

Review Article

Tianma Gouteng Yin as Adjunctive Treatment for Essential Hypertension: A Systematic Review of Randomized Controlled Trials

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Received 11 December 2012; Revised 28 March 2013; Accepted 31 March 2013

Academic Editor: Aiping Lu

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Background. Tianma Gouteng Yin (TGY) is widely used for essential hypertension (EH) as adjunctive treatment. Many randomized clinical trials (RCTs) of TGY for EH have been published. However, it has not been evaluated to justify their clinical use and recommendation based on TCM zheng classification. **Objectives.** To assess the current clinical evidence of TGY as adjunctive treatment for EH with liver yang hyperactivity syndrome (LYHS) and liver-kidney yin deficiency syndrome (LKYDS). **Search Strategy.** 7 electronic databases were searched until November 20, 2012. **Inclusion Criteria.** RCTs testing TGY combined with antihypertensive drugs versus antihypertensive drugs were included. **Data Extraction and Analyses.** Study selection, data extraction, quality assessment, and data analyses were conducted according to the Cochrane standards. **Results.** 22 RCTs were included. Methodological quality was generally low. Except diuretics treatment group, blood pressure was improved in the other 5 subgroups; zheng was improved in angiotensin converting enzyme inhibitors (ACEIs), calcium channel blockers (CCBs), and “CCB + ACEI” treatment groups. The safety of TGY is still uncertain. **Conclusions.** No confirmed conclusion about the effectiveness and safety of TGY as adjunctive treatment for EH with LYHS and LKYDS could be made. More rigorous trials are needed to confirm the results.

1. Introduction

Cardiovascular disease (CVD) is the leading cause of death worldwide [1, 2]. High blood pressure (BP) is the major independent risk factors for CVD [3–5]. Therefore, hypertension and blood-pressure-related disease have become an emerging epidemic and important worldwide public-health challenge [6–12]. Oral antihypertensive drugs are a milestone in the therapy of hypertension and other CVDs. However, the control rates of hypertension are still far from optimal currently [13, 14]. What is more, although treated with intensive medication, uncontrolled hypertension related symptoms (including headache, dizziness, and fatigue) and the side effects of antihypertensive drug therapy (including headache, flushing, dry cough, edema, and sexual dysfunction) are still

the major problems confronting modern medicine [15–18]. Effective treatment of hypertension is limited by availability, cost, and adverse effects of conventional western medicine treatment. Thus, a certain proportion of the population has turned to complementary and alternative medicine (CAM), including traditional Chinese medicine (TCM) [19–23], for lowering BP and improving its related symptoms worldwide [24, 25].

Within Asia, TCM is widely used about 3,000 years ago [26–28]. It has formed a unique theoretical system and control methods [29–31]. TCM zheng (also called as syndrome or zheng differentiation or pattern classification) is the basic unit and the key concept in TCM theory [32–35]. Currently combination of zheng classification and biomedical diagnosis has become a hot topic both in diagnostics and treatment for

the basic and clinical research [36–39]. Recently, increasing number of clinical trials and systematic reviews (SRs) showed that, as compared to antihypertensive therapy alone, Chinese herbal formula combined with antihypertensive drugs (also known as combination therapy) appear to be more effective in improving BP and symptoms in hypertensive patients with certain syndrome [40–43]. There is no doubt that, with more and more rigorous research evidences of effectiveness and safety about combination therapy, clinical studies linking TCM zheng classification and biomedicine diagnosis will lead to personalized therapeutic strategies and innovation in medical sciences [44, 45].

According to TCM theory, liver yang hyperactivity syndrome (LYHS) and liver-kidney yin deficiency syndrome (LKYDS) are the most important and common TCM zheng of essential hypertension (EH) [46]. LYHS is characterized by vertigo, tinnitus, headache, flushing, red eyes, irritability, insomnia, lassitude in lion and legs, bitter mouth, red tongue, and wiry pulse. LKYDS is always characterized by dizziness, tinnitus, headache, low fever, flushing, burning sensation of five centres, hypochondriac pain, hypopsia, lassitude in lion and legs, red tongue with scanty coating, and wiry-rapid pulse. It is worth noting that LYHS is usually caused by LKYDS. And these syndromes often appear together in EH. Molecular mechanism of LYHS and LKYDS in EH may be related to the hyperexpression of tyrosine hydroxylase (TH), and fifteen compounds of the structure and metabolic pathways mainly including amino acids, free fatty acids, and sphingosine by high performance liquid chromatography coupled with time of flight mass spectrometry (HPLC-TOFMS) [47–49]. Our previous studies showed that LYHS and LKYDS are the most important pathogenesis of EH in TCM, which could be well treated by Tianma Gouteng Yin (TGY) [46]. TGY, containing eleven commonly used herbs (*Gastrodia elata*, *Uncaria*, abalone shell, *Eucommia ulmoides* Oliv, achyranthes root, *Loranthus parasiticus*, *Gardenia*, *Scutellaria baicalensis* Georgi, *Leonurus japonicus*, *Poria cocos*, and caulis polygoni multiflori), is a classical Chinese herbal formula noted in *Za Bing Zheng Zhi Xin Yi (New Meanings in Syndrome and Therapy of Miscellaneous Diseases)*. It has been widely used to treat hypertension-related symptoms and signs in clinical practice for decades [46]. The most common symptoms include headache, dizziness, insomnia, and lassitude in lion and legs, red tongue with scanty coating, and wiry-rapid pulse, which belong to LYHS and LKYDS in TCM [46]. The mechanism of the formula may be suppressing liver yang hyperactivity and nourishing the liver and kidney. Recently, modern researches showed that TGY could not only improve hypertension-related symptoms and signs, but also lower BP in vitro and in vivo [50–60]. Biochemically, TGY appears to have good effect in inhibiting vascular smooth muscle cell proliferation and promoting apoptosis by decreasing TGF- β 1 and Bcl-2, improving vascular remodeling, inhibiting left ventricular hypertrophy and myocardial fibrosis, regulating rennin-angiotensin system (RAS) and Ca²⁺ overload in vascular smooth muscle cells, improving SOD, nitric oxide and insulin resistance, and decreasing endothelin, MDA, and IGF-1, so as to lower the arterial pressure [50–60].

Currently, a number of clinical trials have been published in Chinese language by TGY used alone or combined with antihypertensive drugs for EH. However, there is no critically appraised evidence such as SRs or meta-analyses to assess clinical efficacy and safety of TGY combined with antihypertensive drugs as an adjunct therapy for hypertensive patients based on TCM zheng classification. The PAPER aims to evaluate the beneficial and harmful effects of TGY for EH in randomized trials. To our knowledge, this is the first zheng classification-based systematic English review on TGY for EH.

2. Methods

2.1. Database and Search Strategies. Literature searches were conducted in the Cochrane Library (July, 2012), PubMed, EMBASE, Chinese National Knowledge Infrastructure (CNKI), Chinese Scientific Journal Database (VIP), Chinese Biomedical Literature Database (CBM), and Wanfang data. The reference list of retrieved papers was also searched. Since TGY was mainly used and researched in China, four main databases in Chinese were searched to retrieve the maximum possible number of trials of TGY combined with antihypertensive drugs for EH. All of those searches ended on November 20, 2012. Ongoing registered clinical trials were searched in the website of Chinese clinical trial registry (<http://www.chictr.org/en/>) and international clinical trial registry by US national institutes of health (<http://clinicaltrials.gov/>). The following search terms were used individually or combined: “Tianma Gouteng yin,” “Tianma Gouteng decoction,” “Tianma Gouteng tang,” “hypertension,” “essential hypertension,” “clinical trial,” and “randomized controlled trial.” The bibliographies of included studies were searched for additional references.

2.2. Inclusion Criteria. All the parallel randomized controlled trials (RCTs) of all the prescriptions based on “Tianma Gouteng yin” combined with antihypertensive drugs compared to antihypertensive drugs for EH with LYHS and LKYDS were included. According to the principle of the similarity of TCM formula [42, 61], the number of modified herbs should not be more than 5, so that to ensure the similarity is greater than or equal to 0.5. And the key herbs in the modified Tianma Gouteng yin should include *Gastrodia elata*, *Uncaria*, and abalone shell, according to the theory of TCM. There were no restrictions on population characteristics, language and publication type. Duplicated publications reporting the same groups of participants were excluded.

2.3. Data Extraction and Quality Assessment. Two authors conducted the literature searching (X. J. Xiong, W. Liu), study selection (X. J. Xiong, B. Feng), and data extraction (X. J. Xiong, X. C. Yang) independently. The extracted data included authors, title of study, year of publication, study size, age and sex of the participants, details of methodological information, name and component of Chinese herbs, treatment process, details of the control interventions, outcomes,

and adverse effects for each study. Disagreement was resolved by discussion and reached consensus through a third party (J. Wang).

Criteria from the Cochrane Handbook for Systematic Review of Interventions, Version 5.1.0 were used to assess the methodological quality of trials (X. J. Xiong, Y. Zhang) [62]. The items included random sequence generation (selection bias), allocation concealment (selection bias), blinding of participants and personnel (performance bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias), selective reporting (reporting bias), and other bias. The quality of all the included trials was categorized to low/unclear/high risk of bias (“Yes” for a low of bias, “No” for a high risk of bias, “Unclear” otherwise). Then trials were categorized into three levels: low risk of bias (all the items were in low risk of bias), high risk of bias (at least one item was in high risk of bias), unclear risk of bias (at least one item was in unclear risk of bias).

2.4. Data Synthesis. Revman 5.1 software provided by the Cochrane Collaboration was used for data analyses. Dichotomous data were presented as risk ratio (RR) and continuous outcomes as mean difference (MD), both with 95% confidence interval (CI). Heterogeneity was recognized significant when $I^2 \geq 50\%$. Fixed effects model was used if there is no significant heterogeneity of the data; random effects model was used if significant heterogeneity existed ($50\% < I^2 < 85\%$). Publication bias would be explored by funnel plot analysis if sufficient studies were found.

3. Result

3.1. Description of Included Trials. A flow chart depicted the search process and study selection (as shown in Figure 1). After primary searches from the seven databases both in Chinese and English, 1243 articles were retrieved: Cochrane Library ($n = 1$), Pubmed ($n = 6$), EMBASE ($n = 19$), CNKI ($n = 499$), VIP ($n = 247$), CBM ($n = 270$), and Wanfang data ($n = 201$). 505 articles were screened after 746 duplicates were removed. After reading the titles and abstracts, 317 articles of them were excluded. Full texts of 188 articles were retrieved, and 166 articles were excluded with reasons listed as the following: participants did not meet the inclusive criteria ($n = 129$), duplication ($n = 6$), no control group ($n = 2$), the intervention included other Chinese herbal formula ($n = 27$), and no data for extraction ($n = 2$). In the end, 22 RCTs [63–84] were included. All the RCTs were conducted in China and published in Chinese. The characteristics of included trials were listed in Table 1.

1808 patients with EH were included. There was a wide variation in the age of subjects (30–74 years). Twenty-two included clinical trials specified four diagnostic criteria of hypertension, eighteen trials [63–67, 69–74, 76–78, 80, 81, 83, 84] used 1999 WHO-ISH guidelines for the management of hypertension (1999 WHO-ISH GMH), two trials [75, 79] used Chinese Guidelines for the Management of Hypertension-2005 (CGMH-2005), one trial [82] used

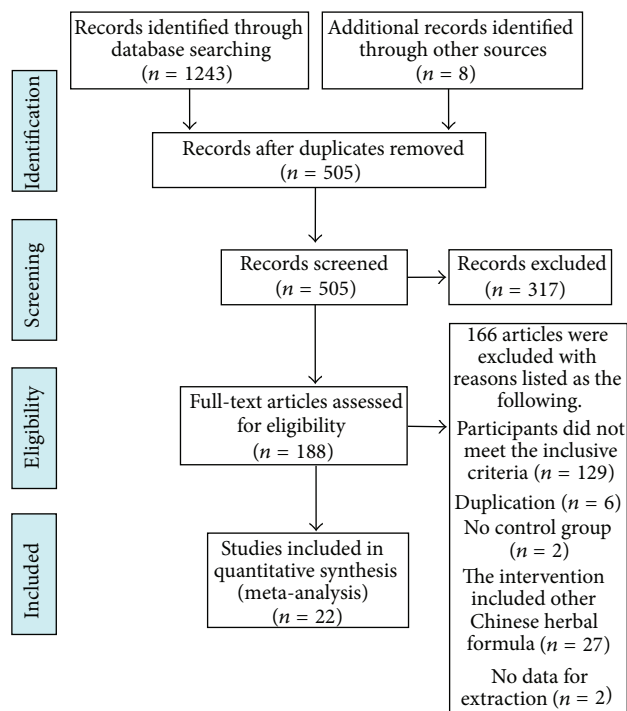


FIGURE 1: PRISMA 2009 flow diagram.

Chinese Guidelines for the Management of Hypertension-1999 (CGMH-1999), and one trial [68] only demonstrated patients with EH without detailed information. Twenty-two (22) trials specified three diagnostic criteria of LYHS and LKYDS in TCM, seventeen trials [64, 66–70, 72–75, 78–84] used Guidelines of Clinical Research of New Drugs of Traditional Chinese Medicine (GCRNDTCM), two trials [71, 76] used Chinese internal medicine (CIM), and three trials [63, 65, 77] only demonstrated patients with LYHS and LKYDS without detailed information about TCM diagnostic criteria.

Interventions included all the prescriptions based on “Tianma Gouteng yin” combined with antihypertensive drugs. The controls included antihypertensive drugs alone. The total treatment duration ranged from 2 to 12 weeks. The variable prescriptions are presented in Table 1. The compositions of Chinese herbal formula Tianma Gouteng yin are presented in Table 2. All of the 22 trials used the BP, including systolic blood pressure (SBP) and diastolic blood pressure (DBP), as the outcome measure. 9 trials [63, 69, 71–75, 78, 81] used TCM zheng to evaluate treatment effects as the other outcome measure.

3.2. Methodological Quality of Included Trials. The majority of the included clinical trials were assessed to be of general poor methodological quality according to the predefined quality assessment criteria. The randomized allocation of participants was mentioned in all trials; however, only seven trials have described the specific methods for sequence generation including random number table [64, 75, 80, 84] and drawing [74, 81]. One trial [67] only reported

TABLE 1: Characteristics and methodological quality of included studies.

Study ID	Sample	Diagnosis standard	Intervention	Control	Course (week)	Outcome measure
Wang et al., 1998 [63]	98	1999 WHO-ISH GMH; TCM diagnostic criteria (unclear)	modified TGY (1 dose/d) + control	captopril (25 mg tid)	4	BP; TCM zheng
Ren and Zhao, 2012 [64]	60	1999 WHO-ISH GMH; GCRNDTCM	modified TGY (300 mL/d) + control	nifedipine sustained release tablets (10 mg bid)	6	BP
Fu, 2005 [65]	116	1999 WHO-ISH GMH; TCM diagnostic criteria (unclear)	modified TGY (250 mL/d) + control	enalapril (10 mg bid)	2	BP
Qin, 2010 [66]	45	1999 WHO-ISH GMH; GCRNDTCM	TGY (1 dose/d) + control	antihypertensive drugs (no detailed information)	4	BP
Hu et al., 2009 [67]	39	1999 WHO-ISH GMH; GCRNDTCM	TGY (1 dose/d) + captopril	captopril (12.5–25 mg bid) + TGY placebo	4	BP
Sun and Huang, 2007 [68]	60	hypertension diagnostic criteria (unclear); GCRNDTCM	TGY (1 dose/d) + control	hydrochlorothiazide (12.5 mg bid)	4	BP
Wang et al., 2008 [69]	80	1999 WHO-ISH GMH; GCRNDTCM	TGY (1 dose/d) + control	captopril (25 mg tid)	4	BP; TCM zheng
Fang et al., 2008 [70]	60	1999 WHO-ISH GMH; GCRNDTCM	TGY (1 dose/d) + control	captopril (25 mg tid)	4	BP
Li, 2006 [71]	80	1999 WHO-ISH GMH; CIM	modified TGY (1 dose/d) + control	captopril (12.5 mg bid)	4	BP; TCM zheng
Liu, 2011 [72]	86	1999 WHO-ISH GMH; GCRNDTCM	modified TGY (1 dose/d) + control	amlodipine besylate (5 mg qd)	8	BP; TCM zheng
Liu et al., 2009 [73]	60	1999 WHO-ISH GMH; GCRNDTCM	TGY (1 dose/d) + control	perindopril (25 mg tid)	4	BP; TCM zheng
Chen, 2009 [74]	100	1999 WHO-ISH GMH; GCRNDTCM	TGY (1 dose/d) + control	captopril (25 mg tid)	6	BP; TCM zheng
Zhang and Yang, 2011 [75]	60	CGMH-2005; GCRNDTCM	modified TGY (1 dose/d) + control	amlodipine besylate (5 mg qd) + lisinopril (10 mg qd)	4	BP; TCM zheng
Liu and Li, 2011 [76]	100	1999 WHO-ISH GMH; CIM	TGY (1 dose/d) + control	nifedipine sustained release tablets (10 mg bid)	4	BP; TCM zheng
Wei, 2012 [77]	98	1999 WHO-ISH GMH; TCM diagnostic criteria (unclear)	TGY (1 dose/d) + control	nifedipine (10 mg bid)	4	BP
Li, 2011 [78]	120	1999 WHO-ISH GMH; GCRNDTCM	TGY (1 dose/d) + control	levamlodipine (5 mg qd)	4	BP
Lin and Liu, 2010 [79]	94	CGMH-2005; GCRNDTCM	TGY (1 dose/d) + control	telmisartan (20 mg qd)	4	BP
Zhou and Zhang, 2011 [80]	72	1999 WHO-ISH GMH; GCRNDTCM	modified TGY (1 dose/d) + control	captopril (25 mg bid)	4	BP
Chen, 2008 [81]	100	1999 WHO-ISH GMH; GCRNDTCM	TGY (1 dose/d) + control	captopril (25 mg tid)	6	BP; TCM zheng
Du, 2012 [82]	100	CGMH-1999; GCRNDTCM	modified TGY (1 dose/d) + control	captopril (25 mg tid)	4	BP
Cheng, 2010 [83]	100	1999 WHO-ISH GMH; GCRNDTCM	modified TGY (1 dose/d) + control	enalapril (10 mg qd)	12	BP
Zhu, 2009 [84]	80	1999 WHO-ISH GMH; GCRNDTCM	TGY (1 dose/d) + control	captopril (25 mg tid)	4	BP

TABLE 2: Composition of formula.

Study ID	Formula	Composition of formula
Wang et al., 1998 [63]	modified TGY	<i>Salvia miltiorrhiza</i> 30 g, red peony root 20 g, <i>Gastrodia elata</i> 12 g, <i>Uncaria</i> 30 g, abalone shell 30 g, <i>Eucommia ulmoides</i> Oliv 15 g, achyranthes root 30 g, <i>Loranthus parasiticus</i> 15 g, <i>Gardenia</i> 12 g, <i>Scutellaria baicalensis</i> Georgi 12 g, <i>Leonurus japonicus</i> 20 g, <i>Poria cocos</i> 15 g, caulis polygoni multiflori 30 g
Ren and Zhao, 2012 [64]	modified TGY	<i>Gastrodia elata</i> 9 g, <i>Uncaria</i> 12 g, abalone shell 18 g, <i>Eucommia ulmoides</i> Oliv 9 g, achyranthes root 12 g, <i>Loranthus parasiticus</i> 9 g, <i>Gardenia</i> 9 g, <i>Scutellaria baicalensis</i> Georgi 9 g, <i>Leonurus japonicus</i> 9 g, <i>scu9</i> g, caulis polygoni multiflori 9 g
Fu, 2005 [65]	modified TGY	<i>Gastrodia elata</i> 18 g, <i>Uncaria</i> 12 g, abalone shell 18 g, <i>Eucommia ulmoides</i> Oliv 9 g, achyranthes root 15 g, <i>Loranthus parasiticus</i> 9 g, <i>Gardenia</i> 9 g, <i>Scutellaria baicalensis</i> Georgi 12 g, <i>Leonurus japonicus</i> 9 g, <i>Poria cocos</i> 9 g, caulis polygoni multiflori 9 g, <i>Prunella vulgaris</i> 12 g
Qin, 2010 [66]	TGY	<i>Gastrodia elata</i> , <i>Uncaria</i> , abalone shell, <i>Eucommia ulmoides</i> Oliv, achyranthes root, <i>Loranthus parasiticus</i> , <i>Gardenia</i> , <i>Scutellaria baicalensis</i> Georgi, <i>Leonurus japonicus</i> , <i>Poria cocos</i> , caulis polygoni multiflori
Hu et al., 2009 [67]	TGY	<i>Gastrodia elata</i> 9 g, <i>Uncaria</i> 12 g, abalone shell 18 g, <i>Eucommia ulmoides</i> Oliv 9 g, achyranthes root 12 g, <i>Loranthus parasiticus</i> 9 g, <i>Gardenia</i> 9 g, <i>Scutellaria baicalensis</i> Georgi 9 g, <i>Leonurus japonicus</i> 9 g, <i>Poria cocos</i> 9 g, caulis polygoni multiflori 9 g
Sun and Huang, 2007 [68]	TGY	<i>Gastrodia elata</i> 9 g, <i>Uncaria</i> 12 g, abalone shell 18 g, <i>Eucommia ulmoides</i> Oliv 9 g, achyranthes root 12 g, <i>Loranthus parasiticus</i> 9 g, <i>Gardenia</i> 9 g, <i>Scutellaria baicalensis</i> Georgi 9 g, <i>Leonurus japonicus</i> 9 g, <i>Poria cocos</i> 9 g, caulis polygoni multiflori 9 g
Wang et al., 2008 [69]	TGY	<i>Gastrodia elata</i> 15 g, <i>Uncaria</i> 30 g, abalone shell 21 g, <i>Eucommia ulmoides</i> Oliv 12 g, achyranthes root 15 g, <i>Loranthus parasiticus</i> 12 g, <i>Gardenia</i> 12 g, <i>Scutellaria baicalensis</i> Georgi 12 g, <i>Leonurus japonicus</i> 12 g, <i>Poria cocos</i> 12 g, caulis polygoni multiflori 12 g
Fang et al., 2008 [70]	TGY	<i>Gastrodia elata</i> 9 g, <i>Uncaria</i> 12 g, abalone shell 18 g, <i>Eucommia ulmoides</i> Oliv 9 g, achyranthes root 12 g, <i>Loranthus parasiticus</i> 9 g, <i>Gardenia</i> 9 g, <i>Scutellaria baicalensis</i> Georgi 9 g, <i>Leonurus japonicus</i> 9 g, <i>Poria cocos</i> 9 g, caulis polygoni multiflori 9 g
Li, 2006 [71]	modified TGY	<i>Gastrodia elata</i> 10 g, <i>Uncaria</i> 12 g, abalone shell 30 g, achyranthes root 15 g, <i>Loranthus parasiticus</i> 15 g, <i>Scutellaria baicalensis</i> Georgi 10 g, <i>Leonurus japonicus</i> 20 g, caulis polygoni multiflori 25 g, white peony root 15 g, <i>Chrysanthemum</i> 12 g
Liu, 2011 [72]	modified TGY	<i>Gastrodia elata</i> 10 g, <i>Uncaria</i> 15 g, abalone shell 20 g, <i>Eucommia ulmoides</i> Oliv 10 g, achyranthes root 15 g, <i>Loranthus parasiticus</i> 15 g, <i>Gardenia</i> 10 g, <i>Scutellaria baicalensis</i> Georgi 10 g, <i>Poria cocos</i> 30 g, caulis polygoni multiflori 15 g, <i>Apocynum</i> 10 g
Liu et al., 2009 [73]	TGY	<i>Gastrodia elata</i> 9 g, <i>Uncaria</i> 12 g, abalone shell 18 g, <i>Eucommia ulmoides</i> Oliv 9 g, achyranthes root 12 g, <i>Loranthus parasiticus</i> 9 g, <i>Gardenia</i> 9 g, <i>Scutellaria baicalensis</i> Georgi 9 g, <i>Leonurus japonicus</i> 9 g, <i>Poria cocos</i> 9 g, caulis polygoni multiflori 9 g
Chen, 2009 [74]	TGY	<i>Gastrodia elata</i> 12 g, <i>Uncaria</i> 9 g, abalone shell 30 g, <i>Eucommia ulmoides</i> Oliv 12 g, achyranthes root 15 g, <i>Loranthus parasiticus</i> 15 g, <i>Gardenia</i> 9 g, <i>Leonurus japonicus</i> 15 g, <i>Poria cocos</i> 15 g, caulis polygoni multiflori 20 g
Zhang and Yang, 2011 [75]	modified TGY	<i>Gastrodia elata</i> 10 g, <i>Uncaria</i> 30 g, abalone shell 30 g, <i>Eucommia ulmoides</i> Oliv 10 g, achyranthes root 15 g, <i>Loranthus parasiticus</i> 15 g, <i>Poria cocos</i> 15 g, caulis polygoni multiflori 15 g, <i>Salvia miltiorrhiza</i> 30 g, <i>Prunella vulgaris</i> 15 g, keel 30 g, oyster 30 g, pearl shell 30 g, <i>Albizia julibrissin</i> 15 g, <i>Glycyrrhiza</i> 6 g
Liu and Li, 2011 [76]	TGY	<i>Gastrodia elata</i> 15 g, <i>Uncaria</i> 30 g, abalone shell 30 g, <i>Eucommia ulmoides</i> Oliv 15 g, achyranthes root 15 g, <i>Loranthus parasiticus</i> 30 g, <i>Scutellaria baicalensis</i> Georgi 15 g, <i>Leonurus japonicus</i> 15 g, <i>Poria cocos</i> 20 g, caulis polygoni multiflori 15 g
Wei, 2012 [77]	TGY	<i>Gastrodia elata</i> 10 g, <i>Uncaria</i> 15 g, abalone shell 20 g, <i>Eucommia ulmoides</i> Oliv 10 g, achyranthes root 15 g, <i>Loranthus parasiticus</i> 15 g, <i>Gardenia</i> 10 g, <i>Scutellaria baicalensis</i> Georgi 10 g, <i>Leonurus japonicus</i> 15 g, <i>Poria cocos</i> 15 g, caulis polygoni multiflori 10 g
Li, 2011 [78]	TGY	<i>Gastrodia elata</i> 10 g, <i>Uncaria</i> 15 g, abalone shell 20 g, <i>Eucommia ulmoides</i> Oliv 10 g, achyranthes root 15 g, <i>Loranthus parasiticus</i> 15 g, <i>Gardenia</i> 10 g, <i>Scutellaria baicalensis</i> Georgi 10 g, <i>Leonurus japonicus</i> 15 g, <i>Poria cocos</i> 15 g, caulis polygoni multiflori 10 g
Lin and Liu, 2010 [79]	TGY	<i>Gastrodia elata</i> 9 g, <i>Uncaria</i> 12 g, abalone shell 30 g, <i>Eucommia ulmoides</i> Oliv 10 g, achyranthes root 12 g, <i>Loranthus parasiticus</i> 12 g, <i>Gardenia</i> 6 g, <i>Scutellaria baicalensis</i> Georgi 9 g, <i>Leonurus japonicus</i> 9 g, <i>Poria cocos</i> 12 g, caulis polygoni multiflori 12 g
Zhou and Zhang, 2011 [80]	modified TGY	<i>Gastrodia elata</i> 12 g, <i>Uncaria</i> 10 g, abalone shell 10 g, <i>Eucommia ulmoides</i> Oliv 10 g, achyranthes root 10 g, <i>Loranthus parasiticus</i> 10 g, <i>Gardenia</i> 9 g, <i>Scutellaria baicalensis</i> Georgi 9 g, <i>Leonurus japonicus</i> 15 g, <i>Poria cocos</i> 10 g, caulis polygoni multiflori 10 g, <i>Gentiana scabra</i> bge 15 g

TABLE 2: Continued.

Study ID	Formula	Composition of formula
Chen, 2008 [81]	TGY	<i>Gastrodia elata</i> 12 g, <i>Uncaria</i> 9 g, abalone shell 30 g, <i>Eucommia ulmoides</i> Oliv 12 g, achyranthes root 15 g, <i>Loranthus parasiticus</i> 15 g, <i>Gardenia</i> 9 g, <i>Leonurus japonicus</i> 15 g, <i>Poria cocos</i> 15 g, caulis polygoni multiflori 20 g
Du, 2012 [82]	modified TGY	<i>Gastrodia elata</i> 15 g, <i>Uncaria</i> 20 g, abalone shell 15 g, <i>Eucommia ulmoides</i> Oliv 10 g, achyranthes root 10 g, <i>Loranthus parasiticus</i> 10 g, <i>Gardenia</i> 6 g, <i>Scutellaria baicalensis</i> Georgi 8 g, <i>Leonurus japonicus</i> 10 g, <i>Poria cocos</i> 10 g, caulis polygoni multiflori 30 g; constipation plus rhubarb 5 g and aloe vera 10 g; liver-kidney yin deficiency plus glossy privet 10 g, wolfberry fruit 15 g, <i>Rehmanniae radix</i> 15 g, root of herbaceous peony 10 g; gan yang hua feng syndrome and dizziness plus antelope horn 3 g, pearl shell 15 g, keel 30 g and oyster 30 g; severe headache, flushed face and congested eyes and coating on the tongue yellow dry plus <i>Gentiana scabra</i> bge 15 g, <i>Chrysanthemum</i> 10 g, cortex moutan radialis 10 g
Cheng, 2010 [83]	modified TGY	<i>Gastrodia elata</i> 12 g, <i>Uncaria</i> 12 g, abalone shell 18 g, <i>Eucommia ulmoides</i> Oliv 12 g, achyranthes root 12 g, <i>Loranthus parasiticus</i> 12 g, <i>Gardenia</i> 12 g, <i>Scutellaria baicalensis</i> Georgi 12 g, <i>Leonurus japonicus</i> 12 g, <i>Poria cocos</i> 12 g, caulis polygoni multiflori 9 g, hawthorn 30 g, giant knotweed 10 g
Zhu, 2009 [84]	TGY	<i>Gastrodia elata</i> 9 g, <i>Uncaria</i> 12 g, <i>Eucommia ulmoides</i> Oliv 9 g, achyranthes root 12 g, <i>Loranthus parasiticus</i> 9 g, <i>Gardenia</i> 9 g, <i>Scutellaria baicalensis</i> Georgi 9 g, <i>Leonurus japonicus</i> 9 g, <i>Poria cocos</i> 9 g, caulis polygoni multiflori 9 g

simple random sampling without concrete information. The remaining fifteen studies [63, 65, 66, 68–73, 76–79, 82, 83] did not mention the random sequence generation. There is also no sufficient information provided to judge whether it was conducted properly or not. Allocation concealment was not reported in all the trials. Only one trial [67] used the blinding of participants and personnel; however, no trial reported blinding of outcome assessment. Three trials [67–69] reported drop-out or withdraw. A pretrial estimation of sample size and followup had not been reported in all of included trials. We have tried to contact with authors by telephone, email, and other ways for further information about the trials; however, no information could be provided until now. The results of the assessment of risk of bias are presented in Table 3.

3.3. Effect of the Interventions. All the included trials [63–84] compared TGY combined with antihypertensive drugs with antihypertensive drugs alone. A change in BP was reported in all the trials. According to the different control drugs, it could be divided into six subgroups.

3.3.1. TGY Plus ACEI versus ACEI. 13 trials compared TGY plus angiotensin converting enzyme inhibitors (ACEIs) versus ACEI (including captopril, enalapril, and perindopril) [63, 65, 67, 69–71, 73, 74, 80–84].

Blood Pressure (BP). 8 trial [65, 71, 73, 74, 80–83] used three classes to evaluate treatment effects on BP: significant effective (DBP decreased by 10 mmHg reaching the normal range, or DBP has not yet returned to normal, but has been reduced ≥ 20 mmHg), effective (DBP decreased to less than 10 mmHg reaching the normal range, or DBP decreased by 10–19 mmHg, but did not reach the normal range, or SBP decreased ≥ 30 mmHg), and ineffective (Not to meet the above standards). The trial showed significant difference between treatment and control group (RR: 3.16 [1.94, 5.14]; $P < 0.00001$) (Table 4).

When it comes to SBP, 5 independent trials [63, 67, 69, 70, 84] showed significant heterogeneity in the results, chi-square = 20.01, ($P = 0.0005$); $I^2 = 80\%$. Thus, random-effects model was used for statistical analysis. The meta-analysis showed that there are significant beneficial effect on the combination group compare to captopril group (WMD: -6.71 [$-6.94, -6.49$]; $P < 0.00001$) (Table 5).

When it comes to DBP, 5 independent trials [63, 67, 69, 70, 84] showed significant heterogeneity in the results, chi-square = 14.66, ($P = 0.005$); $I^2 = 73\%$. Thus, random-effects model was used for statistical analysis. The meta-analysis showed there are significant beneficial effects on the combination group compared to captopril group (WMD: -4.60 [$-5.11, -4.09$]; $P < 0.00001$) (Table 6).

TCM Zheng. 6 trials [63, 69, 71, 73, 74, 81] used three classes to measure TCM zheng (just LYHS and LKYDS): significant effective (The main symptoms such as headache, dizziness, palpitations, insomnia, tinnitus, and irritability disappear, or TCM zheng scores reduced rate $\geq 70\%$), effective (The main

symptoms relieved, or, 70% > TCM zheng scores reduced rate $\geq 30\%$), and ineffective (The main symptoms do not change, or TCM zheng scores reduced rate $< 30\%$). Meta-analysis showed significant difference in favor of the combination group compared to ACEI group (RR: 6.15 [3.38, 11.18]; $P < 0.00001$) (Table 7).

3.3.2. TGY Plus CCB versus CCB. 5 trials compared TGY plus calcium channel blockers (CCB) versus CCB (including nifedipine sustained release tablets, amlodipine besylate, nifedipine, and levamlodipine) [64, 72, 76–78].

Blood Pressure (BP). 2 trials [77, 78] used three classes to evaluate treatment effects on BP. The trials showed significant difference between treatment and control group (RR: 8.97 [2.59, 31.04]; $P = 0.0005$) (Table 4).

When it comes to SBP, 3 independent trials [64, 72, 76] showed significant heterogeneity in the results, chi-square = 10.10, ($P = 0.006$); $I^2 = 80\%$. Thus, random-effects model was used for statistical analysis. The meta-analysis showed there are significant beneficial effects on the combination group compared to captopril group (WMD: -12.03 [$-13.52, -10.54$]; $P < 0.00001$) (Table 5).

When it comes to DBP, 3 independent trials [64, 72, 76] showed significant heterogeneity in the results, chi-square = 12.39, ($P = 0.002$); $I^2 = 84\%$. Thus, random-effects model was used for statistical analysis. The meta-analysis showed there are significant beneficial effects on the combination group compared to captopril group (WMD: -7.98 [$-8.85, -7.12$]; $P < 0.00001$) (Table 6).

TCM Zheng. 2 trials [72, 78] used three classes to evaluate treatment effects on TCM zheng. The trials showed significant difference between treatment and control group (RR: 5.56 [2.50, 12.37]; $P < 0.0001$) (Table 7).

3.3.3. TGY Plus Diuretics versus Diuretics. 1 trial compared TGY plus diuretics versus diuretics (including hydrochlorothiazide) [68]. When it comes to SBP, it [68] showed no applicable heterogeneity in the result. Thus, fixed-effects model was used for statistical analysis. The meta-analysis showed there is no significant beneficial effect on the combination group compared to hydrochlorothiazide group (WMD: 0.28 [$-0.72, 1.28$]; $P = 0.58$) (Table 5).

When it comes to DBP, it [68] showed no applicable heterogeneity in the result. Thus, fixed-effects model was used for statistical analysis. The meta-analysis showed there is no significant beneficial effect on the combination group compared to hydrochlorothiazide group (WMD: 0.44 [$-0.52, 1.40$]; $P = 0.37$) (Table 6).

3.3.4. TGY Plus ARB versus ARB. 1 trial compared TGY plus angiotensin II receptor blockers (ARB) versus ARB (including telmisartan) [79]. When it comes to SBP, it showed no applicable heterogeneity in the result. Thus, fixed-effects model was used for statistical analysis. The meta-analysis showed there is significant beneficial effect on the combination group compared to telmisartan group (WMD: -3.70 [$-3.78, -3.62$]; $P < 0.00001$) (Table 5).

TABLE 3: Quality assessment of included randomized controlled trials.

Included trials	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other sources of bias	Risk of bias
Wang et al., 1998 [63]	Unclear	Unclear	Unclear	Unclear	Yes	No	Unclear	High
Ren and Zhao, 2012 [64]	Table of random number	Unclear	Unclear	Unclear	Yes	No	Unclear	Unclear
Fu, 2005 [65]	Unclear	Unclear	Unclear	Unclear	Yes	No	Unclear	High
Qin, 2010 [66]	Unclear	Unclear	Unclear	Unclear	Yes	No	Unclear	High
Hu et al., 2009 [67]	Simple random sampling	Unclear	Yes	Unclear	No	No	Unclear	Unclear
Sun and Huang, 2007 [68]	Unclear	Unclear	Unclear	Unclear	No	No	Unclear	High
Wang et al., 2008 [69]	Unclear	Unclear	Unclear	Unclear	Yes	No	Unclear	High
Fang et al., 2008 [70]	Unclear	Unclear	Unclear	Unclear	No	No	Unclear	High
Li, 2006 [71]	Unclear	Unclear	Unclear	Unclear	Yes	No	Unclear	High
Liu, 2011 [72]	Unclear	Unclear	Unclear	Unclear	Yes	No	Unclear	High
Liu et al., 2009[73]	Unclear	Unclear	Unclear	Unclear	Yes	No	Unclear	High
Chen, 2009 [74]	Drawing	Unclear	Unclear	Unclear	No	No	Unclear	Unclear
Zhang and Yang, 2011 [75]	Table of random number	Unclear	Unclear	Unclear	Yes	No	Unclear	Unclear
Liu and Li, 2011 [76]	Unclear	Unclear	Unclear	Unclear	No	No	Unclear	High
Wei, 2012 [77]	Unclear	Unclear	Unclear	Unclear	Yes	No	Unclear	High
Li, 2011 [78]	Unclear	Unclear	Unclear	Unclear	Yes	No	Unclear	High
Lin and Liu, 2010 [79]	Unclear	Unclear	Unclear	Unclear	Yes	No	Unclear	High
Zhou and Zhang, 2011 [80]	Table of random number	Unclear	Unclear	Unclear	No	No	Unclear	Unclear
Chen, 2008 [81]	Drawing	Unclear	Unclear	Unclear	No	No	Unclear	Unclear
Du, 2012 [82]	Unclear	Unclear	Unclear	Unclear	Yes	No	Unclear	High
Cheng, 2010 [83]	Unclear	Unclear	Unclear	Unclear	Yes	No	Unclear	High
Zhu, 2009 [84]	Table of random number	Unclear	Unclear	Unclear	No	No	Unclear	Unclear

TABLE 4: Analyses of blood pressure.

Trials	Intervention (n/N)	Control (n/N)	RR [95% CI]	P Value
TGY plus ACEI versus ACEI				
modified TGY plus enalapril versus enalapril	56/60	44/56	3.82 [1.15, 12.66]	0.03
modified TGY plus captopril versus captopril	44/48	21/32	5.76 [1.64, 20.25]	0.006
TGY plus perindopril versus perindopril	29/30	26/30	4.46 [0.47, 42.51]	0.19
TGY plus captopril versus captopril	45/50	44/50	1.23 [0.35, 4.32]	0.75
modified TGY plus captopril versus captopril	34/36	30/36	3.40 [0.64, 18.13]	0.15
TGY plus captopril versus captopril	45/50	44/50	1.23 [0.35, 4.32]	0.75
modified TGY plus captopril versus captopril	48/50	42/50	4.57 [0.92, 22.73]	0.06
modified TGY plus enalapril versus enalapril	48/50	39/50	6.77 [1.42, 32.37]	0.02
Meta-Analysis	349/374	290/354	3.16 [1.94, 5.14]	<0.00001
TGY plus CCB versus CCB				
TGY plus nifedipine versus nifedipine	48/49	40/49	10.80 [1.31, 88.92]	0.03
TGY plus levamlodipine versus levamlodipine	58/60	47/60	8.02 [1.72, 37.33]	0.008
Meta-Analysis	106/109	87/109	8.97 [2.59, 31.04]	0.0005
TGY plus antihypertensive drugs versus antihypertensive drugs				
TGY plus antihypertensive drugs versus antihypertensive drugs	20/22	17/23	3.53 [0.63, 19.83]	0.01
Meta-Analysis	20/22	17/23	3.53 [0.63, 19.83]	0.01

TABLE 5: Analyses of systolic blood pressure.

Trial	MD [95% CI]	P Value	
TGY plus ACEI versus ACEI			
modified TGY plus captopril versus captopril	1	-9.70 [-11.80, -7.60]	<0.00001
TGY plus captopril versus captopril	1	-6.20 [-7.03, -5.37]	<0.00001
TGY plus captopril versus captopril	1	-8.76 [-10.02, -7.50]	<0.00001
TGY plus captopril versus captopril	1	-5.30 [-9.88, -0.72]	0.02
TGY plus captopril versus captopril	1	-6.65 [-6.89, -6.41]	<0.00001
Meta-Analysis	5	-6.71 [-6.94, -6.49]	<0.00001
TGY plus CCB versus CCB			
modified TGY plus nifedipine sustained release tablets versus nifedipine sustained release tablets	1	-13.00 [-14.48, -11.52]	<0.00001
modified TGY plus amlodipine besylate versus amlodipine besylate	1	-12.60 [-13.69, -11.51]	<0.00001
TGY plus nifedipine sustained release tablets versus nifedipine sustained release tablets	1	-10.68 [-11.62, -9.74]	<0.00001
Meta-Analysis	3	-12.25 [-13.52, -10.54]	<0.00001
TGY plus diuretics versus diuretics			
modified TGY plus hydrochlorothiazide versus hydrochlorothiazide	1	0.28 [-0.72, 1.28]	0.58
Meta-Analysis	1	0.28 [-0.72, 1.28]	0.58
TGY plus ARB versus ARB			
TGY plus telmisartan versus telmisartan	1	-3.70 [-3.78, -3.62]	<0.00001
Meta-Analysis	1	-3.70 [-3.78, -3.62]	<0.00001
TGY plus "CCB + ACEI" versus "CCB + ACEI"			
modified TGY plus amlodipine besylate and lisinopril versus amlodipine besylate and lisinopril	1	-11.03 [-12.72, -9.34]	<0.00001
Meta-Analysis	1	-11.03 [-12.72, -9.34]	<0.00001

TABLE 6: Analyses of diastolic blood pressure.

Trials	MD [95% CI]	P Value	
TGY plus ACEI versus ACEI			
modified TGY plus captopril versus captopril	1	-6.10 [-9.06, -3.14]	<0.0001
TGY plus captopril versus captopril	1	-5.00 [-5.89, -4.11]	<0.00001
TGY plus captopril versus captopril	1	-3.69 [-4.44, -2.94]	<0.00001
TGY plus captopril versus captopril	1	-3.30 [-7.12, 0.52]	0.09
TGY plus captopril versus captopril	1	-6.28 [-7.55, -5.01]	<0.00001
Meta-Analysis	5	-4.60 [-5.11, -4.09]	<0.00001
TGY plus CCB versus CCB			
modified TGY plus nifedipine sustained release tablets versus nifedipine sustained release tablets	1	-10.00 [-12.53, -7.47]	<0.00001
modified TGY plus amlodipine besylate versus amlodipine besylate	1	-8.20 [-8.58, -7.82]	<0.00001
TGY plus nifedipine sustained release tablets versus nifedipine sustained release tablets	1	-7.34 [-7.73, -6.95]	<0.00001
Meta-Analysis	3	-7.98 [-8.85, -7.12]	<0.00001
TGY plus diuretics versus diuretics			
modified TGY plus hydrochlorothiazide versus hydrochlorothiazide	1	0.44 [-0.52, 1.40]	0.37
Meta-Analysis	1	0.44 [-0.52, 1.40]	0.37
TGY plus ARB versus ARB			
TGY plus telmisartan versus telmisartan	1	-0.80 [-1.57, -0.03]	0.04
Meta-Analysis	1	-0.80 [-1.57, -0.03]	0.04
TGY plus "CCB + ACEI" versus "CCB + ACEI"			
modified TGY plus amlodipine besylate and lisinopril versus amlodipine besylate and lisinopril	1	-6.87 [-7.60, -6.14]	<0.00001
Meta-Analysis	1	-6.87 [-7.60, -6.14]	<0.00001

TABLE 7: Analyses of TCM zheng.

Trials	Intervention (n/N)	Control (n/N)	RR [95% CI]	P Value
TGY plus ACEI versus ACEI				
modified TGY plus captopril versus captopril	1 48/50	36/48	8.00 [1.68, 38.00]	0.009
TGY plus captopril versus captopril	1 38/40	28/40	8.14 [1.69, 39.22]	0.009
modified TGY plus captopril versus captopril	1 44/48	21/32	5.76 [1.64, 20.25]	0.006
TGY plus perindopril versus perindopril	1 29/30	23/30	8.83 [1.01, 76.96]	0.05
TGY plus captopril versus captopril	1 47/50	38/50	4.95 [1.30, 18.81]	0.02
TGY plus captopril versus captopril	1 47/50	39/50	4.42 [1.15, 16.97]	0.03
Meta-Analysis	6 253/268	185/250	6.15 [3.38, 11.18]	<0.00001
TGY plus CCB versus CCB				
modified TGY plus amlodipine besylate versus amlodipine besylate	1 42/46	26/40	5.65 [1.68, 19.04]	0.005
TGY plus levamlodipine versus levamlodipine	1 55/60	40/60	5.50 [1.90, 15.89]	0.002
Meta-Analysis	2 97/106	66/100	5.56 [2.50, 12.37]	<0.00001
TGY plus "CCB + ACEI" versus "CCB + ACEI"				
modified TGY plus amlodipine besylate and lisinopril versus amlodipine besylate and lisinopril	1 29/30	22/30	10.55 [1.23, 90.66]	0.03
Meta-Analysis	1 29/30	22/30	10.55 [1.23, 90.66]	0.03

When it comes to DBP, it showed no applicable heterogeneity in the result. Thus, fixed-effects model was used for statistical analysis. The meta-analysis showed there is significant beneficial effect on the combination group compared to telmisartan group (WMD: -0.80 [$-1.57, -0.03$]; $P = 0.04$) (Table 6).

3.3.5. TGY Plus “CCB + ACEI” versus “CCB + ACEI”. 1 trial [75] compared TGY plus “CCB + ACEI” versus “CCB + ACEI” (including amlodipine besylate and lisinopril).

Blood Pressure (BP). When it comes to SBP, it showed no applicable heterogeneity in the result. Thus, fixed-effects model was used for statistical analysis. Meta-analysis showed there is significant beneficial effect on the combination group compared to “amlodipine besylate and lisinopril” group (WMD: -11.03 [$-12.72, -9.34$]; $P < 0.00001$) (Table 5).

When it comes to DBP, it showed no applicable heterogeneity in the result. Thus, fixed-effects model was used for statistical analysis. Meta-analysis showed there is significant beneficial effect on the combination group compared to “amlodipine besylate and lisinopril” group (WMD: -6.87 [$-7.60, -6.14$]; $P < 0.00001$) (Table 6).

TCM Zheng. 1 trial [75] used three classes to evaluate treatment effects on TCM zheng. It showed significant difference between treatment and control group (RR: 10.55 [$1.23, 90.66$]; $P = 0.03$) (Table 7).

3.3.6. TGY Plus Antihypertensive Drugs versus Antihypertensive Drugs. 1 trial [66] compared TGY plus antihypertensive drugs versus antihypertensive drugs with no detailed information. It used three classes to evaluate treatment effects on BP. The trial showed significant difference between combination group and antihypertensive drugs group (RR: 3.53 [$0.63, 19.83$]; $P = 0.01$) (Table 4).

3.4. Publication Bias. The number of trials was too small to conduct any sufficient additional analysis of publication bias.

3.5. Adverse Effect. Eight out of twenty-two trials mentioned the adverse effect [67, 68, 70, 74, 76, 80, 81, 84]. Eight trials reported five specific symptoms including cough, vomiting, flushing, rash, and edema. Among them, no adverse events were found in one trial [80]. Two trials reported cough and vomiting in combination group and antihypertensive drugs group, respectively [67, 68]. Three trials reported cough in both TGY plus captopril group and captopril group [70, 74, 81]. One trial mentioned flushing in both TGY plus nifedipine sustained release tablets group and nifedipine sustained release tablets group [76]. One trial mentioned cough, rash, and edema in TGY plus captopril group, and cough and rash in captopril group [84].

4. Discussion

Due to the potential side effects of antihypertensive drugs, natural herbal products have been favored by people all over the world. Chinese herbal formula has made great

contributions to the health and well-being of the people for their unique advantages in preventing and curing diseases, rehabilitation and health care. Currently, with increasing popularity of TCM [85, 86], more and more systematic reviews (SRs) and meta-analysis have been conducted to assess the efficiency of TCM for EH [87–93]. It is demonstrated that Chinese herbal medicine could not only contribute to low BP smoothly, recover the circadian rhythm of BP, but also improve symptoms and TCM zheng especially [94]. The health-enhancing qualities of TGY, a classical Chinese formula, have been dispensed and used in China for many years. As an adjunctive treatment to antihypertensive drugs, TGY is a popular classical TCM formula for EH. And until now, more and more researches about TGY have been conducted in China including 2 SRs [95, 96]. Among them, one is published in English in Cochrane library [95], and the other is in Chinese [96]. However, due to different search strategies and databases both in English and Chinese, no trial was got in this Cochrane Database of Systematic Reviews, and thus no conclusions can be made about the role of TGY in the treatment of EH [95]. Another one compared TGY plus enalapril with enalapril with positive conclusion [96]. However, as a famous adjunctive treatment in EH, the role of TGY is still unclear. This study aims to assess the current clinical evidence of TGY for EH with LYHS and LKYDS based on TCM zheng classification.

This systematic review included 22 randomized trials and a total of 1808 participants. As compared to ACEI, positive results in SBP (WMD: -6.71 [$-6.94, -6.49$]; $P < 0.00001$), DBP (WMD: -4.60 [$-5.11, -4.09$]; $P < 0.00001$), BP (RR: 3.16 [$1.94, 5.14$]; $P < 0.00001$), and TCM zheng (RR: 6.15 [$3.38, 11.18$]; $P < 0.00001$) were found about TGY plus ACEI, indicating that SBP and DBP could be decreased by 6.71 mmHg and 4.60 mmHg, respectively, and TCM zheng (just LYHS and LKYDS) could be improved after the combination therapy. As compared to CCB, positive results in SBP (WMD: -12.25 [$-13.52, -10.54$]; $P < 0.00001$), DBP (WMD: -7.98 [$-8.85, -7.12$]; $P < 0.00001$), BP (RR: 8.97 [$2.59, 31.04$]; $P = 0.0005$), and TCM zheng (RR: 5.56 [$2.50, 12.37$]; $P < 0.0001$) were found about TGY plus CCB, indicating that SBP and DBP could be decreased by 12.25 mmHg and 7.98 mmHg, respectively, and TCM zheng could be improved after the combination therapy. As compared to diuretics, there is no difference between TGY plus diuretics and diuretics in SBP (WMD: 0.28 [$-0.72, 1.28$]; $P = 0.58$) and DBP (WMD: 0.44 [$-0.52, 1.40$]; $P = 0.37$), indicating that no more beneficial effect was found in the combination therapy. As compared to ARB, positive results in SBP (WMD: -3.70 [$-3.78, -3.62$]; $P < 0.00001$) and DBP (WMD: -0.80 [$-1.57, -0.03$]; $P = 0.04$) were found about TGY plus ARB, indicating that SBP and DBP could be decreased by 3.70 mmHg and 0.80 mmHg, respectively, after the combination therapy. As compared to “CCB + ACEI,” positive results in SBP (WMD: -11.03 [$-12.72, -9.34$]; $P < 0.00001$), DBP (WMD: -6.87 [$-7.60, -6.14$]; $P < 0.00001$), and TCM zheng (RR: 10.55 [$1.23, 90.66$]; $P = 0.03$) were found about TGY plus “CCB + ACEI,” indicating that SBP and DBP could be decreased by 11.03 mmHg and 6.87 mmHg, respectively, and TCM zheng could be improved

after the combination therapy. As compared to antihypertensive drugs, positive results in BP (RR: 3.53 [0.63, 19.83]; $P = 0.01$) was found about TGY plus antihypertensive drugs, indicating that BP could be improved after the combination therapy. In conclusion, except diuretics treatment group, BP was improved in the other 5 subgroups; TCM zheng was improved in ACEI, CCB, and “CCB + ACEI” treatment groups. However, although the meta-analysis showed positive results, no confirmed conclusion about the effectiveness and safety of TGY as adjunctive treatment for EH could be made according to current evidence due to the small sample size, poor methodological qualities, and significant heterogeneity of included trials.

The following limitations of this review should be considered. Firstly, according to the predefined evaluation criteria, the quality of methodology is generally low in most of the included trials. There is insufficient reporting of generation methods of the allocation sequence and allocation concealment, which might lead to potential selection bias. Although it is claimed that patients were randomly assigned into two groups, we are still unable to judge if it is conducted really. Most of clinical trials have not implemented double blind in this review, and only one trial used blinding of participants and personnel, which might lead to potential performance bias and detection bias. Therefore, assessment of outcomes was prone to significant systemic errors. Only 1 trial out of the 22 included studies has placebo control. T. J. Kaptchuk once pointed out that, in alternative medicine, the main question regarding placebo has been whether a given therapy has more than a placebo effect [97]. It also regarded that only prospective trials directly comparing the placebo effects of unconventional and mainstream medicine can provide reliable evidence to support such claims [97, 98]. In this review, the result would be positive because of nonspecific placebo effects. In our opinion, the reason why placebo is not implemented may be related to the characteristics of Chinese herbs including appearance, taste, and smell [99]. Drop-out was only reported in 3 trials, and most of the trials havenot reported intention to treat analysis in details. Thus, results generated from these trials should be interpreted with caution. Additionally, most of the trials were small sample size and single-center. None of the trials have reported the sample size estimation, which placed the statistical analysis's validity in doubt.

Secondly, only 8 out of 22 trials mentioned the adverse effects, and most of the trials havenot realized the importance of adverse effects of either Chinese herbal formula or herb-drug interaction. Herb-drug interaction, just botanical and chemical drugs, is an emerging issue of integrative medicine [100–104]. It has raised more and more concern. In this review, almost all the reported adverse events such as cough, vomiting, flushing, rash, and edema in combination group may partially be related to the adverse events of antihypertensive drugs. Thus, a definite conclusion about the safety of TGY combined with antihypertensive drugs still cannot be drawn.

Thirdly, zheng is a unique concept in TCM [105, 106]. It is identified from a comprehensive analysis of clinical information by TCM practitioner from four main diagnostic

TCM methods: observation, listening, questioning, and pulse analyses [107]. In other words, zheng classification is a traditional diagnostic method to categorize patients based on their different conditions. All diagnostic and therapeutic methods in TCM are based on the differentiation of TCM syndrome, and this concept has been used for thousands of years in China [108]. Clinical trials based on TCM zheng classification may lead to more valid conclusions about Chinese herbal formula [109–114]. In our review, TGY combined with antihypertensive drugs appeared to be more effective than antihypertensive drugs alone for LYHS and LKYDS in EH. However, 3 trials did not provide detailed information about TCM diagnostic criteria, and only 9 trials used TCM zheng to evaluate treatment effects as the other outcome measure. Thus, clear diagnostic criteria and objective evaluation of TCM zheng are warranted in further clinical trials.

In conclusion, this is the first zheng classification-based meta-analysis of randomized, controlled trials to assess the efficacy and safety of TGY as adjunctive treatment in patients with EH. However, current clinical evidence of TGY for EH with LYHS and LKYDS was so weak. More rigorous trials with high quality are needed to generate high level of evidence and confirm the results.

Conflict of Interests

All authors declare that they have no conflict of interests.

Authors' Contribution

J. Wang, B. Feng, X. Yang, W. Liu, Y. Liu, Y. Zhang, G. Yu, S. Li, and Y. Zhang contributed equally to this paper.

Acknowledgments

The current work was partially supported by the National Basic Research Program of China (973 Program, no. 2003CB517103) and the National Natural Science Foundation Project of China (no. 90209011). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the paper.

References

- [1] K. Sliwa, S. Stewart, and B. J. Gersh, “Hypertension: a global perspective,” *Circulation*, vol. 123, no. 24, pp. 2892–2896, 2011.
- [2] G. Mancia, G. De Backer, A. Dominiczak et al., “2007 Guidelines for the Management of Arterial Hypertension. The Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC),” *Journal of Hypertension*, vol. 25, no. 6, pp. 1105–1187, 2007.
- [3] Y. Wu, R. Huxley, L. Li et al., “Prevalence, awareness, treatment, and control of hypertension in China data from the China National Nutrition and Health Survey 2002,” *Circulation*, vol. 118, no. 25, pp. 2679–2686, 2008.
- [4] D. Gu, K. Reynolds, X. Wu et al., “Prevalence, awareness, treatment, and control of hypertension in China,” *Hypertension*, vol. 40, no. 6, pp. 920–927, 2002.

- [5] G. Mancia, S. Laurent, E. Agabiti-Rosei et al., "Reappraisal of European guidelines on hypertension management: a European Society of Hypertension Task Force document," *Journal of Hypertension*, vol. 27, no. 11, pp. 2121–2158, 2009.
- [6] M. H. Alderman and T. Ogihara, "Global challenge for overcoming high blood pressure: Fukuoka Statement, 19 October 2006," *Journal of Hypertension*, vol. 25, no. 3, p. 727, 2007.
- [7] M. Ezzati, A. D. Lopez, A. Rodgers, S. Vander Hoorn, and C. J. L. Murray, "Selected major risk factors and global and regional burden of disease," *Lancet*, vol. 360, no. 9343, pp. 1347–1360, 2002.
- [8] P. M. Kearney, M. Whelton, K. Reynolds, P. Muntner, P. K. Whelton, and J. He, "Global burden of hypertension: analysis of worldwide data," *Lancet*, vol. 365, no. 9455, pp. 217–223, 2005.
- [9] S. MacMahon, M. H. Alderman, L. H. Lindholm, L. Liu, R. A. Sanchez, and Y. K. Seedat, "Blood-pressure-related disease is a global health priority," *Lancet*, vol. 371, no. 9623, pp. 1480–1482, 2008.
- [10] D. Yach, C. Hawkes, C. L. Gould, and K. J. Hofman, "The global burden of chronic diseases: overcoming impediments to prevention and control," *Journal of the American Medical Association*, vol. 291, no. 21, pp. 2616–2622, 2004.
- [11] S. Yusuf, S. Reddy, S. Ôunpuu, and S. Anand, "Global burden of cardiovascular diseases," *Circulation*, vol. 104, pp. 2855–2864, 2001.
- [12] C. M. Lawes, S. V. Hoorn, and A. Rodgers, "Global burden of blood-pressure-related disease, 2001," *Lancet*, vol. 371, no. 9623, pp. 1513–1518, 2008.
- [13] P. M. Kearney, M. Whelton, K. Reynolds, P. K. Whelton, and J. He, "Worldwide prevalence of hypertension: a systematic review," *Journal of Hypertension*, vol. 22, no. 1, pp. 11–19, 2004.
- [14] C. Farsang, L. Naditch-Brule, A. Avogaro et al., "Where are we with the management of hypertension? From science to clinical practice," *Journal of Clinical Hypertension*, vol. 11, no. 2, pp. 66–73, 2009.
- [15] A. V. Chobanian, G. L. Bakris, H. R. Black et al., "Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure," *Hypertension*, vol. 42, no. 6, pp. 1206–1252, 2003.
- [16] M. Baumhäkel, N. Schlimmer, and M. Böhm, "Effect of irbesartan on erectile function in patients with hypertension and metabolic syndrome," *International Journal of Impotence Research*, vol. 20, no. 5, pp. 493–500, 2008.
- [17] L. C. Keene and P. H. Davies, "Drug-related erectile dysfunction," *Adverse Drug Reactions and Toxicological Reviews*, vol. 18, no. 1, pp. 5–24, 1999.
- [18] I. N. Mohamed, P. J. Helms, C. R. Simpson, and J. S. McLay, "Using routinely collected prescribing data to determine drug persistence for the purpose of pharmacovigilance," *Journal of Clinical Pharmacology*, vol. 51, no. 2, pp. 279–284, 2011.
- [19] F. Cheung, "TCM: made in China," *Nature*, vol. 480, no. 7378, supplement, pp. S82–S83, 2011.
- [20] H. Xu and K. Chen, "Integrative medicine: the experience from China," *Journal of Alternative and Complementary Medicine*, vol. 14, no. 1, pp. 3–7, 2008.
- [21] J. M. Crow, "The healthy gut feeling," *Nature*, vol. 480, no. 7378, supplement, pp. S88–S89, 2011.
- [22] L. Liu, "The clinical trial barriers," *Nature*, vol. 480, no. 7378, supplement, p. S100, 2011.
- [23] H. Xu and K. J. Chen, "Complementary and alternative medicine: is it possible to be mainstream?" *Chinese Journal of Integrative Medicine*, vol. 18, no. 6, pp. 403–404, 2012.
- [24] R. Nahas, "Complementary and alternative medicine approaches to blood pressure reduction: an evidence-based review," *Canadian Family Physician*, vol. 54, no. 11, pp. 1529–1533, 2008.
- [25] E. Ernst, "Complementary/alternative medicine for hypertension: a mini-review," *Wiener Medizinische Wochenschrift*, vol. 123, pp. 386–391, 2005.
- [26] M. Y. Liu and K. J. Chen, "Convergence: the tradition and the modern," *Chinese Journal of Integrative Medicine*, vol. 18, no. 3, pp. 164–165, 2012.
- [27] K. J. Chen, "Where are we going?" *Chinese Journal of Integrative Medicine*, vol. 16, no. 2, pp. 100–101, 2010.
- [28] H. L. Park, H. S. Lee, B. C. Shin et al., "Traditional medicine in China, Korea, and Japan: a brief introduction and comparison," *Evidence-Based Complementary and Alternative Medicine*, vol. 2012, Article ID 429103, 9 pages, 2012.
- [29] P. Tian, "Where west meets east," *Nature*, vol. 480, no. 7378, supplement, pp. S84–S86, 2011.
- [30] A. P. Lu, H. W. Jia, C. Xiao, and Q. P. Lu, "Theory of traditional Chinese medicine and therapeutic method of diseases," *World Journal of Gastroenterology*, vol. 10, pp. 1854–1856, 2004.
- [31] X. J. Xiong, F. Y. Chu, H. X. Li, and Q. Y. He, "Clinical application of the TCM classic formulae for treating chronic bronchitis," *Journal of Traditional Chinese Medicine*, vol. 31, no. 1, pp. 69–72, 2011.
- [32] M. Jiang, C. Zhang, G. Zheng et al., "Traditional Chinese medicine Zheng in the era of evidence-based medicine: a literature analysis," *Evidence-Based Complementary and Alternative Medicine*, vol. 2012, Article ID 409568, 9 pages, 2012.
- [33] M. Jiang, C. Lu, C. Zhang et al., "Syndrome differentiation in modern research of traditional Chinese medicine," *Journal of Ethnopharmacology*, vol. 140, pp. 634–642, 2012.
- [34] M. Jiang, C. Zhang, H. Cao, K. Chan, and A. Lu, "The role of Chinese medicine in the treatment of chronic diseases in China," *Planta Medica*, vol. 77, no. 9, pp. 873–881, 2011.
- [35] J. Wang, P. Q. Wang, and X. J. Xiong, "Current situation and re-understanding of syndrome and formula syndrome in Chinese medicine," *Internal Medicine*, 2012.
- [36] A. P. Lu, M. Jiang, C. Zhang, and K. Chan, "An integrative approach of linking traditional Chinese medicine pattern classification and biomedicine diagnosis," *Journal of Ethnopharmacology*, vol. 141, no. 2, pp. 549–556, 2012.
- [37] J. Wang and X. J. Xiong, "Current situation and perspectives of clinical study in integrative medicine in China," *Evidence-Based Complementary and Alternative Medicine*, vol. 2012, Article ID 268542, 11 pages, 2012.
- [38] K. J. Chen, "Clinical service of Chinese medicine," *Chinese Journal of Integrative Medicine*, vol. 14, no. 3, pp. 163–164, 2008.
- [39] A. P. Lu and K. J. Chen, "Integrative medicine in clinical practice: from pattern differentiation in traditional Chinese medicine to disease treatment," *Chinese Journal of Integrative Medicine*, vol. 15, no. 2, p. 152, 2009.
- [40] H. Li, L. T. Liu, W. M. Zhao et al., "Effect of traditional and integrative regimens on quality of life and early renal impairment in elderly patients with isolated systolic hypertension," *Chinese Journal of Integrative Medicine*, vol. 16, no. 3, pp. 216–221, 2010.
- [41] G. W. Zhong, M. J. Chen, Y. H. Luo et al., "Effect of Chinese herbal medicine for calming Gan and suppressing hyperactive yang on arterial elasticity function and circadian rhythm of blood pressure in patients with essential hypertension," *Chinese Journal of Integrative Medicine*, vol. 17, no. 6, pp. 414–420, 2011.

- [42] X. J. Xiong, X. C. Yang, W. Liu et al., “Banxia Baizhu Tianma decoction for essential hypertension: a systematic review of randomized controlled trials,” *Evidence-Based Complementary and Alternative Medicine*, vol. 2012, Article ID 271462, 10 pages, 2012.
- [43] J. Wang, K. W. Yao, X. C. Yang et al., “Chinese patent medicine liu wei di huang wan combined with antihypertensive drugs, a new integrative medicine therapy, for the treatment of essential hypertension: a systematic review of randomized controlled trials,” *Evidence-Based Complementary and Alternative Medicine*, vol. 2012, Article ID 714805, 7 pages, 2012.
- [44] A. P. Lu and K. J. Chen, “Chinese medicine pattern diagnosis could lead to innovation in medical sciences,” *Chinese Journal of Integrative Medicine*, vol. 17, no. 11, pp. 811–817, 2011.
- [45] H. Xu and K. J. Chen, “Integrating traditional medicine with biomedicine towards a patient-centered healthcare system,” *Chinese Journal of Integrative Medicine*, vol. 17, no. 2, pp. 83–84, 2011.
- [46] J. Wang and X. J. Xiong, “Control strategy on hypertension in Chinese medicine,” *Evidence-Based Complementary and Alternative Medicine*, vol. 2012, Article ID 284847, 6 pages, 2012.
- [47] H. Q. Jiang, Y. L. Li, and J. Xie, “Urine metabonomic study on hypertension patients of ascendant hyperactivity of gan yang syndrome by high performance liquid chromatography coupled with time of flight mass spectrometry,” *Zhongguo Zhong Xi Yi Jie He Za Zhi*, vol. 32, no. 3, pp. 333–337, 2012.
- [48] Y. Jin, S. Hu, and D. Yan, “Study on molecular mechanism of ganyang shangkang syndrome in hypertension,” *Chinese Journal of Integrated Traditional and Western Medicine*, vol. 20, no. 2, pp. 87–90, 2000.
- [49] C. H. Yang, J. M. Lin, J. Xie, H. Q. Jiang, and Y. L. Li, “Study on the metabolin difference of hypertension patients of gan-yang hyperactivity syndrome and yin-yang deficiency syndrome,” *Zhongguo Zhong Xi Yi Jie He Za Zhi*, vol. 32, no. 9, pp. 1204–1207, 2012.
- [50] W. L. Li, X. Y. Chen, and X. L. Wu, “Effects of Tianma Gouteng decoction on mRNA expression of CaL- α 1C and PM-CA1 in vascular smooth muscle cells of spontaneously hypertensive rat,” *Zhong Cheng Yao*, vol. 31, no. 8, pp. 1175–1179, 2009.
- [51] C. L. Cai, M. Y. Li, Z. H. Xing, W. P. Liu, H. Y. Tan, and C. Zhang, “Effects of Tianma Gouteng decoction on SOD and MDA in hypertensive patients with liver yang hyperactivity syndrome,” *Jia Ting Yi Xue Za Zhi*, vol. 21, no. 3, pp. 321–322, 2005.
- [52] Z. Z. Lin, Z. H. Xing, C. L. Cai, H. Y. Tan, and C. Zhang, “Effects of tianma gouteng decoction on the plasma endothelin of patients with primary hypertension of hyperactivity of the liver yang,” *Chinese Journal of Clinical Rehabilitation*, vol. 8, no. 27, pp. 5992–5993, 2004.
- [53] Z. H. Xing, C. L. Cai, H. Y. Tan, and Z. Z. Lin, “Effect of Tianma Gouteng decoction on the curative efficacy and quality of life in patients with essential hypertension,” *Chinese Journal of Clinical Rehabilitation*, vol. 8, no. 15, pp. 2880–2881, 2004.
- [54] X. N. Mo, Y. B. Yang, S. X. Huang, and J. C. Liu, “Effects of Tianma Gouteng decoction on vascular remodeling in hypertensive rat,” *Zhongguo Shi Yan Fang Ji Xue Za Zhi*, vol. 17, no. 9, pp. 149–152, 2011.
- [55] X. J. Duan, X. Zeng, X. Zhang, and R. M. Ou, “Effects of Tianma Gouteng decoction on Ang II, ALD and liver protein expression in spontaneously hypertensive rats with liver yang hyperactivity syndrome,” *Zhongguo Shi Yan Fang Ji Xue Za Zhi*, vol. 16, no. 16, pp. 160–162, 2010.
- [56] J. H. Sun, “Effect of Tianma Gouteng decoction on myocardial fibrosis in spontaneously hypertensive rats,” *Guangzhou Zhong Yi Yao Da Xue Xue Bao*, vol. 25, no. 5, pp. 438–441, 2008.
- [57] Y. P. Gong, M. W. Ni, X. H. Song, Z. Q. Cheng, and H. P. Gu, “Experimental study of Tianma Gouteng decoction on insulin resistance in spontaneously hypertensive rats with liver yang hyperactivity syndrome,” *Zhejiang Zhong Yi Xue Yuan Xue Bao*, vol. 29, no. 2, pp. 62–64, 2005.
- [58] Q. Y. Yang and H. R. Sun, “Effect and clinical significance of Tianma Gouteng decoction on TGF- β 1 and Bcl-2 in patients with essential hypertension,” *Zhong Yi Yan Jiu*, vol. 19, no. 7, pp. 24–26, 2006.
- [59] Z. Z. Lin and Z. H. Xing, “A clinical observation on the therapeutic effect of Tianma Gouteng decoction on the plasma level of endothelin among patients with hypertension,” *Hunan Zhong Yi Xue Yuan Xue Bao*, vol. 23, no. 1, pp. 13–14, 2003.
- [60] W. P. Liu, Z. H. Xing, and Z. Z. Lin, “Effect of Tianma Gouteng decoction on plasma nitric oxide of the patients with essential hypertension,” *Zhongguo Kang Fu*, vol. 18, no. 5, pp. 291–292, 2003.
- [61] Y. B. Li, M. Cui, Y. Yang et al., “Similarity of traditional Chinese medicine formula,” *Zhong Hua Zhong Yi Yao Xue Kan*, vol. 30, no. 5, pp. 1096–1097, 2012.
- [62] J. P. T. Higgins and S. Green, “Cochrane handbook for systematic reviews of interventions, version 5.1.0 [updated March 2011],” *The Cochrane Collaboration*, 2009, <http://www.cochrane-handbook.org/>.
- [63] S. F. Wang, Q. F. Li, J. G. Wang, and N. Mei, “A clinical observation on the therapeutic effect of Dan Shao Tianma Gouteng decoction combined with captopril on hypertension,” *Heilongjiang Zhong Yi Yao*, no. 4, pp. 10–11, 1998.
- [64] B. W. Ren and X. M. Zhao, “Effect of modified Tianma Gouteng yin on 30 cases of essential hypertension with liver yang hyperactivity syndrome,” *Zhongguo Yao Ye*, vol. 21, no. 16, p. 89, 2012.
- [65] R. Fu, “Effect of modified Tianma Gouteng yin on essential hypertension with liver yang hyperactivity syndrome,” *Liaoning Zhong Yi Xue Yuan Xue Bao*, vol. 7, no. 6, p. 595, 2005.
- [66] F. L. Qin, “The Clinical effects comparision of Tianma Gouteng yin and Tianma Gouteng particle on treating hypertension,” *Zhongguo Dang Dai Yi Yao*, vol. 17, no. 10, pp. 72–73, 2010.
- [67] S. Y. Hu, S. X. Xian, L. C. Zhao, Z. Yu, Y. H. Wu, and Y. H. Qi, “Effect of Tianma Gouteng yin decoction on serum procollagen III and aldosterone and angiotensin II in essential hypertension,” *Zhong Xi Yi Jie He Xin Nao Xue Guan Bing Za Zhi*, vol. 7, no. 5, pp. 512–513, 2009.
- [68] J. H. Sun and X. W. Huang, “Clinical studies of Tianma Gouteng yin decoction combined with hydrochlorothiazide for the treatment of elderly patients with hypertension,” *Zhong Yao Xin Yao Yu Lin Chuang Yao Li*, vol. 18, no. 5, pp. 412–414, 2007.
- [69] Q. Wang, F. Li, and X. M. Fang, “Effect of Tianma Gouteng yin decoction and captopril on blood pressure and inflammatory factor in patients with essential hypertension,” *Zhong Yi Za Zhi*, vol. 49, no. 1, pp. 32–34, 2008.
- [70] X. M. Fang, F. Li, J. S. He, and Q. Wang, “Effect of Tianma Gouteng yin decoction and captopril on 30 cases of hypertensive patients,” *Shanxi Zhong Yi*, vol. 29, no. 3, pp. 308–310, 2008.
- [71] M. X. Li, “A clinical observation on the therapeutic effect of modified Tianma Gouteng yin on 48 cases of essential hypertension with liver yang hyperactivity syndrome,” *Jilin Zhong Yi Yao*, vol. 26, no. 5, pp. 15–16, 2006.

- [72] Y. F. Liu, "Effect of Tianma Gouteng yin decoction combined with amlodipine on hypertension with liver yang hyperactivity syndrome," *Shenzhen Zhong Xi Yi Jie He Za Zhi*, vol. 21, no. 4, pp. 239–241, 2011.
- [73] C. B. Liu, L. J. Wang, H. B. Ren, and X. C. Jiang, "Effect of Tianma Gouteng yin decoction combined with perindopril on 30 cases of hypertension," *Zhong Yi Yao Xue Bao*, vol. 37, no. 1, pp. 55–56, 2009.
- [74] X. J. Chen, "Effect of Tianma Gouteng yin decoction combined with captopril on 50 patients with essential hypertension," *Shanxi Zhong Yi*, vol. 30, no. 6, pp. 681–683, 2009.
- [75] S. Y. Zhang and X. Y. Yang, "A clinical observation on the therapeutic effect of Tianma Gouteng yin decoction combined with western medicine on hypertension with anxiety," *Tianjin Zhong Yi Yao*, vol. 28, no. 3, pp. 191–193, 2011.
- [76] L. Y. Liu and R. Li, "A clinical observation on the therapeutic effect of Tianma Gouteng yin decoction on 100 cases of hypertension with liver yang hyperactivity syndrome," *Ya Tai Chuan Tong Yi Yao*, vol. 7, no. 6, pp. 58–59, 2011.
- [77] Y. L. Wei, "Effect of Tianma Gouteng yin decoction on 49 cases of hypertension with liver yang hyperactivity syndrome," *Shenzhen Zhong Xi Yi Jie He Za Zhi*, vol. 22, no. 5, pp. 310–312, 2012.
- [78] M. F. Li, "A clinical observation on the therapeutic effect of Tianma Gouteng yin decoction on 120 cases of hypertension with liver yang hyperactivity syndrome," *Zhong Yi Yao Dao Bao*, vol. 17, no. 7, pp. 38–39, 2011.
- [79] J. Z. Lin and Y. Y. Liu, "A clinical observation on the therapeutic effect of Tianma Gouteng yin decoction on hypertension of young and middle-aged," *Zhong Xi Yi Jie He Xin Nao Xue Guan Bing Za Zhi*, vol. 8, no. 6, p. 649, 2010.
- [80] Y. L. Zhou and Y. K. Zhang, "Effect of integrative medicine on 36 cases of essential hypertension with liver yang hyperactivity syndrome," *Shanxi Zhong Yi*, vol. 27, no. 2, p. 24, 2011.
- [81] X. J. Chen, "The clinical observation on high blood pressure with combined treatment of traditional Chinese medicine and western medicine: a report of 50 cases," *Shanxi Zhong Yi*, vol. 24, no. 7, pp. 27–28, 2008.
- [82] W. X. Du, "Effect of integrative medicine on 50 cases of essential hypertension," *Hunan Zhong Yi Za Zhi*, vol. 28, no. 4, pp. 30–31, 2012.
- [83] M. Cheng, "A clinical observation on the therapeutic effect of integrative medicine on 50 cases of essential hypertension," *Zhong Yi Yao Dao Bao*, vol. 16, no. 9, pp. 46–47, 2010.
- [84] X. Q. Zhu, "Clinical effects on integrative Chinese and western medicine in treating essential hypertension," *Hunan Zhong Yi Yao Da Xue Xue Bao*, vol. 29, no. 12, pp. 67–69, 2009.
- [85] H. Xu and K. J. Chen, "Making evidence-based decisions in the clinical practice of integrative medicine," *Chinese Journal of Integrative Medicine*, vol. 16, no. 6, pp. 483–485, 2010.
- [86] X. J. Xiong, "Study on the history of formulas corresponding to syndromes," *Journal of Chinese Integrative Medicine*, vol. 8, no. 6, pp. 581–588, 2010.
- [87] J. I. Kim, J. Y. Choi, H. Lee, M. S. Lee, and E. Ernst, "Moxibustion for hypertension: a systematic review," *BMC Cardiovascular Disorders*, vol. 10, article 33, 2010.
- [88] J. Wang, X. C. Yang, B. Feng et al., "Is Yangxue Qingnao Granule combined with antihypertensive drugs, a new integrative medicine therapy, more effective than antihypertensive therapy alone in treating essential hypertension?" *Evidence-Based Complementary and Alternative Medicine*, vol. 2013, Article ID 540613, 8 pages, 2013.
- [89] M. S. Lee, T. Y. Choi, B. C. Shin, J. I. Kim, and S. S. Nam, "Cupping for hypertension: a systematic review," *Clinical and Experimental Hypertension*, vol. 32, no. 7, pp. 423–425, 2010.
- [90] M. S. Lee, M. H. Pittler, R. E. Taylor-Piliae, and E. Ernst, "Tai chi for cardiovascular disease and its risk factors: a systematic review," *Journal of Hypertension*, vol. 25, no. 9, pp. 1974–1975, 2007.
- [91] X. J. Xiong, X. C. Yang, B. Feng et al., "Zhen gan xi feng decoction, a traditional Chinese herbal formula, for the treatment of essential hypertension: a systematic review of randomized controlled trials," *Evidence-Based Complementary and Alternative Medicine*, vol. 2013, Article ID 982380, 9 pages, 2013.
- [92] M. S. Lee, M. H. Pittler, R. Guo, and E. Ernst, "Qigong for hypertension: a systematic review of randomized clinical trials," *Journal of Hypertension*, vol. 25, no. 8, pp. 1525–1532, 2007.
- [93] M. S. Lee, E. N. Lee, J. I. Kim, and E. Ernst, "Tai chi for lowering resting blood pressure in the elderly: a systematic review," *Journal of Evaluation in Clinical Practice*, vol. 16, no. 4, pp. 818–824, 2010.
- [94] X. J. Xiong, X. C. Yang, Y. M. Liu, Y. Zhang, P. Q. Wang, and J. Wang, "Chinese herbal formulas for treating hypertension in traditional Chinese medicine: perspective of modern science," *Hypertension Research*, 2013.
- [95] H. W. Zhang, J. Tong, G. Zhou, H. Jia, and J. Y. Jiang, "Tianma Gouteng Yin Formula for treating primary hypertension," *Cochrane Database of Systematic Reviews*, no. 6, Article ID CD008166, 2012.
- [96] D. X. Dong, S. L. Yao, N. Yu, and B. Yang, "Systematic review and meta-analysis of Tianma Gouteng Yin combined with enalapril for essential hypertension," *Zhongguo Zhong Yi Ji Zheng*, vol. 20, no. 5, pp. 762–764, 2011.
- [97] T. J. Kaptchuk, "The placebo effect in alternative medicine: can the performance of a healing ritual have clinical significance?" *Annals of Internal Medicine*, vol. 136, no. 11, pp. 817–825, 2002.
- [98] H. Brody and F. G. Miller, "Lessons from recent research about the placebo effect: from art to science," *Journal of the American Medical Association*, vol. 306, no. 23, pp. 2612–2613, 2011.
- [99] W. Chen, C. E. Danforn Lin, H. J. Kang, and J. P. Liu, "Chinese herbal medicines for the treatment of Type A H1N1 Influenza: a systematic review of randomized controlled trials," *Plos ONE*, vol. 6, no. 12, Article ID e28093.
- [100] J. Wang and X. J. Xiong, "Outcome measures of Chinese herbal medicine for hypertension: an overview of systematic reviews," *Evidence-Based Complementary and Alternative Medicine*, vol. 2012, Article ID 697237, 7 pages, 2012.
- [101] X. J. Xiong and J. Wang, "Discussion of related problems in herbal prescription science based on objective indications of herbs," *Journal of Chinese Integrative Medicine*, vol. 8, no. 1, pp. 20–24, 2010.
- [102] H. Xu and K. J. Chen, "Herb-drug interaction: an emerging issue of integrative medicine," *Chinese Journal of Integrative Medicine*, vol. 16, no. 3, pp. 195–196, 2010.
- [103] X. J. Xiong, J. Wang, and Q. Y. He, "Application status and safety countermeasures of traditional Chinese medicine injections," *Journal of Chinese Integrative Medicine*, vol. 8, no. 4, pp. 307–311, 2010.
- [104] X. Xiong, J. Wang, and Q. He, "Thinking about reducing adverse reactions based on idea of formula corresponding to syndromes," *Zhongguo Zhongyao Zazhi*, vol. 35, no. 4, pp. 536–538, 2010.

- [105] A. P. Lu, Z. X. Bian, and K. J. Chen, "Bridging the traditional Chinese medicine pattern classification and biomedical disease diagnosis with systems biology," *Chinese Journal of Integrative Medicine*, vol. 18, no. 12, pp. 883–890, 2012.
- [106] A. Ferreira, "Integrative medicine for hypertension: the earlier the better for treating who and what are not yet ill," *Hypertension Research*, 2013.
- [107] M. Jiang, J. Yang, C. Zhang et al., "Clinical studies with traditional Chinese medicine in the past decade and future research and development," *Planta Medica*, vol. 76, no. 17, pp. 2048–2064, 2010.
- [108] A. P. Lu, X. R. Ding, and K. J. Chen, "Current situation and progress in integrative medicine in China," *Chinese Journal of Integrative Medicine*, vol. 14, no. 3, pp. 234–240, 2008.
- [109] C. Lu, C. Xiao, G. Chen et al., "Cold and heat pattern of rheumatoid arthritis in traditional Chinese medicine: distinct molecular signatures indentified by microarray expression profiles in CD4-positive T cell," *Rheumatology International*, vol. 32, pp. 61–68, 2012.
- [110] X. J. Xiong and J. Wang, "Explaining syndromes of decoction for removing blood stasis in chest," *Zhongguo Zhong Yao Za Zhi*, vol. 36, no. 21, pp. 3026–3031, 2011.
- [111] M. Jiang, C. Xiao, G. Chen et al., "Correlation between cold and hot pattern in traditional Chinese medicine and gene expression profiles in rheumatoid arthritis," *Frontiers of Medicine*, vol. 5, no. 2, pp. 219–228, 2011.
- [112] X. Xiong and J. Wang, "Thought and method of treating dyslipidemia," *Zhongguo Zhongyao Zazhi*, vol. 35, no. 10, pp. 1349–1351, 2010.
- [113] X. J. Xiong and J. Wang, "Experience of diagnosis and treatment of exogenous high-grade fever," *Journal of Chinese Integrative Medicine*, vol. 9, no. 6, pp. 681–687, 2011.
- [114] B. C. Shin, S. Kim, and Y. H. Cho, "Syndrome pattern and its application in parallel randomized controlled trials," *Chinese Journal of Integrative Medicine*, vol. 19, no. 3, pp. 163–171, 2013.