroenterol Hepatol* 2012; **27**: 1808-1815 [PMID: 22775479 DOI: 10.1111/j.1440-1746.2012.07215.x]
98 **Zhou T**, Zhang SS, Cui C. [Clinical study of comprehensive treatment of Chinese medicine in treating ulcerative colitis based on two steps according to the stage of disease]. *Zhongguo Zhongxiyi Jiehe Zazhi* 2012; **32**: 172-175 [PMID: 22574586]
99 **Tong ZQ**, Yang B, Tong XY. [A multi-center randomized double-blinded, placebo-controlled clinical study on efficacy of composite sophora colon-soluble capsules in treating ulcerative colitis of internal dampness-heat accumulation syndrome type]. *Zhongguo Zhongxiyi Jiehe Zazhi* 2011; **31**: 172-176 [PMID: 21425568]
100 **Tong ZQ**, Yang B, Chen BY, Zhao ML. A multi-center, randomized, single-blind, controlled clinical study on the efficacy of composite sophora colon-soluble capsules in treating ulcerative colitis. *Chin J Integr Med* 2010; **16**: 486-492 [PMID: 21110172 DOI: 10.1007/s11655-010-0562-5]
101 **Chen ZS**, Nie ZW, Sun QL. [Clinical study in treating intractable ulcerative colitis with traditional Chinese medicine]. *Zhongguo Zhongxiyi Jiehe Zazhi* 1994; **14**: 400-402 [PMID: 7950223]
102 **Ling XH**, Yu X, Kong DJ, Hu CY, Hong Y, Yang XM. Treatment of inflammatory bowel disease with Chinese drugs administered by both oral intake and retention enema. *Chin J Integr Med* 2010; **16**: 222-228 [PMID: 20694776 DOI: 10.1007/s11655-010-0222-0]
103 **Liu JP**, McIntosh H, Lin H. Chinese medicinal herbs for chronic hepatitis B. *Cochrane Database of Systematic Reviews* 2000; **4**: CD001940
104 **Liu JP**, Manheimer E, Tsutani K, Gluud C. Medicinal herbs for hepatitis C virus infection. *Cochrane Database of Systematic Reviews* 2001; **4**: CD003183
105 **Xia Y**, Luo H, Liu JP, Gluud C. Phyllanthus species versus antiviral drugs for chronic hepatitis B virus infection. *Cochrane Database of Systematic Reviews* 2013; **4**: CD009004
106 **Liu P**, Hu YY, Liu C, Xu LM, Liu CH, Sun KW, Hu DC, Yin YK, Zhou XQ, Wan MB, Cai X, Zhang ZQ, Ye J, Zhou RX, He J, Tang BZ. Multicenter clinical study on Fuzhenghuayu capsule against liver fibrosis due to chronic hepatitis B. *World J Gastroenterol* 2005; **11**: 2892-2899 [PMID: 15902724 DOI: 10.3748/wjg.v11.i19.2892]
107 **Liu P**, Hu YY, Liu C, Xu LM, Liu CH, Sun KW, Hu DC, Yin YK, Zhou XQ, Wan MB, Cai X, Zhang ZQ, Ye J, Tang BZ, He J. [Multicenter clinical study about the action of Fuzheng Huayu Capsule against liver fibrosis with chronic hepatitis B]. *Zhongxiyi Jiehe Xuebao* 2003; **1**: 89-98, 102 [PMID: 15339577]
108 **Deng X**, Liang J, Wu FS, Li YB, Zhang YP, Tang YF. Influence of Fuzheng Huayu Tablet on mental state and social function of patients with post-hepatitis B liver cirrhosis. *Chin J Integr Med* 2012; **18**: 466-472 [PMID: 22821660 DOI: 10.1007/s11655-012-1112-0]
109 **Tang LL**, Sheng JF, Xu CH, Liu KZ. Clinical and experimental effectiveness of Astragali compound in the treatment of chronic viral hepatitis B. *J Int Med Res* 2009; **37**: 662-667 [PMID: 19589248 DOI: 10.1177/147323000903700308]
110 **Xiao HJ**, Shi CG, Zhang AP, Li P, Fan ZS. [Effects of Kang Gang Qian Granule (KGQG) on clinical and pathological features in chronic hepatitis B patients]. *Zhonghua Shiyan He Linchuang Bingduxue Zazhi* 2007; **21**: 369-371 [PMID: 18322606]
111 **Yang HY**, Li J, Yi M. [Study on chronical hepatitis B with treatment of integrative traditional Chinese and Western medicine]. *Zhongguo Zhongyao Zazhi* 2006; **31**: 1277-1280 [PMID: 17048576]
112 **Mollison L**, Totten L, Flexman J, Beaman M, Batey R. Randomized double blind placebo-controlled trial of a Chinese herbal therapy (CH100) in chronic hepatitis C. *J Gastroenterol Hepatol* 2006; **21**: 1184-1188 [PMID: 16824073 DOI: 10.1111/j.1440-1746.2006.04320.x]
113 **Chen JJ**, Tang BX, Wang LT. [Clinical study on effect of bushen granule combined with marine injection in treating chronic hepatitis B of Gan-shen deficiency with damp-heat syndrome type]. *Zhongguo Zhongxiyi Jiehe Zazhi* 2006; **26**: 23-27 [PMID: 16466167]
114 **Jakkula M**, Boucher TA, Beyendorff U, Conn SM, Johnson JE, Nolan CJ, Peine CJ, Albrecht JH. A randomized trial of Chinese herbal medicines for the treatment of symptomatic hepatitis C. *Arch Intern Med* 2004; **164**: 1341-1346 [PMID: 15226169 DOI: 10.1001/archinte.164.12.1341]
115 **Zhang CP**, Tian ZB, Liu XS, Zhao QX, Wu J, Liang YX. Effects of Zhaoyangwan on chronic hepatitis B and posthepatic cirrhosis. *World J Gastroenterol* 2004; **10**: 295-298 [PMID: 14716843]
116 **Liu P**, Hu YY, Liu C, Zhu DY, Xue HM, Xu ZQ, Xu LM, Liu CH, Gu HT, Zhang ZQ. Clinical observation of salvianolic acid B in treatment of liver fibrosis in chronic hepatitis B. *World J Gastroenterol* 2002; **8**: 679-685 [PMID: 12174378]
117 **Chen C**, Guo SM, Liu B. A randomized controlled trial of kurorinone versus interferon-alpha2a treatment in patients with

chronic hepatitis B. *J Viral Hepat* 2000; **7**: 225-229 [PMID: 10849265 DOI: 10.1046/j.1365-2893.2000.00216.x]
118 **Akbar N**, Tahir RA, Santoso WD, Soemarno HM, Liu G. Effectiveness of the analogue of natural Schisandrin C (HpPro) in treatment of liver diseases: an experience in Indonesian patients. *Chin Med J* (Engl) 1998; **111**: 248-251 [PMID: 10374427]
119 **Batey RG**, Bensoussan A, Fan YY, Bollipo S, Hossain MA. Preliminary report of a randomized, double-blind placebo-controlled trial of a Chinese herbal medicine preparation CH-100 in the treatment of chronic hepatitis C. *J Gastroenterol Hepatol* 1998; **13**: 244-247 [PMID: 9570235 DOI: 10.1111/j.1440-1746.1998.01550.x]
120 **Mao Q**, Su Y, Wu C, Duan Z, Tang J, Gu C, Liang H, Yang J, Huang L, Zheng Y, Wang M, Gong X. [Sustained efficacy of alpha-interferon therapy combined with Yixuesheng Capsule in treatment of chronic hepatitis B]. *Zhongguo Zhongyao Zazhi* 2012; **37**: 537-540 [PMID: 22667159]
121 **Zhang T**, Wang Y, Sun KW. [Effects of entecavir and Shenxian Yiganling combination therapy on patients with HBeAg-positive chronic hepatitis B for 48 weeks]. *Zhongguo Zhongxiyi Jiehe Zazhi* 2012; **32**: 180-182 [PMID: 22574588]
122 **Qiu H**, Mao DW, Wei AL. [Clinical study on Baihua Xianglian detoxification recipe combined with adefovir dipivoxil in treating HBeAg positive chronic hepatitis]. *Zhongguo Zhongxiyi Jiehe Zazhi* 2012; **32**: 176-179 [PMID: 22574587]
123 **Tang CL**, Zhou Z, Shi WQ. [Effects of Fuzheng Huayu Capsule on the ratio of TGF-beta1/BMP-7 of chronic viral hepatitis B fibrosis patients of Gan-Shen insufficiency blood-stasis obstruction syndrome]. *Zhongguo Zhongxiyi Jiehe Zazhi* 2012; **32**: 20-24 [PMID: 22500384]
124 **Hu XY**, Zhang Y, Chen G, Zhong S, Fan XJ. [A prospective cohort study on the influence of high doses of herbs for clearing heat and resolving stasis on survival rates in patients with hepatitis B-related acute-on-chronic liver failure]. *Zhongxiyi Jiehe Xuebao* 2012; **10**: 176-185 [PMID: 22313885 DOI: 10.3736/jcim20120208]
125 **Tang BZ**, Li M, Gao YQ. [Curative effect of Yidu Recipe in treating chronic hepatitis B patients of gan-shen yin-deficiency and damp-heat syndrome type and its influence of T-cell subsets]. *Zhongguo Zhongxiyi Jiehe Zazhi* 2010; **30**: 823-827 [PMID: 21038650]
126 **Li Y**, Wang L, Su C, Sun HN. Clinical observation on the treatment of chronic severe hepatitis B by retention enema with Huchang Jiedu Decoction. *Chin J Integr Med* 2010; **16**: 348-352 [PMID: 20697947 DOI: 10.1007/s11655-010-0519-8]
127 **Liang JX**, Zeng WT, Zhu KL, Zhang H, Wei JJ. [Effects of Danqi Huogan Capsule in protecting the liver, promoting circulation and removing clots in patients with chronic hepatitis B]. *Nanfang Yike Daxue Xuebao* 2010; **30**: 379-381 [PMID: 20159729]
128 **Chi XL**, Wu LM, Jiang JM, Chen PQ, Tian GJ, Xiao HM, Cai GS, Chen Y, Qian Y. [Evaluation of Chai Shao Liu Jun Tang for the treatment of chronic hepatitis B]. *Zhonghua Ganzangbing Zazhi* 2009; **17**: 440-442 [PMID: 19567023]
129 **Wang YL**. [Yiqi Huoxue Recipe combined with polyene phosphatidycholine capsule in treating 50 patients with non-alcoholic fatty hepatitis]. *Zhongguo Zhongxiyi Jiehe Zazhi* 2007; **27**: 162-164 [PMID: 17343008]
130 **Deng G**, Kurtz RC, Vickers A, Lau N, Yeung KS, Shia J, Cassileth B. A single arm phase II study of a Far-Eastern traditional herbal formulation (sho-sai-ko-to or xiao-chai-hu-tang) in chronic hepatitis C patients. *J Ethnopharmacol* 2011; **136**: 83-87 [PMID: 21527335]
131 **Ye F**, Liu Y, Qiu G, Zhao Y, Liu M. [Clinical study on treatment of cirrhosis by different dosages of salvia injection]. *Zhongyaocai* 2005; **28**: 850-854 [PMID: 16447879]
132 **Wang XB**, Jiang YY, Zhao CY. [Clinical research of xinganbao capsule on the treatment of chronic hepatitis B liver fibrosis]. *Zhongguo Zhongxiyi Jiehe Zazhi* 2012; **32**: 325-328 [PMID: 22686076]
133 **Zhou ZH**, Li M, Huang LY. [Study of xiaozhang recipe combined with lamivudine in treatment of 84 chronic viral hepatitis B patients with compensated liver cirrhosis]. *Zhongguo Zhongxiyi Jiehe Zazhi* 2011; **31**: 1220-1223 [PMID: 22013800]
134 **Long Y**, Lin XT, Zeng KL, Zhang L. Efficacy of intramuscular matrine in the treatment of chronic hepatitis B. *Hepatobiliary Pancreat Dis Int* 2004; **3**: 69-72 [PMID: 14969841]
135 **Li W**, Wang C, Zhang J. Effects of da ding feng zhu decoction in 30 cases of liver fibrosis. *J Tradit Chin Med* 2003; **23**: 251-254 [PMID: 14719288]
136 **Hu YH**, Liao ZR, Zou GM. [Clinical and experimental study on effect of ganyan IV in treatment of chronic active hepatitis complicated with hyperbilirubinemia]. *Zhongguo Zhongxiyi Jiehe Zazhi* 1996; **16**: 210-212 [PMID: 9206242]
137 **Yang HZ**, Wang FL, Wang YZ, Shen WS, Xu GL, Yang YW, Huang XL. [The clinical study on chronic hepatitis B treated by the four-step therapeutics of Traditional Chinese Medicine]. *Zhongyaocai* 2006; **29**: 748-752 [PMID: 17059015]
138 **Yang H**, Guo K, Shen W, Li Y, Dai M. [Clinical observation of the treatment of 654-2 injection and "ganxian tui huang recipe" on liver cirrhosis with intractable jaundice]. *Zhongyaocai* 2003; **26**: 385-387 [PMID: 14535021]
139 **Gan T**, Chen J, Jin SJ, Wang Y. Chinese medicinal herbs for cholelithiasis. *Cochrane Database of Systematic Reviews* 2013; **6**: CD004547
140 **Ma XM**, Fu QJ, Qu SX. [Effects of Jinhuang Yidan Granule on the bile compositions of primary bile duct pigment calculus patients]. *Zhongguo Zhongxiyi Jiehe Zazhi* 2012; **32**: 25-28 [PMID: 22500385]
141 **Cui NQ**, Wu XZ, Zheng XL. [Effect of li dan ling in decreasing jaundice and improving liver function in patients with obstructive jaundice]. *Zhongxiyi Jiehe Zazhi* 1989; **9**: 137-140, 131 [PMID: 2736696]
142 **Wu Y**, Yao DK, Zhu L. [Clinical observation on the safety and efficacy of ursodeoxycholic acid and fuzheng huayu capsule in the treatment of primary biliary cirrhosis]. *Zhongguo Zhongxiyi Jiehe Zazhi* 2012; **32**: 1477-1482 [PMID: 23359968]
143 **Tong GD**, Tang HH, Wei CS, Chen YJ, He JS, Zhou XZ, Zheng YJ, Zhou DQ. Efficacy of ursodeoxycholic acid combined with Tongdan Decoction () on immunological indices and histopathological changes in primary biliary cirrhosis patients. *Chin J Integr Med* 2012; **18**: 16-22 [PMID: 22231705 DOI: 10.1007/s11655-0112-0962-9]
144 **Qi YZ**, Zhang LZ, Liu Y. Eighty cases of chronic cholecystitis treated by oral administration of dan an tang. *J Tradit Chin Med* 2009; **29**: 288-290 [PMID: 20112492 DOI: 10.1016/S0254-6272(09)60086-8]
145 **Jiang J**, He M. [Clinical features of primary biliary cirrhosis and treatment of it by integrated traditional Chinese and western medicine]. *Zhongxiyi Jiehe Xuebao* 2003; **1**: 99-102 [PMID: 15339578 DOI: 10.3736/jcim20030205]
146 **Zhou LY**, Shan ZZ, You JL. Clinical observation on treatment of colonic cancer with combined treatment of chemotherapy and Chinese herbal medicine. *Chin J Integr Med* 2009; **15**: 107-111 [PMID: 19407947 DOI: 10.1007/s11655-009-0107-y]
147 **Liu J**, Wang WP, Zhou YY. [Observation on therapeutic effect of jianpi huoxue herbs combined with chemotherapy in treating post-operational colonic cancer patients]. *Zhongguo Zhongxiyi Jiehe Zazhi* 2005; **25**: 207-209 [PMID: 15842137]
148 **Cao GW**, Yang WG, Du P. [Observation of the effects of LAK/IL-2 therapy combining with Lycium barbarum polysaccharides in the treatment of 75 cancer patients]. *Zhonghua Zhongliu Zazhi* 1994; **16**: 428-431 [PMID: 7720497]
149 **Guo Z**. [Clinical observation on treatment of 38 cases of postoperational large intestinal cancer by fuzheng yiai decoction combined with chemotherapy]. *Zhongguo Zhongxiyi Jiehe Zazhi* 1999; **19**: 20-22 [PMID: 11783254]
150 **Li NQ**. [Clinical and experimental study on shen-qi injection with

chemotherapy in the treatment of malignant tumor of digestive tract]. *Zhongguo Zhongxiyi Jiehe Zazhi* 1992; **12**: 588-592, 579 [PMID: 1302539]
151 **Wu GL**, Zhang L, Li TY, Chen J, Yu GY, Li JP. Short-term effect of combined therapy with Jinlong Capsule and transcatheter arterial chemoembolization on patients with primary hepatic carcinoma and its influence on serum osteopontin expression. *Chin J Integr Med* 2010; **16**: 109-113 [PMID: 20473734 DOI: 10.1007/s11655-010-0109-9]
152 **Oka H**, Yamamoto S, Kuroki T, Harihara S, Marumo T, Kim SR, Monna T, Kobayashi K, Tango T. Prospective study of chemoprevention of hepatocellular carcinoma with Sho-saiko-to (TJ-9). *Cancer* 1995; **76**: 743-749 [PMID: 8625175]
153 **Yamamoto S**, Oka H, Kanno T, Mizoguchi Y, Kobayashi K. [Controlled prospective trial to evaluate Syosakiko-to in preventing hepatocellular carcinoma in patients with cirrhosis of the liver]. *Gan To Kagaku Ryoho* 1989; **16**: 1519-1524 [PMID: 2543309]
154 **Huang Z**, Wang Y, Chen J, Wang R, Chen Q. Effect of Xiaoaiping injection on advanced hepatocellular carcinoma in patients. *J Tradit Chin Med* 2013; **33**: 34-38 [PMID: 23596809 DOI: 10.1016/S0254-6272(13)60097-7]
155 **Yen Y**, So S, Rose M, Saif MW, Chu E, Liu SH, Foo A, Jiang Z, Su T, Cheng YC. Phase I/II study of PHY906/capecitabine in advanced hepatocellular carcinoma. *Anticancer Res* 2009; **29**: 4083-4092 [PMID: 19846955]
156 **Chen Z**, Zhai XF, Su YH, Wan XY, Li J, Xie JM, Gao B. [Clinical observation of cinobufacini injection used to treat moderate and advanced primary liver cancer]. *Zhongxiyi Jiehe Xuebao* 2003; **1**: 184-186 [PMID: 15339556 DOI: 10.3736/jcim20030311]
157 **Peng ZS**, Rao RS, Gong ZF. [Clinical effects of perfusing drugs into hepatic artery to promote blood circulation in late stage of hepatocarcinoma]. *Zhongguo Zhongxiyi Jiehe Zazhi* 1993; **13**: 330-332, 323 [PMID: 8257834]
158 **Saif MW**, Lansigan F, Ruta S, Lamb L, Mezes M, Elligers K, Grant N, Jiang ZL, Liu SH, Cheng YC. Phase I study of the botanical formulation PHY906 with capecitabine in advanced pancreatic and other gastrointestinal malignancies. *Phytomedicine* 2010; **17**: 161-169 [PMID: 20092990 DOI: 10.1016/j.phymed.2009.12.016]
159 **Zhai XF**, Chen Z, Li B, Shen F, Fan J, Zhou WP, Yang YK, Xu J, Qin X, Li LQ, Ling CQ. Traditional herbal medicine in preventing recurrence after resection of small hepatocellular carcinoma: a multicenter randomized controlled trial. *J Integr Med* 2013; **11**: 90-100 [PMID: 23506690 DOI: 10.3736/jintegrmed2013021]
160 **Zhao HJ**, Du J, Chen X. [Clinical study of Fuzheng Yiliu Recipe combined with microwave ablation on hepatocellular carcinoma]. *Zhongguo Zhongxiyi Jiehe Zazhi* 2012; **32**: 32-34 [PMID: 22500387]
161 **Feng YL**, Ling CQ, Li B. [Clinical study on integrative medicine for preventing and treating post-transcatheter arterial chemoembolization]. *Zhongguo Zhongxiyi Jiehe Zazhi* 2005; **25**: 534-536 [PMID: 16025970]
162 **Wang H**. [Clinical observation on effect of comprehensive immunotherapy in treating hepatic carcinoma after embolism chemotherapy]. *Zhongguo Zhongxiyi Jiehe Zazhi* 1998; **18**: 411-413 [PMID: 11477817]
163 **Zheng C**, Feng G, Liang H. Bletilla striata as a vascular embolizing agent in interventional treatment of primary hepatic carcinoma. *Chin Med J* (Engl) 1998; **111**: 1060-1063 [PMID: 11263363]
164 **Tian HQ**, Li HL, Wang B, Liang GW, Huang XQ, Huang ZQ, Lang JM, Zhang YP, Chen XZ, Chen YS. Treatment of middle/late stage primary hepatic carcinoma by Chinese medicine comprehensive therapy: A prospective randomized controlled study. *Chin J Integr Med* 2010; **16**: 102-108 [PMID: 20473733 DOI: 10.1007/s11655-010-0102-3]
165 **Wang B**, Tian HQ, Liang GW. [Effect of ganji recipe combined with Fructus Bruceae oil emulsion intervention on quality of life in patients with advanced primary hepatic cancer]. *Zhongguo Zhongxiyi Jiehe Zazhi* 2009; **29**: 257-260 [PMID: 19548447]
166 **Hou EC**, Lu YX. [Primary hepatocarcinoma treated by traditional Chinese medicine combined with transcatheter arterial chemoembolization]. *Zhongguo Zhongxiyi Jiehe Zazhi* 2009; **29**: 225-227 [PMID: 19548439]
167 **Lin LZ**, Zhou DH, Liu K, Wang FJ, Lan SQ, Ye XW. [Analysis on the prognostic factors in patients with large hepatocarcinoma treated by shentao ruangan pill and hydroxycamptothecine]. *Zhongguo Zhongxiyi Jiehe Zazhi* 2005; **25**: 8-11 [PMID: 15719740]
168 **Xu K**, Li Z, Zhu D. The effect of gan fu le in interventional treatment of hepatocarcinoma. *J Tradit Chin Med* 2000; **20**: 185-186 [PMID: 11038979]
169 **Han JQ**, Chen SD, Zhai LM. [Clinical study of combined Chinese herbal medicine with move stripe field radiation in treating primary hepatocellular carcinoma]. *Zhongguo Zhongxiyi Jiehe Zazhi* 1997; **17**: 465-466 [PMID: 10322831]
170 **Chen ZX**, Zhang SJ, Hu HT, Sun BG, Yin LR. [Clinical study of method of strengthening body resistance and disintoxication disintoxication in patients with HCC of post-TACE]. *Zhongguo Zhongyao Zazhi* 2007; **32**: 1211-1213 [PMID: 17802890]
171 **Wu D**, Bao WG, Ding YH. [Clinical and experimental study of xiaoshui decoction in the treatment of primary liver cancer caused ascites]. *Zhongguo Zhongxiyi Jiehe Zazhi* 2005; **25**: 1066-1069 [PMID: 16398423]
172 **Lin JJ**, Jin CN, Zheng ML, Ouyang XN, Zeng JX, Dai XH. Clinical study on treatment of primary hepatocellular carcinoma by Shenqi mixture combined with microwave coagulation. *Chin J Integr Med* 2005; **11**: 104-110 [PMID: 16150196 DOI: 10.1007/BF02836465]
173 **Xu BP**, Zhang YQ, Li SP. [Effect of relieving blood stasis, strengthening spleen and soothing liver therapy in improving hepatic function in patients after liver-carcinomectomy]. *Zhongguo Zhongxiyi Jiehe Zazhi* 2001; **21**: 742-743 [PMID: 12575605]
174 **Lao Y**. [Clinical study on effect of matrine injection to protect the liver function for patients with primary hepatic carcinoma after trans-artery chemo-embolization (TAE)]. *Zhongyaocai* 2005; **28**: 637-638 [PMID: 16252735]
175 **Zhang B**, Huang G, Zhang Y, Chen X, Hu P, Xu B. [Clinical observation on prevention of "jia wei si jun zi tang" from damage of hepatic reserving function after intervention of liver cancer]. *Zhong Yao Cai* 2004; **27**: 387-389 [PMID: 15376398]
176 **Shao ZX**, Cheng ZG, Yin X. [Clinical study on treatment of middle-advanced stage liver cancer by combined treatment of hepatic artery chemoembolization with gan'ai no. I and no. II]. *Zhongguo Zhongxiyi Jiehe Zazhi* 2001; **21**: 168-170 [PMID: 12577328]
177 **Liu B**, Piao X, Guo L. Effect of herbal formula xiao pi-II on functional dyspepsia. *J Tradit Chin Med* 2013; **33**: 298-302 [PMID: 24024322 DOI: 10.1016/S0254-6272(13)60168-5]
178 **Zhang SS**, Zhao LQ, Wang HB, Wu B, Wang CJ, Huang SP, Shen H, Wei W, Lai YL. Efficacy of Gastrosis No.1 compound on functional dyspepsia of spleen and stomach deficiency-cold syndrome: a multi-center, double-blind, placebo-controlled clinical trial. *Chin J Integr Med* 2013; **19**: 498-504 [PMID: 23818201 DOI: 10.1007/s11655-013-1503-x]
179 **Xiao L**, Li Y. [Randomized controlled trial of modified banxia houpo decoction in treating functional dyspepsia patients with psychological factors]. *Zhongguo Zhongxiyi Jiehe Zazhi* 2013; **33**: 298-302 [PMID: 23713238]
180 **Fan YH**, Cai LJ, Xu GP. [Treatment of functional dyspepsia by Chinese medical syndrome typing: a randomized control research]. *Zhongguo Zhongxiyi Jiehe Zazhi* 2012; **32**: 1592-1597 [PMID: 23469593]
181 **Zhang S**, Zhao L, Wang H, Wang C, Huang S, Shen H, Wei W, Tao L, Zhou T. Efficacy of modified LiuJunZi decoction on functional dyspepsia of spleen-deficiency and qi-stagnation syndrome: a randomized controlled trial. *BMC Complement Altern Med* 2013; **13**: 54 [PMID: 23453018 DOI: 10.1186/1472-6882-13-54]
182 **Wu H**, Jing Z, Tang X, Wang X, Zhang S, Yu Y, Wang Z, Cao H, Huang L, Yu Y, Wang Y. To compare the efficacy of two kinds of

Zhizhu pills in the treatment of functional dyspepsia of spleen-deficiency and qi-stagnation syndrome: a randomized group sequential comparative trial. *BMC Gastroenterol* 2011; **11**: 81 [PMID: 21762493 DOI: 10.1186/1471-230X-11-81]

183 **Xia LY**, Ge WJ, Liu WJ. [Therapeutic effect of hewei xiaopi capsule for treatment of dyskinesis functional dyspepsia]. *Zhongguo Zhongxiyi Jiehe Zazhi* 2008; **28**: 454-456 [PMID: 18672777]

184 **Tatsuta M**, Iishi H. Effect of treatment with liu-jun-zi-tang (TJ-43) on gastric emptying and gastrointestinal symptoms in dyspeptic patients. *Aliment Pharmacol Ther* 1993; **7**: 459-462 [PMID: 8218760 DOI: 10.1111/j.1365-2036.1993.tb00120.x]

185 **Gu Z**, Wang X, Wang Q. [Determination of gastric emptying time of functional dyspepsia and clinical study on therapeutic effect of Weihuigui decoction on functional dyspepsia]. *Zhongguo Zhongxiyi Jiehe Zazhi* 1998; **18**: 724-726 [PMID: 11475718]

186 **Gao LM**, Yao SK, Zhang RX. [Effect of Qingre Liqi Granule on clinical therapeutic efficacy, electrogastrogram and gastric emptying in patients with functional dyspepsia]. *Zhongguo Zhongxiyi Jiehe Zazhi* 2007; **27**: 505-508 [PMID: 17633361]

187 **Li H**, Yang ZY, Li Y. The therapeutic effect of Xiaopi-I on functional dyspepsia. *Chin J Integr Med* 2013; **19**: 223-227 [PMID: 22370870 DOI: 10.1007/s11655-011-0951-4]

188 **Zhao L**, Gan AP. Clinical and psychological assessment on xinwei decoction for treating functional dyspepsia accompanied with depression and anxiety. *Am J Chin Med* 2005; **33**: 249-257 [PMID: 15974484 DOI: 10.1142/S0192415X05002801]

189 **Ge Y**, Cui JC, Zhou RL. [Clinical and experimental study on separately decocted and mingly decocted jianweishu granule]. *Zhongguo Zhongxiyi Jiehe Zazhi* 2002; **22**: 420-422 [PMID: 12585184]

190 **el-Omar EM**, Banerjee S, Wirz A, McColl KE. The Glasgow Dyspepsia Severity Score--a tool for the global measurement of dyspepsia. *Eur J Gastroenterol Hepatol* 1996; **8**: 967-971 [PMID: 8930560 DOI: 10.1097/00042737-199610000-00006]

191 **Qin F**, Huang X, Ren P. Chinese herbal medicine modified xiaoyao san for functional dyspepsia: meta-analysis of randomized controlled trials. *J Gastroenterol Hepatol* 2009; **24**: 1320-1325 [PMID: 19702899 DOI: 10.1111/j.1440-1746.2009.05934.x]

192 **Liu JP**, Yang M, Liu Y, Wei ML, Grimsgaard S. Herbal medicines for treatment of irritable bowel syndrome. *Cochrane Database of Systematic Reviews* 2006; **1**: CD004116

193 **Bensoussan A**. Establishing evidence for Chinese medicine: a case example of irritable bowel syndrome. *Zhonghua Yixue Zazhi* (Taipei) 2001; **64**: 487-492 [PMID: 11768276]

194 **Bensoussan A**, Talley NJ, Hing M, Menzies R, Guo A, Ngu M. Treatment of irritable bowel syndrome with Chinese herbal medicine: a randomized controlled trial. *JAMA* 1998; **280**: 1585-1589 [PMID: 9820260 DOI: 10.1001/jama.280.18.1585]

195 **Pan F**, Zhang T, Zhang YH, Xu JJ, Chen FM. Effect of Tongxie Yaofang Granule in treating diarrhea-predominate irritable bowel syndrome. *Chin J Integr Med* 2009; **15**: 216-219 [PMID: 19568715 DOI: 10.1007/s11655-009-0216-7]

196 **Leung WK**, Wu JC, Liang SM, Chan LS, Chan FK, Xie H, Fung SS, Hui AJ, Wong VW, Che CT, Sung JJ. Treatment of diarrhea-predominant irritable bowel syndrome with traditional Chinese herbal medicine: a randomized placebo-controlled trial. *Am J Gastroenterol* 2006; **101**: 1574-1580 [PMID: 16863563 DOI: 10.1111/j.1572-0241.2006.00576.x]

197 **Zhang SS**, Wang HB, Li ZH. [A multi-center randomized controlled trial on treatment of diarrhea-predominant irritable bowel syndrome by Chinese medicine syndrome-differentiation therapy]. *Zhongguo Zhongxiyi Jiehe Zazhi* 2010; **30**: 9-12 [PMID: 20353023]

198 **Wu B**, Zhang SS. [Effect of TCM therapy for invigorating Pi, soothing Gan, eliminating dampness and resolving blood stasis on the short-term quality of life in patients with diarrhea type irritable bowel syndrome]. *Zhongguo Zhongxiyi Jiehe Zazhi* 2008; **28**: 894-896 [PMID: 19123325]

199 **Sperber AD**, Gwee KA, Hungin AP, Corazziari E, Fukudo S, Gerson C, Ghoshal UC, Kang JY, Levy RL, Schmulson M, Dumitrascu D, Gerson MJ, Chen M, Myung SJ, Quigley EM, Whorwell PJ, Zarzar K, Whitehead WE. Conducting multinational, cross-cultural research in the functional gastrointestinal disorders: issues and recommendations. A Rome Foundation working team report. *Aliment Pharmacol Ther* 2014; **40**: 1094-1102 [PMID: 25175998 DOI: 10.1111/apt.12942]

200 **Su X**, Tang Y, Zhang J, Dong Y, Wei W, Bai Y, Liu Y. Curative effect of warming kidney and fortifying spleen recipe on diarrhea-predominant irritable bowel syndrome. *J Tradit Chin Med* 2013; **33**: 615-619 [PMID: 24660584 DOI: 10.1016/S0254-6272(14)60030-3]

201 **Lv YH**, Wang YP. [Observe effect of treating C-IBS by Tongyouqing]. *Zhongguo Zhongyao Zazhi* 2008; **33**: 691-693, 717 [PMID: 18590203]

202 **Bian ZX**, Cheng CW, Zhu LZ. Chinese herbal medicine for functional constipation: a randomised controlled trial. *Hong Kong Med J* 2013; **19** Suppl 9: 44-46 [PMID: 24473591]

203 **Cheng CW**, Bian ZX, Zhu LX, Wu JC, Sung JJ. Efficacy of a Chinese herbal proprietary medicine (Hemp Seed Pill) for functional constipation. *Am J Gastroenterol* 2011; **106**: 120-129 [PMID: 21045817 DOI: 10.1038/ajg.2010.305]

204 **Jia G**, Meng MB, Huang ZW, Qing X, Lei W, Yang XN, Liu SS, Diao JC, Hu SY, Lin BH, Zhang RM. Treatment of functional constipation with the Yun-chang capsule: a double-blind, randomized, placebo-controlled, dose-escalation trial. *J Gastroenterol Hepatol* 2010; **25**: 487-493 [PMID: 20370727 DOI: 10.1111/j.1440-1746.2009.06189x]

205 **Gao WY**, Lin YF, Chen SQ, Lu YP, Yang Z, Gong Y, Liu Y, Wang LX, Wang CH. [Effects of Changjishu soft elastic capsule in treatment of diarrhea-predominant irritable bowel patients with liver-qi stagnation and spleen deficiency syndrome: a randomized double-blinded controlled trial]. *Zhongxiyi Jiehe Xuebao* 2009; **7**: 212-217 [PMID: 19284948 DOI: 10.3736/jcim20090303]

206 **Zhang RM**, Wang L, Yang XN, Xia Q, Jiang MD, Fan ZJ, Zhang FX, Zhang HR, Yu Z, Li TQ. [Dinggui Oil Capsule in treating irritable bowel syndrome with stagnation of qi and cold: a prospective, multi-center, randomized, placebo-controlled, double-blind trial]. *Zhongxiyi Jiehe Xuebao* 2007; **5**: 392-397 [PMID: 17631801 DOI: 10.3736/jcim20070406]

207 **Gao WY**, Wang CH, Lin YF. [Effect of jianpi tiaogan wenshen recipe in treating diarrhea-predominant irritable bowel syndrome]. *Zhongguo Zhongxiyi Jiehe Zazhi* 2010; **30**: 13-17 [PMID: 20353024]

208 **Shen Y**, Cai G, Sun X. [Randomized controlled clinical study on effect of Chinese compound changjitai in treating diarrheic irritable bowel syndrome]. *Zhongguo Zhongxiyi Jiehe Zazhi* 2003; **23**: 823-825 [PMID: 14666762]

209 **Wang G**, Li TQ, Wang L, Xia Q, Chang J, Zhang Y, Wan MH, Guo J, Cheng Y, Huang X, Zhang RM. Tong-xie-ning, a Chinese herbal formula, in treatment of diarrhea-predominant irritable bowel syndrome: a prospective, randomized, double-blind, placebo-controlled trial. *Chin Med J* (Engl) 2006; **119**: 2114-2119 [PMID: 17199964]

210 **Huang CH**, Su YC, Li TC, Lee SC, Lin JS, Chiu TY, Lue HC. Treatment of constipation in long-term care with Chinese herbal formula: a randomized, double-blind placebo-controlled trial. *J Altern Complement Med* 2011; **17**: 639-646 [PMID: 21711205 DOI: 10.1089/acm.2010.0150]

211 **Brinkhaus B**. [Traditional Chinese phytotherapy for irritable bowel syndrome]. *Forsch Komplementarmed* 1999; **6**: 157-158 [PMID: 10490340]

212 **Zhang CX**. [Clinical observation on treatment of functional constipation with compound plantain-senna granules]. *Zhongguo Zhongxiyi Jiehe Zazhi* 2009; **29**: 1119-1122 [PMID: 20214337]

213 **Li CX**. [Effect of tongbian navel paste on colonic motility in children with constipation of slow transmission type]. *Zhongguo Zhongxiyi Jiehe Zazhi* 2009; **29**: 158-160 [PMID: 19382480]

214 **Wang BX**, Wang MG, Jiang MZ, Xu CD, Shao CH, Jia LY, Huang ZH, Xu XH. [Forlax in the treatment of childhood constipation:

a randomized, controlled, multicenter clinical study]. *Zhongguo Dangdai Erke Zazhi* 2007; **9**: 429-432 [PMID: 17937851]

215 **Jin ZH**, Duan JH, Zhao HC. [Clinical study on colonic transmission time and the effect of sini powder on it in functional constipation patients]. *Zhongguo Zhongxiyi Jiehe Zazhi* 2006; **26**: 896-898 [PMID: 17121040]

216 **Yu SP**, Ye H, Ha NL, Ding SQ, Chen G. Effect of modified Sinisan on anorectal manometry of the constipation predominant type of irritable bowel syndrome. *Chin J Integr Med* 2005; **11**: 27-30 [PMID: 15975303 DOI: 10.1007/BF02835744]

P- Reviewer: Chowdhury P **S- Editor**: Ma YJ **L- Editor**: Wang TQ
E- Editor: Liu XM

Published by **Baishideng Publishing Group Inc**
8226 Regency Drive, Pleasanton, CA 94588, USA
Telephone: +1-925-223-8242
Fax: +1-925-223-8243
E-mail: bpgoffice@wjgnet.com
Help Desk: http://www.wjgnet.com/esps/helpdesk.aspx
http://www.wjgnet.com

ISSN 1007-9327
15>