The Clinical Efficacy of Phytochemical Medicines Containing Tanshinol and Ligustrazine in the Treatment of Stable Angina: A Systematic Review and Meta-Analysis

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Background. Phytochemical medicines containing tanshinol and ligustrazine are commonly used in the treatment of stable angina in China, but their clinical effectiveness and risk have not been adequately assessed. In this paper, we conducted a systematic review and meta-analysis to evaluate the clinical efficacy. Methods. Relevant randomized controlled trials (RCTs) of phytochemical medicines containing tanshinol and ligustrazine in the treatment of stable angina were searched in electronic databases. The search date was up to March 31, 2020, and the languages of the RCTs were limited to English and Chinese. Results. A total of 28 studies, including 2518 patients, were included in the meta-analysis. It was shown that the adjunctive therapy of phytochemical medicines containing tanshinol and ligustrazine was better than the conventional therapies in the improvement of stable angina according to the clinical efficacy in symptoms (n = 2518, RR = 1.24, 95% CI: 1.20 to 1.29, P < 0.01) and clinical efficacy in electrocardiography (n = 1766, RR = 1.29, 95% CI: 1.19 to 1.40, P < 0.01).

Conclusion. The meta-analysis supported the use of phytochemical medicines containing tanshinol and ligustrazine in the treatment of stable angina. However, quality of the evidence for this finding was low due to a high risk of bias in the included studies. Therefore, well-designed RCTs are still needed to further evaluate the efficacy.

1. Introduction

Stable angina is caused by fixed blockages in coronary arteries [1]. It typically occurs during activities, and the main symptoms are chest tightness and shortness of breath, which can be alleviated after a rest or administration of sublingual nitroglycerin [2–4]. Stable angina is a chronic coronary disease compared with unstable angina; however, it seriously affects patients’ lives, such as restricting daily activities [5]. Then, the treatment aims to reduce morbidity and improve symptoms.

Currently, the main treatment of stable angina is medicine, such as nitroglycerin, beta-blockers, or calcium channel blockers, which focus on decreasing heart’s workload and prevent episodes [6–9]. In China, phytochemical medicines are also used by many physicians. For example, Shao et al. [10] conducted a meta-analysis to assess the efficacy of danshen injection (main component: salvianic aid A) in the treatment of angina pectoris and concluded that it is more effective than antiangiual agents alone. Yu et al. [11] and Wang et al. [12] conducted randomized controlled trials in the treatment of stable angina, respectively, and found that xinxuekang capsule (main component: steroidal saponins) had a better efficacy compared with danshen tablets. In addition, for the treatment of unstable angina, many researchers have supported different phytochemical medicines, such as puerarin injection [13], safflower yellow injection [14], and danshen chuanxionggin injection [15].

In these phytochemical medicines, tanshinol and ligustrazine are the commonly used components. Tanshinol is also named salvianic aid A, with a molecular formula C9H10O5 [16]. Ligustrazine’s molecular formula is C8H12N2.
Tanshinol has antioxidant capacity [18]; it can attenuate oxidative stress by decreasing the expressions of FoxO3a signaling [19] and improve cardiovascular injury by scavenging reactive oxygen species [20]. In addition, tanshinol can attenuate endothelial cell apoptosis, which helps reduce the aortic atherosclerotic lesion area [21]. Ligustrazine has effects on calcium channels; the research of Ren et al. [22] showed that ligustrazine could significantly suppress calcium transient and contraction in rabbits. It was also reported that the ligustrazine exhibits an anti-inflammatory effect; as Guo et al. described, the salvia ligustrazine injection could decrease high-sensitivity C-reactive protein and interleukin-6 levels [17, 23]. Ligustrazine was also found to suppress acid-sensing ion channels and reduce ischemia-induced infarct size in rats with angina [24]. The combination of tanshinol and ligustrazine has efficacy in dilating coronary arteries, reducing blood viscosity, promoting blood circulation, and removing blood stasis through synergistic action [25–27]. Ye et al. [28] investigated the anti-inflammatory effect of danshen, chuanxiong, and their combination and found that their combination has a dual anti-inflammatory effect on macrophages and endothelial cells. All these findings provide a biological basis of tanshinol and ligustrazine in the treatment of angina.

Tanshinol and ligustrazine are the main compounds of danshen and chuanxiong. There are several phytochemical medicines whose main components are tanshinol and ligustrazine, such as danshen chuanxiongqin injection, guanxinning injection, and shenxiong glucose injection. Several systematic reviews have been conducted to evaluate the efficacy of these medicines in the treatment of angina pectoris. Jia et al. [29] analyzed eligible RCTs using guanxinning injection, Zhang et al. [15] assessed danshen chuanxiongqin injection in treating unstable angina pectoris, and Liu and Ding [30] assessed shenxiong glucose injection in the treatment of unstable angina pectoris. In addition, many randomized controlled trials have been published to support the use of danshen and chuanxiongqin in the treatment of stable angina. However, in the treatment of stable angina, no relevant meta-analysis has been conducted to assess the clinical efficacy or the risk of phytochemical medicines containing tanshinol and ligustrazine. Therefore, in this study, a meta-analysis was conducted to evaluate the efficacy of phytochemical medicines in the treatment of stable angina.

2. Methods

The protocol of this study was registered in PROSPERO with the registration number CRD42018105921.

2.1. Database and Search Strategies. The following electronic databases were searched by two independent reviewers (Gao L. and Wang J.): Web of Science, Cochrane Library, PubMed, Chinese Biomedical Literature Database, Chinese National Knowledge Infrastructure, Chinese Scientific Journal Database, and Wanfang Database. The search date was up to March 31, 2020, and the languages of the publications were limited to English and Chinese. The following search terms were used: (tanshinol OR salvianic acid A OR β-(3,4-dihydroxyphenyl) lactic acid OR danshensu OR danshen OR radix salvia OR salvia miltiorrhiza) AND (ligustrazine OR chuanxiong OR chuanxiongzine OR tetramethylpyrazine) AND (stable angina OR angina OR angina pectoris OR stenocardia OR angor pectoris) AND (randomized controlled trial).

2.2. Inclusion Criteria. The included studies must be RCTs.

Participants: patients who were diagnosed with stable angina were included. The stable angina was diagnosed according to the criteria [31, 32], with tests such as electrocardiography (ECG), exercise ECG, and symptoms of the patients.

Interventions: interventions using phytochemical medicines containing tanshinol and ligustrazine as a main treatment were chosen. The dosages of tanshinol and ligustrazine should be described specifically.

Comparators: the control groups received conventional treatments, such as taking medicines to treat and prevent angina attacks. Placebos were also included.

Outcomes: the primary outcome was the clinical efficacy in symptoms and ECG; the secondary outcome is adverse event.

2.3. Exclusion Criteria. The exclusion criteria in the meta-analysis included (a) non-RCTs, case studies, experience summaries, animal experiments, and unpublished or repeated studies; (b) studies that used herbal medicines as the main intervention in addition to tanshinol and ligustrazine; (c) studies that used acupuncture or cupping as combined therapies; (d) patients who were identified as unstable angina; and (e) patients who have complications of heart failure, diabetes, stroke, or some other serious organic diseases.

2.4. Data Extraction and Quality Assessment. Four reviewers (Gao L, Wu T, Jia C, and Xiao Z) independently performed the data extraction and quality assessments. Meta-analysis was conducted using RevMan 5.3 software, and the risk of bias was assessed according to the Cochrane handbook [33]. Any disagreement was resolved by discussions among all reviewers.

3. Results

3.1. Description of the Included Studies. In this meta-analysis, 1613 studies were identified through database searching. But 500 repeated studies were excluded and 882 irrelevant studies were excluded through title and abstract reviewing. The full texts of 231 studies were assessed and 203 studies were excluded, including 75 studies that used some other herbal medicines in addition to tanshinol and ligustrazine in the intervention group, 96 studies included patients with unstable angina, 2 study lacked data on the dosages of...
tanshinol and ligustrazine, 1 study lacked data to judge the
efficacy, and 29 studies had patients with complications. At
last, a total of 28 studies [34–61] were included in the meta-
analysis. The screening process is summarized in a PRISMA
flow diagram (Figure 1).

Details of the 28 studies are summarized in Table 1. There were 2518 patients in total, including 1276 patients in the
intervention group and 1242 patients in the control
group. Sample sizes of the studies were small, and only 8
studies had sample sizes greater than 100 patients. The
youngest patient in these studies was 46 years old, while
most of the studies reported patients older than 60 years old.
Many patients had a long course of the disease, and the
longest course was 25 years. In the control group, con-
ventional treatments were used, such as nitroglycerin, beta-
blockers, and calcium channel blockers. No study used a
placebo. In the intervention group, phytochemical medi-
cines containing tanshinol and ligustrazine were used based
on the control group, except that one study that used a
phytochemical medicine containing tanshinol and lig-
ustrazine alone. The uses of tanshinol and ligustrazine were
in different forms, 21 studies used danshen chuanxiongqin
injection (DCI), 5 studies used shenxiong glucose injection
(SGI), and 2 studies used danshen injection (DI) combined
with ligustrazine injection (LI). The nature of constituents is
botanical. 1 ml DCI contains 0.4 mg tanshinol and 20 mg
ligustrazine, 1 ml SGI contains 0.2 mg tanshinol and 1 mg
ligustrazine, and 1 ml DI contains 0.2 mg tanshinol. Details
of the constituents of the 28 included studies are shown in
Appendix table (available here). The treatment duration
lasted from 7 days to 30 days. All the studies used clinical
efficacy in symptoms as the main outcome, and 18 studies
used clinical efficacy in ECG.

3.2. Risk of Bias. The risk of bias was high in the included
studies (Figure 2). All the studies were described using
randomization, but only five of these studies [35, 38, 44, 47, 55] reported using an appropriate method of random
sequence generation. None of the studies described the
method for allocation concealment, blinding of partic-
ips and personnel, and blinding of the outcome
assessment.

3.3. Outcome Measurements. The outcome measurements of
the included studies include clinical efficacy in symptoms,
clinical efficacy in ECG, and adverse events.

3.3.1. Clinical Efficacy in Symptoms. The criteria for clinical
efficacy in symptoms are defined as follows [62]: effective
(the frequency of angina or the amount of nitroglycerine
used is reduced by more than 50%) and no effect (the
frequency of angina or the amount of nitroglycerine
used is reduced by less than 50%).

All the studies showed that phytochemical medicines
containing tanshinol and ligustrazine have better clinical
efficacy in symptoms. Since low heterogeneity was observed
in the meta-analysis ($I^2 = 43\%$, which is lower than 50\%), a
model of fixed effects was used to calculate the pooled es-
timation with an analysis of the dichotomous data using
relative risk (RR), including 95% confidence intervals (CIs).
The total meta-analysis showed favorable effects of phyto-
chemical medicines on clinical efficacy ($n = 2518, RR = 1.24$,
95% CI: 1.20 to 1.29, $P < 0.01$) compared with the control
group (Figure 3).

3.3.2. Clinical Efficacy in ECG. The criteria for clinical ef-
cicacy in ECG are defined as follows [62]: effective (recovery
of ST-segment depression is more than 0.05 mV, or am-
plitude of the inverted T wave reduces more than 50%, or the
shape of T wave changes from flat to upright) and no effect
(no improvements in ECG compared with before).

Since high heterogeneity was observed in the meta-
analysis ($I^2 = 64\%$, which is higher than 50\%), a model of
random effects was used. The total meta-analysis showed
favorable effects of phytochemical medicines on ECG
($n = 1766, RR = 1.29, 95\%$ CI: 1.19 to 1.40, $P < 0.01$) com-
pared with the control group (Figure 4).

3.3.3. Adverse Events (AEs). Only 10 studies reported AEs,
of which 7 studies [35, 39, 40, 49, 54, 56, 59] reported that
there were no AEs. In the other three studies [38, 42, 55], two
studies reported AEs in the intervention group, including 2
cases of skin rash, 1 case of epigastric discomfort, 1 case of
insomnia, and 1 case of tiredness, and three studies reported
AEs in the control group, including 2 cases of nausea, 1 case of
stomachache, 1 case of dizziness, 2 cases of skin rash, 4
cases of epigastric discomfort, 3 cases of insomnia, and 3
cases of tiredness. Other studies did not report AEs.

4. Discussion

Currently, phytochemical medicines containing tanshinol
and ligustrazine have been widely utilized by physicians to
treat stable angina in China. However, it is controversial
since there was no systematic review to assess the therapy’s
clinical efficacy. Therefore, this meta-analysis aimed to
evaluate the efficacy or risk of phytochemical medicines in
the treatment of stable angina.

In this meta-analysis, DCI and SGI were used by most
studies. Both DCI and SGI consist of tanshinol and lig-
ustrazine. As reported, DCI and SGI have been studied in the
treatment of acute myocardial infarction [63], myocardial
ischemia/reperfusion injury [64], and focal cerebral isch-
emia [65]. In the theory of traditional Chinese medicine,
angina pectoris should be treated by supplementing qi and
activating blood circulation. Tanshinol and ligustrazine are
extracted from danshen and chuanxiong, which are two
commonly used herbs in the treatment of cardiac diseases in
China.

Tanshinol is the drug used for promoting blood cir-
culation and removing blood stasis, which can improve
cardiac function by increasing coronary blood flow and
slowing the heart rate down [66]. Clinical practice has
proved that salvia has a curative effect on myocardial
hypoxia caused by myocardial infarction, and it plays a role
Table 1: Details of the 28 included studies on phytochemical medicines containing tanshinol and ligustrazine in the treatment of stable angina.

| Study          | Sample size | Age (years) | Course of disease (years) | Intervention group | Control group | Treatment duration (days) | Main outcomes |
|----------------|-------------|-------------|---------------------------|--------------------|---------------|---------------------------|---------------|
| Cao and Wang   | 118 (59/59) | 63.0 ± 14.0 | 61.5 ± 14.5               | NR DCI (10 ml) + TCR | Nifedipine 30–60 mg/d; metoprolol 100–200 mg/d; aspirin 100–300 mg/d; nitroglycerin when necessary | 14 | CES + ECG |
| Chen           | 100 (50/50) | 57.24 ± 9.64| NR DCI (10 ml)             |                    | Aspirin 100 mg/d; atorvastatin 20 mg/d; trimetazidine 60 mg/d; nitroglycerin 10 mg/d | 7 | CES |
| Ding           | 60 (30/30)  | 56–72       | NR DCI (10 ml) + TCR       |                    | Nitroglycerin | 10 | CES |
| Han            | 60 (30/30)  | 64.9 ± 5.89 | 65.7 ± 7.93               | NR DCI (10 ml) + TCR | Nitrates; aspirin; calcium channel blockers | 14 | CES |
| He and Li      | 70 (35/35)  | 48.2 ± 2.1  | NR DCI (10 ml) + TCR       |                    | Aspirin; nitrates | 14 | CES |
| Hu             | 58 (30/28)  | 60 ± 8      | 59 ± 9                    | NR DCI (10 ml) + TCR | Nitrates; beta-blockers; calcium channel blockers; aspirin Isosorbide mononitrate 25 mg/d; quinapril 10 mg/d; metoprolol 50 mg/d; aspirin 100 mg/d | 14 | CES + ECG |
| Hua et al.     | 70 (35/35)  | 64.7 ± 8.4  | 63.3 ± 8.3                | NR DCI (10 ml) + TCR | Isosorbide mononitrate 25 mg/d; quinapril 10 mg/d; metoprolol 50 mg/d; aspirin 100 mg/d | 14 | CES + ECG |
### Table 1: Continued.

| Study       | Sample size | Age (years) | Course of disease (years) | Intervention group | Control group | Treatment duration (days) | Main outcomes |
|-------------|-------------|-------------|---------------------------|--------------------|---------------|---------------------------|---------------|
| Jia [41]    | 76 (38/38)  | 62.04 ± 2.15 | 61.92 ± 2.13              | NR                 | DCI (10 ml) + TCR | Aspirin 100 mg/d; atorvastatin 20 mg/d; trimetazidine 60 mg/d; isosorbide mononitrate 40 mg/d | 7 | CES           |
| Lan [42]    | 216 (116/100) | 57.6 ± 4.6  | 58.1 ± 5.2                | 7.62 ± 3.87        | 8.91 ± 4.28    | DCI (10 ml) + TCR          | 14 | CES + ECG     |
| Li et al. [43] | 80 (40/40) | 67.3 ± 6.20 | 3.5 ± 1.6                 | DCI (10 ml) + TCR  | Aspirin 100 mg/d; atorvastatin 20 mg/d; trimetazidine 60 mg/d; isosorbide mononitrate 40 mg/d | 7 | CES           |
| Li and Li [44] | 80 (40/40) | 58.93 ± 2.07 | 58.42 ± 2.31              | 4.45 ± 1.43        | 4.37 ± 1.52    | DCI (10 ml) + TCR          | 7 | CES           |
| Li [45]     | 216 (108/108)| 64.7 ± 4.8  | 10.6 ± 1.2                | DCI (10 ml) + TCR  | Aspirin; calcium channel blockers; beta-blockers; nitrates | 14 | CES + ECG     |
| Liu and Li [46] | 60 (30/30) | 63.7 ± 7.7  | 64.9 ± 9.4                | NR                 | SGI (100 ml) + TCR | Nitrates; aspirin; beta-blockers; calcium channel blockers; ACE inhibitors; ARBs | 14 | CES           |
| Ma et al. [47] | 80 (40/40) | NR           | NR                        | DCI (10 ml) + TCR  | Nitrates; beta-blockers; calcium channel blockers; aspirin | 14 | CES + ECG     |
| Ma et al. [48] | 104 (52/52) | 63.74 ± 11.83 | 62.34 ± 10.63             | NR                 | SGI (100 ml) + TCR | Aspirin 100 mg/d; isosorbide mononitrate 40 mg/d; metoprolol 50 mg/d; atorvastatin 20 mg/d; nitrates | 14 | CES           |
| Ou [49]     | 60 (30/30)  | 60.33 ± 10.04 | 61.21 ± 9.36              | 0.08–12            | 0.16–13        | SGI (100 ml) + TCR         | 14 | CES + ECG     |
| Pang and Liu [50] | 64 (32/32) | 77.2 ± 5.6   | 6–20                      | SGI (200 ml) + TCR | Nitrates; beta-blockers; calcium channel blockers; antiplatelet drug | 14 | CES + ECG     |
| Sun [51]    | 80 (40/40)  | 72.3 ± 0.2   | 71.9 ± 0.4                | 5.2 ± 0.6          | 5.1 ± 0.4      | DCI (5 ml) + TCR           | 30 | CES + ECG     |
| Tian [52]   | 62 (32/30)  | 61.68 ± 10.98 | 60.39 ± 9.76              | NR                 | DCI (20 ml) + TCR | Nitrates; calcium channel blockers | 14 | CES           |
| Wang and Wang [54] | 62 (31/31) | 46–58        | 3–18                      | DI (20 ml) + LI (80 mg) + TCR | Nitrates; beta-blockers; calcium channel blockers | 14 | CES + ECG     |
| Wang and Lian [53] | 105 (56/49) | 51–75        | 1.6–25                    | DCI (10 ml) + TCR  | Nitrates; beta-blockers; calcium channel blockers; aspirin | 14 | CES + ECG     |
| Xi [55]     | 80 (40/40)  | 59.3 ± 6.4   | 62.4 ± 5.3                | 5.9 ± 0.6          | 4.8 ± 0.8      | DCI (10 ml) + TCR           | 14 | CES           |
| Xie and Zhu [56] | 104 (52/52) | 51–79        | 1.6–25                    | DI (20–30 ml) + LI (40–80 mg) + TCR | Nitrates; beta-blockers; calcium channel blockers; aspirin | 14 | CES + ECG     |
| Xing [57]   | 100 (50/50) | 66.2 ± 5.60  | 2.8 ± 1.8                 | DCI (10 ml) + TCR  | Nitrates; beta-blockers; calcium channel blockers; aspirin | 14 | CES + ECG     |
| Xiong and Wang [58] | 85 (46/39) | 52–71        | 1.6–25                    | DCI (10 ml) + TCR  | Nitrates; beta-blockers; calcium channel blockers; aspirin | 14 | CES + ECG     |
in anticoagulation by dilating peripheral vessels to reduce blood pressure and improving cAMP (cyclic adenosine monophosphate) in cells [67, 68]. Ligustrazine is a kind of active alkaloid, which is effective to dilate coronary arteries and reduce coronary resistance. Ligustrazine is efficient in increasing coronary blood flow and improving myocardial oxygen supply, making it commonly to be used to inhibit platelet aggregation and depolymerize the aggregated platelets [69, 70]. In the treatment of cardiac diseases, tanshinol and ligustrazine can promote blood circulation, dilate coronary arteries, and inhibit platelet aggregation [29, 71], which provides a rationale in the treatment of stable angina.

Heterogeneity in this meta-analysis was moderate, with clinical efficacy in symptoms of $I^2 = 43\%$, and clinical efficacy in ECG of $I^2 = 64\%$. The reasons for this may be that different
Figure 3: Forest plot of the clinical efficacy in symptoms of phytochemical medicines containing tanshinol and ligustrazine in the treatment of stable angina.

Figure 4: Forest plot of the clinical efficacy in ECG of phytochemical medicines containing tanshinol and ligustrazine in the treatment of stable angina.
conventional treatments were used in different control groups. Therapies in the intervention group were based on the control group; different therapies make the efficacy hard to be assessed.

The high risk of bias of the included studies makes the methodological quality for this finding low. There are several limitations to this systematic review. First, for most of the included studies, the methods for randomization, allocation concealment, and blinding were not reported clearly. Second, in the 28 included studies, only 8 studies had sample sizes greater than 100 patients, and the small sample sizes in most studies made meaningful conclusions difficult to be drawn. Third, clinical efficacy was the main outcome measurement for most studies, but a bias from the physicians may decrease the reliability and validity of the studies. Fourth, all the studies were published in China, which may limit the generalization of the findings.

5. Conclusion
In conclusion, this meta-analysis included 28 studies that used phytochemical medicines containing tanshinol and ligustrazine in the treatment of stable angina, and the results supported their clinical application. However, the studies analyzed to date are of relatively low quality. More rigorous RCTs with large sample sizes are needed to further evaluate the clinical efficacy and the adverse effects.

Abbreviations
RCTs: Randomized controlled trials
ECG: Electrocardiography
DCI: Danshenchuanxiongqininjection
SGI:Shenxiongglucoseinjection
DI:Dansheninjection
LI:Ligustrazineinjection
CIs:Confidenceintervals
AEs:Adverseevents
TCR:Treatmentsinthecontrolgroup
ACE:Angiotensin-convertingenzyme
ARBs:Angiotensinreceptorblockers
CES:Clinicalefficacyinsymptoms.

Data Availability
All data generated or analyzed during this study are included in this published article and its supplementary information files.

Additional Points
Highlights. (i) It was the first meta-analysis assessing the efficacy of phytochemical medicines containing tanshinol and ligustrazine in the treatment of stable angina. (ii) The clinical efficacy and safety of phytochemical medicines containing tanshinol and ligustrazine in the treatment of stable angina were comprehensively assessed. (iii) The efficacy of phytochemical medicines containing tanshinol and ligustrazine in the treatment of stable angina needed to be further evaluated.

Conflicts of Interest
The authors declare that they have no conflicts of interest.

Authors’ Contributions
LG contributed to conception, acquisition, analysis, and interpretation; TW contributed to acquisition, analysis, and interpretation; JW contributed to interpretation; ZX contributed to acquisition and analysis; CJ contributed to acquisition and analysis; WW contributed to conception and interpretation. All authors drafted manuscript, revised manuscript, gave final approval, and agreed to be accountable for all aspects of work ensuring integrity and accuracy.

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Supplementary Materials
File name: Appendix table. Title of data: summary table of the constituents of the 28 included studies. Description of data: statements of the constituents of the included studies. (Supplementary Materials)

References
[1] R. Al-Lamee, D. Thompson, H.-M. Dehbi et al., “Percutaneous coronary intervention in stable angina (ORBITA): a double-blind, randomised controlled trial,” The Lancet, vol. 391, no. 10115, pp. 31–40, 2018.
[2] D. Tousoulis, “Editorial (hot topics: stable angina pectoris: novel therapeutic insights),” Current Pharmaceutical Design, vol. 19, no. 9, p. 1549, 2013.
[3] S. V. Arnold, D. L. Bhatt, G. W. Barsness et al., “Clinical management of stable coronary artery disease in patients with type 2 diabetes mellitus: a scientific statement from the American heart association,” Circulation, vol. 141, no. 19, 2020.
[4] T. A. Rousan and U. Thadani, “Stable angina medical therapy management guidelines: a critical review of guidelines from the European society of cardiology and national institute for health and care excellence,” European Cardiology Review, vol. 14, no. 1, pp. 18–22, 2019.
[5] G. Andrikopoulos, J. Parissis, G. Filippatos et al., “Hellenic cardiovasc res S: medical management of stable angina,” Hellenic Journal of Cardiology, vol. 55, no. 4, pp. 272–280, 2014.
[6] M. Glezer, V. Vasyuk, and Y. Karpov, “Efficacy of ivabradine in combination with beta-blockers versus uptitration of beta-blockers in patients with stable Angina (CONTROL-2 study),” Advances in Therapy, vol. 35, no. 3, pp. 341–352, 2018.
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[7] T. A. Rousan, S. T. Mathew, and U. Thadani, "Drug therapy for stable angina pectoris," Drugs, vol. 77, no. 3, pp. 265–284, 2017.

[8] K. L. Gould and N. P. Johnson, "Nitroglycerine and angina," Circulation, vol. 136, no. 1, pp. 35–38, 2017.

[9] W. Liao, X. Ma, J. Li et al., "A review of the mechanism of action for dantong of the treatment of chronic stable angina," Biomedicine & Pharmacotherapy, vol. 109, pp. 690–700, 2019.

[10] H. Shao, M. Li, F. Chen, L. Chen, Z. Jiang, and L. Zhao, "The efficacy of danshen injection as adjunctive therapy in treating angina pectoris: a systematic review and meta-analysis," Heart Lung and Circulation, vol. 27, no. 4, pp. 433–442, 2018.

[11] Y. N. Yu, S. Y. Hu, G. X. Li et al., "Comparative effectiveness of di’ao xin xue kang capsule and compound danshen tablet in patients with symptomatic chronic stable angina," Scientific Reports, vol. 4, no. 7058, 2014.

[12] L.-Y. Wang, J.-Y. Tang, J. Liu et al., "Dynamic changes in phenotypic groups in patients with stable angina pectoris after treatment with thunzexuekang capsule: a randomized controlled trial," Current Vascular Pharmacology, vol. 13, no. 4, pp. 492–503, 2015.

[13] Z. Gao, B. Wei, and C. Qian, "Puerarin injection for treatment of unstable angina pectoris: a meta-analysis and systematic review," International Journal of Clinical and Experimental Medicine, vol. 8, no. 9, pp. 14577–14594, 2015.

[14] D. Kong, W. Xia, Z. Zhang et al., "Safflower yellow injection combined with conventional therapy in treating unstable angina pectoris: a meta-analysis," Journal of Traditional Chinese Medicine, vol. 33, no. 5, pp. 553–561, 2013.

[15] X. Zhang, J. Wu, B. Zhang, and W. Zhou, "Danshenchuaxiongqin injection in the treatment of unstable angina pectoris: a systematic review and meta-analysis," Journal of Traditional Chinese Medicine = Chung I Tsai Chih Ying Wen Pan, vol. 36, no. 2, pp. 144–150, 2016.

[16] Y. Wang, X. Huang, F. Qin et al., "A strategy for detecting optimal ratio of cardioprotection-dependent three compounds as quality control of Guan-Xin-Er-Hao formula," Journal of Ethnopharmacology, vol. 133, no. 2, pp. 735–742, 2011.

[17] M. Guo, Y. Liu, and D. Shi, "Cardiovascular actions and therapeutic potential of tetramethylylprazLINE (active component isolated from rhizoma chuanxiong): roles and mechanisms," Biomedi Research International, vol. 2016, Article ID 2430329, 9 pages, 2016.

[18] Y. S. Sun, H. F. Zhu, J. H. Wang, Z. B. Liu, and J. J. Bi, "Isolation and purification of salvianolic acid A and salvianolic acid B from Salvia miltiorrhiza by high-speed counter-current chromatography and comparison of their antioxidative activity," Journal of Chromatography B, vol. 877, no. 8-9, pp. 733–737, 2009.

[19] Y. Yang, Y. Su, D. Wang et al., "Tanshinol attenuates the deleterious effects of oxidative stress on osteoblastic differentiation via Wnt/FoxO3a signaling," Oxidative Medicine and Cellular Longevity, vol. 2013, Article ID 351895, 18 pages, 2013.

[20] J. Ho and C.-Y. Hong, "Salvinorin acids: small compounds with multiple mechanisms for cardiovascular protection," Journal of Biomedical Science, vol. 18, no. 1, p. 30, 2011.

[21] C. Chen, G. Cheng, X. Yang, C. Li, R. Shi, and N. Zhao, "Tanshinol suppresses endothelial cells apoptosis in mice with atherosclerosis via lncRNA TUG1 up-regulating the expression of miR-26a," American Journal of Translational Research, vol. 8, no. 7, pp. 2981–2991, 2016.

[22] Z. Ren, J. Ma, P. Zhang et al., "The effect of ligustrazine on L-type calcium current, calcium transient and contractility in rabbit ventricular myocytes," Journal of Ethnopharmacology, vol. 144, no. 3, pp. 555–561, 2012.

[23] W. Wu, X. Yu, X.-P. Luo, S.-H. Yang, and D. Zheng, "Tetramethylpyrazine protects against scopoline-induced memory impairments in rats by reversing the cAMP/PKA/CREB pathway," Behavioural Brain Research, vol. 253, pp. 212–216, 2013.

[24] Z. G. Zhang, X. L. Zhang, X. Y. Wang, Z. R. Luo, and J. C. Song, "Inhibition of acid sensing ion channel by ligustrazine on angina model in rat," American Journal of Translational Research, vol. 7, no. 10, pp. 1798–1811, 2015.

[25] X. Lv, H. Lu, M. Cao, X. Liu, and W. She, "Application of danshenchuaxiongquin injection," Chinese Journal of Practical Internal Medicine, vol. 29, no. S2, pp. 219–221, 2009.

[26] R. Wang, Q. Han, Y. Jia, and J. Lv, "Effect of danshen chuanxiongquin injection on the myocardial damage of unstable angina patients undergoing percutaneous coronary intervention," Chinese Journal of Integrated Traditional and Western Medicine, vol. 31, no. 7, pp. 899–902, 2011.

[27] Z. Liu, Y. Wu, X. Jiang et al., "Pharmacokinetic study of Tanshinol’s impact on ligustigene hydrochloride from Salvia miltiorrhiza ligustigene hydrochloride injection in rats," West China Journal of Pharmaceutical Sciences, vol. 32, no. 2, pp. 182–185, 2017.

[28] T. Ye, Y. Li, D. Xiong et al., "Combination of Danshen and ligustrazine has dual anti-inflammatory effect on macrophages and endothelial cells," Journal of Ethnopharmacology, vol. 266, Article ID 113425, 2021.

[29] Y. L. Jia, S. W. Leung, M. Y. Lee, G. Z. Cui, X. H. Huang, and F. H. Pan, "The efficacy of guanxinming injection in treating angina pectoris: systematic review and meta-analysis of randomized controlled trials," Evidence-Based Complementary and Alternative Medicine, vol. 2013, Article ID 282707, 16 pages, 2013.

[30] G. Liu and B. Ding, "Meta-analysis of shenqi glucose injection in the treatment of unstable angina pectoris," Journal of Emergency in Traditional Chinese Medicine, vol. 25, no. 2, pp. 272–275, 2016.

[31] T. D. Fraker, S. D. Fihn, R. J. Gibbons et al., "2007 chronic angina focused update of the ACC/AHA 2002 guidelines for the management of patients with chronic stable angina," Circulation, vol. 116, no. 23, pp. 2762–2772, 2007.

[32] F. H. Messerli, G. Mancia, C. R. Conti, and C. J. Pepine, "Guidelines on the management of stable angina pectoris: executive summary: the task force on the management of stable angina pectoris of the European society of cardiology," European Heart Journal, vol. 27, no. 23, pp. 2902–2903, 2006.

[33] J. P. T. Higgins, D. G. Altman, P. C. Gotzsche et al., "The cochrane collaboration’s tool for assessing risk of bias in randomised trials," BMJ, vol. 343, p. d5928, 2011.

[34] Y. Cao and Z. Wang, "Therapeutic effect of danshen ligustrazine injection on angina pectoris," Contemporary Medical Symposium, vol. 15, no. 16, pp. 175–176, 2017.

[35] X. Chen, "Clinical analysis of 50 cases of angina pectoris treated by danshen ligustrazine injection," China Practical Medicine, vol. 12, no. 11, pp. 145–146, 2017.

[36] X. Ding, "Treatment of 30 cases of angina pectoris in the elderly by danshen ligustrazine injection," For All Health, vol. 10, no. 35, pp. 149–150, 2016.

[37] J. Han, "Effect of danshen ligustrazine injection on angina pectoris in the elderly," World Latest Medicine Information, vol. 16, no. 79, p. 208, 2016.
